eBreast

eBreast

Práctica Cáncer de Mama

MANUAL PRÁCTICO PARA LA CONSULTA DE PACIENTES CON CÁNCER DE MAMA

NOVARTIS

ES2208313850

Coordinadores y autores

Eduardo Martínez de Dueñas, Hospital Provincial de Castelló, Castelló

Santiago Olmos Antón, Hospital Provincial de Castelló, Castelló

Autores

Vicente Carañana Ballerini, Hospital Arnau de Vilanova, Valencia

Sonia del Barco Berron, Institut Català d'Oncologia, Girona

Joaquín Gavilá Gregori, Instituto Valenciano de Oncología, Valencia

Mireia Margelí Vila, Institut Català d'Oncologia, Badalona, Barcelona

Serafín Morales Murillo, Hospital Universitari Arnau de Vilanova, Lleida

Ana Santaballa Bertrán, Hospital Universitari i Politècnic la Fe de Valencia

Avales

PARA INFORMACIÓN ADICIONAL, CONSULTAR EL RESTO DE LOS CAPÍTULOS

ISBN: 978-84-09-22045-8

PRÓLOGO

eBreast nace como signo de los tiempos.

No es un libro.

No es una app.

Es la respuesta a las nuevas formas de aprender, enseñar y estudiar.

Signo de los tiempos por la importancia y el impacto que tiene el cáncer de mama en nuestra sociedad y en nuestro sistema sanitario.

Signo de los tiempos por la incesante llegada de nuevos profesionales que tienen la gran responsabilidad de cuidar a nuestras pacientes afectas de cáncer de mama y con la necesidad de adquirir un conocimiento riguroso, actualizado y de acceso inmediato, a veces en la propia consulta, para poder ofrecer las mejores opciones que la evidencia científica nos proporciona.

Signo de los tiempos por la forma de enfrentarse a la información. La aparición y expansión de nuevas TIC (Tecnologías de la información y comunicación), algunas de ellas rápidamente absorbidas por las nuevas generaciones, hace preciso adaptarse a ellas.

Signo de los tiempos por el enorme volumen de información que se genera a diario y que hace precisa la intervención de revisores autorizados en cada materia, sobre todo para los clínicos. El fondo de conocimiento médico es inabarcable. Y el conocimiento y el progreso oncológicos son, actualmente, de los más importantes en la medicina moderna: por volumen de publicaciones, recursos que se destinan, impacto social, consecuencias de la enfermedad…

eBreast está dirigido a todos aquellos profesionales que atienden una consulta médica de cáncer de mama, sobre todo a los que se inician en la patología, a los que atienden a estas pacientes de forma más esporádica o simplemente a los que desean mantenerse actualizados. eBreast proporciona una consulta rápida, sencilla y, sobre todo, muy visual e interactiva. Y con este proyecto nos comprometemos a revisar periódicamente los contenidos, actualizando los datos tras los principales acontecimientos científicos del año.

Los coordinadores quisiéramos agradecer el inmenso esfuerzo realizado por todos los autores, así como el apoyo proporcionado por Novartis, y a las sociedades GEICAM, SEOM, SOLTI y a la Universidad CEU Cardenal Herrera por su aval.

No queremos dejar de olvidar el apoyo de nuestras familias y, sobre todo, a LOS/LAS PACIENTES afectos de cáncer de mama, que son el objeto de todos nuestros esfuerzos, estudios y desvelos profesionales y por tanto, los beneficiarios finales de este proyecto, que pretende ser novedoso.

Santiago Olmos Antón **Eduardo Martínez de Dueñas**

ABREVIATURAS

A	Antraciclina
AC	Adriamicina/doxorrubina, ciclofosfamida
ACT	Antraciclina-ciclofosfamida y taxano concurrente
AC-T	Antraciclina-ciclofosfamida y taxano secuencial
AC-D	Adriamicina, ciclofosfamida, docetaxel
AL	Adriamicina Liposomal
ALND	*Axillary lymph node dissection*
AMH	Agente modulador del hueso
ANA	Anastrozol
AO	Ablación ovárica
AP	Adriamicina,paclitaxel
APBI	Radioterapia parcial acelerada
AP-CMF-Q(x)	Adriamicina y paclitaxel-quimioterapia de ciclofosfamida, metotrexato y 5-FU
AP-CMF	Adriamicina y paclitaxel, ciclofosfamida, metotrexato y 5-FU
ASCO	*Sociedad Americana de Clínica Oncología*
AxRT:	*Axillary radiotherapy*
B	Bevacizumab
BAG	Biopsia con aguja gruesa
BAV	Biopsia asistida por vacío
BC	Beneficio clínico
BCS	Supervivencia específica por cáncer de mama
BOADICEA	*Breast and Ovarian Analysis of Disease Incidence and Carrier Estimation Algorithm*
BSGC	Biopsia selectiva del ganglio centinela
CAF/FAC	Ciclofosfamida, adriamicina y 5-FU
CAFM	Ciclofosfamida, adriamicina, 5-FU y metroxetato
C	Cirugía/Carboplatino
CAP	Capecitabina
CC	Cirugía conservadora
CDDP	Cisplatino
CDI	Carcinoma ductal invasivo

CDIS	Carcinoma ductal *in situ*
CDK	Cinasas dependientes de ciclinas
CEA	Antígeno carcinoembriónico
CEF/FEC	Ciclofosfamida, epirrubicina, 5-FU
CLI	Carcinoma lobulillar infiltrante
CM	Cáncer de mama
CMAJ	*Canadian Medical Association Journal*
CMF	Ciclofosfamida, metotrexato y 5-FU
CMI	Cáncer de mama inflamatorio
CMLA	Cáncer de mama localmente avanzado
CMM	Cáncer de mama metastásico
CMTN	Cáncer de mama triple negativo
cN+	Ganglios linfáticos positivos clínicamente
C-A-CMF	Cirugía-antraciclina-ciclofosfamida, metotrexato y 5-FU
C-AP-CMF	Cirugía-adriamicina, paclitaxel-ciclofosfamida, metotrexato y 5-FU
D	Docetaxel
ddAC	Dosis densas adriamicina y ciclofosfamida
DMO	Densidad mineral ósea
DX	Doxorrubicina
EBCTCG	*Early Breast Cancer Trialists' Collaborative Group*
EC	Epirrubicina, ciclofosfamida
ECG	Electrocardiograma
ECO	Ecografía
ED	Epirrubicina, docetaxel
ESA	Agente estimulador de la eritropoyesis
ESMO	European Society for Medical Oncology
EXE	Exemestano
F	Fulvestrant
FEVI	Fracción de eyección ventricular izquierda
FN	Fiebre neutropénica
GC	Ganglio centinela
GnRH	Hormona liberadora de gonadotropina

G-CSF	Factor estimulante de colonias de granulocitos
TR	Trastuzumab
HD	Altas dosis
HER/EGFR	Receptor de factor de crecimiento epidérmico humano
HNA	Hormonoterapia neoadyuvante
HR	*Hazard ratio*
HT	Hormonoterapia
IA	Inhibidores aromatasa
IAE	Inhibidor no esteroideo de la aromatasa
IANE	Inhibidor de la no esteroideo de la aromatasa
IC	Intervalo de confianza
ICT	Células tumorales aisladas
IHQ	Inmunohistoquímico
ILE	Intervalo libre de enfermedad
IPM	Irradiación parcial de la mama
ISH	Hibridación *in situ*
L	Lapatinib
LA	Linfadenectomía axilar
LET	Letrozol
LHRH	Hormona liberadora de la hormona luteinizante
LR-SLP	Supervivencia libre de progresión locorregional
MMSE	*Mini-Mental State Examination*
MNA	*Mini nutritional assessment*
MRM	Mastectomía radical modificada
MT	Marcadores tumorales
N.A	No aportado
NAB-P	nab-paclitaxel (paclitaxel unido a albúmina)
NCCN	*National Comprehensive Cancer Network*
NCI	*National Cancer Institute*
NCI-CTCAE	*National Cancer Institute Common Terminology Criteria for Adverse Events*
N.S	No significativo
NSABP	*National Surgical Adjuvant Breast and Bowel Project*

OCCR	*Ovarian Cancer Cluster Region*
OR	*Odds Ratio*
ORR	*Objective response rate*
OSNA	*One step nucleic acid amplification*
P	Paclitaxel
PA	Palbociclib
PAAF	Punción aspiración con aguja fina
PE	Progresión de la enfermedad/pertuzumab
PEPI	*Preoperative Endocrine Prognostic Index*
PER	Pertuzumab
PET	Tomografía por emisión de positrones
PF	Preservación de la fertilidad
Post-Op	Postoperatorio
PP	Profilaxis primaria
pRC	Respuesta patológica completa
Pre-Op	Preoperatorio
pRP	Respuesta parcial patológica
pRPmic	Respuesta parcial patológica microscópica
PS	Profilaxis secundaria
QoL	Calidad de vida
QT	Quimioterapia
RANKL	Ligando del receptor activador del factor nuclear k-B
RC	Respuesta completa
RCB	*Residual Cancer Burden* (enfermedad residual posquimioterapia)
RE	Receptor de estrógeno
RFS	Supervivencia libre de recaída
RH	Receptor hormonal
RMN	Resonancia magnética nuclear
ROI	Rastreo óseo isotópico/ gamma o escintigrafía ósea
RP	Receptor de progesterona/Respuesta parcial
RR	Riesgo de recaída
RS	Recurrence score

RT	Radioterapia
Rx	Radiografía
SBRT	Radioterapia estereotáctica de cuerpo
SC	Subcutáneo
SERD	Inhibidor selectivo del RE
SERMS	Modulador selectivo del receptor estrogénico
SG	Supervivencia global
SLE	Supervivencia libre de enfermedad
SLP	Supervivencia libre de progresión
SLR	Supervivencia libre de recaída
SNP	*Single nucleotide polymorphism*
SPPB	Batería corta de rendimiento físico
ST	Tratamiento sistémico
T	Taxano
TA	Tratamiento adyuvante
TAC	Tomografía axial computarizada o Docetaxel, adriamicina, ciclofosfamida
TAM	Tamoxifeno
TBCRC	*Translational Breast Cancer Research Consortium*
TC	Docetaxel y ciclofosfamida
TCH	Docetaxel, carboplatino, trastuzumab
T-DM1	Trastuzumab emtansina
TE	Terapia endocrina
TIL	*Tumor Infiltrating Lymphocites*
THP	Tiempo hasta progresión
TMA	Transplante de células madre autólogo
TN	Triple negativo
TNA	Tratamiento neoadyuvante
TR	Trastuzumab
UCGC	Unidad de consejo genético en cáncer
UI	Unidades Internacionales
V	Vinorelbina

CAPÍTULO 3. CARCINOMA *IN SITU* Y QUIMIOPREVENCIÓN

VER RESUMEN

3. Carcinoma *in situ* y quimioprevención

a) Carcinoma *in situ*.

A. CARCINOMA *IN SITU*

¿Qué es el carcinoma lobulillar *in situ* y cuál es su tratamiento?

¿Qué es el carcinoma ductal *in situ*?

¿Cuál es el tratamiento quirúrgico del carcinoma ductal *in situ*?

¿Cuándo debe hacerse tratamiento radioterápico y hormonoterápico en el carcinoma *in situ*?

¿Qué es el carcinoma lobulillar *in situ* y cuál es su tratamiento?

CARCINOMA LOBULILLAR *IN SITU*

El carcinoma lobulillar *in situ* debe considerarse como un factor de riesgo de desarrollar un carcinoma de mama. Este riesgo es de un 21 % a los 15 años, raramente se trata de carcinomas infiltrantes (5 %) y su supervivencia es del 99 % (83).

El carcinoma lobulillar *in situ* presenta características clínicas, morfológicas y moleculares que lo distinguen del carcinoma ductal *in situ*. Sin embargo, en la nueva clasificación de la OMS es un tipo de neoplasia lobular.

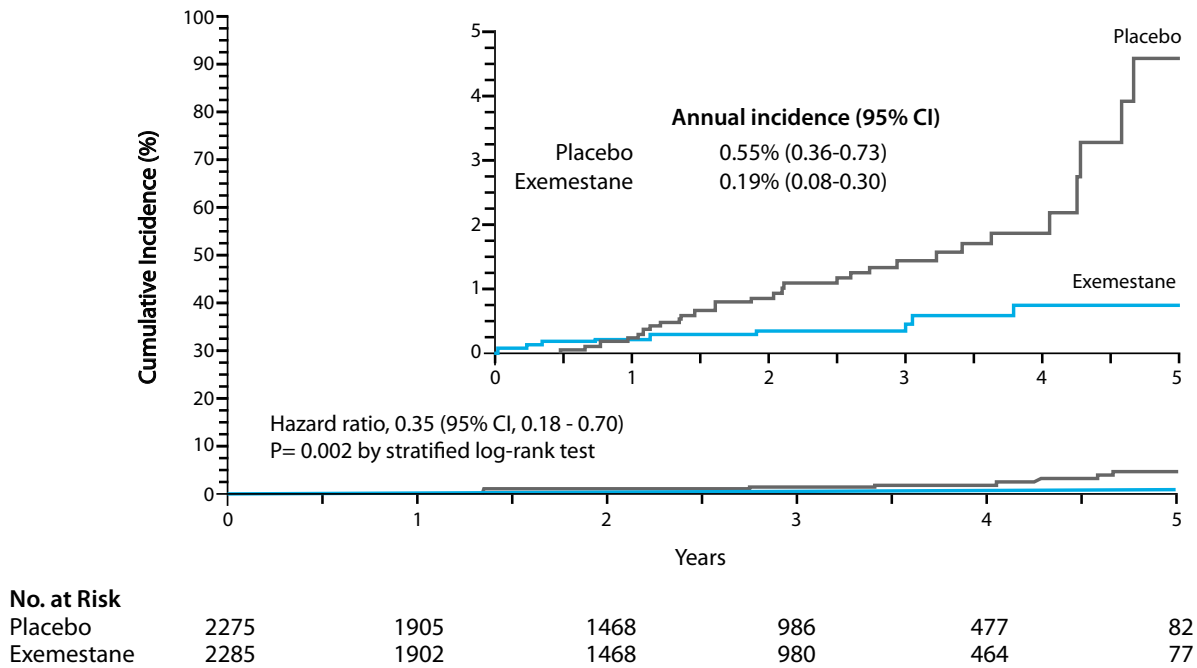
Tratamiento

En este contexto, la administración de tamoxifeno 20 mg/día durante 5 años ha demostrado reducir el riesgo global de desarrollar cáncer invasivo en un 49 % (HR 0,51; IC 95 % 0,39-0,66) (84, 85).

También los inhibidores de la aromatasa han demostrado beneficio en este contexto en pacientes posmenopáusicas. Es el caso de:

- Exemestano en caso de factores de riesgo (hiperplasia ductal con atipia, hiperplasia lobulillar con atipia, carcinoma lobulillar *in situ* o carcinoma ductal *in situ* tratado con mastectomía), demostró una reducción en la incidencia anual de cáncer de mama invasivo de un 65 % (0,19 % vs. 0,55 %; HR 0,35; p=0,002) (86) (Figura 1).

Figura 1. Incidencia acumulada de carcinoma de mama invasivo. ***Basada en Goss P.E et al. (86).***



No. at Risk						
Placebo	2275	1905	1468	986	477	82
Exemestane	2285	1902	1468	980	464	77

- También el anastrozol durante cinco años ha demostrado beneficios en la disminución del riesgo de incidencia de cáncer de mama en pacientes posmenopáusicas de alto riesgo (a un seguimiento de cinco años, 2 % en el grupo de anastrozol vs. 4 % en el de placebo, HR 0,47, P: 0,0001) (87).

Existe una variante pleomórfica del carcinoma lobulillar *in situ*, en la que se recomienda que el tratamiento sea el mismo que en el Carcinoma ductual *in situ* (CDIS), en cuanto a la indicación de cirugía (88).

¿Qué es el carcinoma ductal *in situ*?

CARCINOMA DUCTAL *IN SITU*

Diagnóstico e incidencia

El carcinoma ductal *in situ* (CDIS) constituye un 20-30 % de los diagnósticos de cáncer cada año, y frecuentemente se diagnostica por la mamografía de cribado poblacional. Los datos preliminares muestran un aumento en las tasas de detección de carcinoma *in situ* del 20 % al 30 % a través de los programas de cribado de población en España, siendo la única variable que ha cambiado durante ese período la incorporación de la mamografía digital.

Dependiendo del grado de atipia nuclear, la presencia de necrosis, la actividad mitótica y la presencia de microcalcificaciones, el CDIS se divide en tres grados:

- **Bajo grado.** Se caracteriza por una proliferación homogénea de células con núcleos redondos de tamaño uniforme, un ligero aumento en la relación núcleo-citoplasma (relación de Carolina del Norte), un nucléolo que no es muy evidente y la mitosis ocasional.
- **Grado intermedio.** Muestra características intermedias entre las que se encuentran las de los tipos anteriores. Como se ha mencionado anteriormente, en la reciente revisión de la OMS, los casos de bajo grado nuclear con necrosis son también diagnosticados de carcinoma ductal ***in situ*** de grado intermedio.
- **Alto grado.** Se caracteriza por células con alta atipia nuclear: los núcleos son grandes y pleomórficos con un patrón de cromatina gruesa. La mitosis es generalmente abundante y la necrosis es común, aunque ninguna de estas dos variables es esencial para el diagnóstico.

Tabla 17. Índice pronóstico de Van Nuys. ***Adaptada de Silverstein M.J. et al. (89).***

ÍNDICE	1	2	3
Tamaño	≤ 15 mm	16-40 mm	> 40 mm
Margen de resección	≥ 10 mm	1-9 mm	< 1 mm
Grado	1-2 sin necrosis	1-2 sin necrosis	Grado 3
Edad del paciente	> 60	40-60	< 40

El índice de Van Nuys se calcula con la suma de los valores de cada categoría. El resultado final estará entre 4 y 12 puntos. El índice pronóstico de Van Nuys es una herramienta de uso común para el enfoque terapéutico del carcinoma ductal *in situ*. La edad de la paciente, el tamaño del tumor, los márgenes del tumor y el grado histológico se utilizan con el fin de estratificar a los pacientes en tres grupos relacionados con el riesgo de recidiva local: riesgo bajo, intermedio y alto (89). Sin embargo, pese a su utilidad, se trata de un índice solo validado de forma retrospectiva y, por tanto, con un valor limitado.

El riesgo de desarrollar un cáncer de mama tras el diagnóstico de un CDIS es bajo.

Se trata de una enfermedad heterogénea, los objetivos futuros se basan en la individualización del tratamiento, evitando el sobretratamiento en los casos de bajo riesgo y ajustando el tratamiento en los casos de alto riesgo.

En este sentido, diferentes estudios han evaluado biomarcadores moleculares para predecir la recurrencia después de un diagnóstico de CDIS, en varias cohortes de CDIS; sin embargo, ninguno está en la práctica clínica, principalmente debido a una combinación de falta de validación en cohortes independientes y/o bajo valor predictivo. La mayoría de los estudios realizados tienen poca potencia para la detección precisa del valor predictivo (90, 91). Así, se han evaluado diferentes marcadores por inmunohistoquímica, siendo algunos de los candidatos con mayor evidencia HER2, COX2, Ki67 (> 10% de células positivas) y p16. (92-94)

También la firma genética OncotypeDX se ha evaluado para su predicción del riesgo de recurrencia del CDIS. OncotypeDX fue evaluado en dos cohortes. En ambas, OncotypeDX demostró un valor pronóstico en los análisis multivariados, sin embargo, el grupo de bajo riesgo todavía tenía una probabilidad de recurrencia de 10 a 13 % a los 10 años. Ningún estudio pudo demostrar ninguna diferencia en el resultado entre los grupos de riesgo intermedio y alto. Sin embargo, estos estudios presentan limitaciones importantes como son: solo pudieron ser evaluados 50% de los pacientes de cada cohorte, los datos clínicos patológicos eran incompletos, y los datos procedían de cohortes retrospectivas antiguas (1994-2003), desde las que se han producido importantes avances en técnicas quirúrgicas y de radioterapia (94, 95). En un estudio posterior, Rakovitch *et al*. también evaluó el efecto predictivo de Oncotype en el beneficio de la radioterapia. El grupo de bajo riesgo no se benefició mucho de la adición de radioterapia, mientras que los grupos de mayor riesgo sí se beneficiaron (94).

En definitiva, la biología del CDIS todavía no se comprende bien. El CDIS no es una sola enfermedad, sino que varía según el estado hormonal, el estado del receptor del factor de crecimiento, la tasa de proliferación y las características genéticas. En particular, es necesario dilucidar mejor la interacción de todos estos factores con el microambiente en el inicio de la neoplasia y en la progresión a la enfermedad invasiva

¿Cuál es el tratamiento quirúrgico del carcinoma ductal *in situ*?

Tratamiento

En la mayoría de los casos, la cirugía conservadora de la mama, la radioterapia y el tratamiento hormonal constituyen el tratamiento de elección en el carcinoma intraductal.

Cirugía conservadora vs. mastectomía

La posibilidad de conservar la mama depende del tamaño del tumor y la relación entre el tamaño del tumor y el volumen del pecho del paciente.

Existen, sin embargo, algunos casos en los que la cirugía conservadora no estará indicada y se realizará una mastectomía, como son:

- La existencia de un carcinoma ductal *in situ* multifocal
- La alta probabilidad de un resultado estético pobre debido a un tumor grande en una mama pequeña
- El deseo de la paciente de someterse a una mastectomía
- Índice pronóstico USC/ Van Nuys 10, que implica alto riesgo de recurrencia pese a la radioterapia adyuvante
- Dos primeros trimestres de embarazo

Aunque la cirugía conservadora constituye la opción más frecuente, algunos estudios sugieren un incremento de la mastectomía, así como de la mastectomía contralateral profiláctica, en especial en mujeres más jóvenes, en presencia de comorbilidades y alto grado tumoral. Algunos estudios también relacionan este hecho con la posibilidad de realizar una reconstrucción inmediata de alta calidad (96, 97).

Márgenes de resección

Los márgenes de resección constituyen el factor predictivo más importante de recidiva local; esta recidiva será en forma de carcinoma intraductal en un 50 % de los casos, pero en el otro 50 %, en forma de carcinoma infiltrante. Existe controversia acerca de la definición de margen libre en el caso del carcinoma ductal *in situ*. Según las guías *National Comprehensive Cancer Network (NCCN)*, los márgenes < 1 mm se consideran inadecuados; los márgenes > 10 mm se consideran adecuados (pero posiblemente excesivos). Los márgenes a < 1 mm de la pared torácica o de la piel no obligan a hacer una nueva ampliación quirúrgica, pero sí a valorar una mayor dosis de radioterapia local. Algunas recomendaciones, como las de St. Gallen, consideran que la ausencia de tinta china en el tumor debe ser criterio suficiente para la no ampliación de los márgenes de resección (98).

Un metaanálisis con un total de 12 estudios retrospectivos y 2902 pacientes con un seguimiento medio de 86,4 meses, evaluó la recidiva local tras la mastectomía por carcinoma *in situ*. Los autores encontraron que el rango de recidivas locales es de un 5,3% en caso de márgenes cercanos o positivos frente a un 1,6% en caso de márgenes libres, siendo el 93,7% de recidivas tumores invasivos. Los autores concluyeron que el estado de los márgenes de resección tiene un gran impacto en la recidiva local. Sin embargo, la tasa de recurrencia fue insuficiente para justificar una recomendación de radioterapia postmastectomía en pacientes con márgenes positivos o cercanos (85).

Ganglio centinela

En general, la disección axilar no está indicada en el tratamiento del carcinoma ductal *in situ*, pero sí la realización de la biopsia del ganglio centinela en caso de que exista alto riesgo de áreas de infiltración en la pieza quirúrgica. Así, se considera su realización en los siguientes casos (99):

- CDIS tratados con mastectomía,
- CDIS con focos de microinvasión en el análisis anatomopatológico,
- CDIS de gran tamaño (≥ 5 cm) y en CDIS de alto grado.

¿Cuándo debe hacerse tratamiento radioterápico y hormonoterápico en el carcinoma *in situ*?

Radioterapia

En general, la radioterapia adyuvante está indicada tras la cirugía conservadora de un carcinoma *in situ* dado que disminuye significativamente el riesgo de eventos mamarios ipsilaterales, in situ o invasivos, lo que sustenta su papel establecido en pacientes con carcinoma ductal *in situ* (CDIS). A la espera de resultado de estudios en seguimiento se recomienda agregar *boost* en lecho tumoral a la irradiación de toda la mama en presencia de características clínico-patológicas adversas, y se respalda el uso de esquemas de fraccionamiento de la dosis de toda la mama con hipofracción moderada.

Radioterapia hipofraccionada

Algunos estudios evalúan el papel de la radioterapia hipofraccionada en el tratamiento del carcinoma *in situ*. Así, el estudio internacional, aleatorizado, fase III BIG 3- 07/ TROG 07.1, incluyó 1608 pacientes con CDIS de no bajo riesgo sometidas a cirugía conservadora, siendo aleatorizadas a recibir un *boost* en lecho tumoral (16 Gy en 8 fracciones diarias) o no; tras radioterapia convencional (50Gys en 25 fracciones diarias) o hipofraccionada (42.5 Gy en 16 fracciones diarias). Los resultados comunicados, aun no publicados, con una mediana de seguimiento de 6,6 años, muestran que el *boost* redujo significativamente la recurrencia local, pero no hubo diferencias en las recurrencias locales entre los grupos de irradiación mamaria total convencionalmente fraccionada e hipofraccionada (100). En cuanto a los resultados cosméticos, la administración del *boost* se asoció con un riesgo > 2 veces mayor de deterioro cosmético (P<0,001), y la irradiación hipofraccionada de toda la mama logró una estética a los 3 años estadísticamente similar en comparación con la irradiación convencional de toda la mama (P≥ 0,18). Además, el impacto cosmético adverso del refuerzo no se asoció significativamente con los programas de fraccionamiento de la dosis para toda la mama (interacción P≥0,30)(100).

El estudio fase III de no inferioridad DBCG HYPO trial comparó la administración de dosis de radioterapia de 50 Gy en 25 fracciones frente a 40 Gys en 15 fracciones en pacientes sin afectacion ganglionar o carcinoma in situ. Los resultados de seguimiento no muestran diferencias en riesgo de recidiva locorregional a nueve años . La terapia de 40 Gys no presentó peores resultados que la terapia estándar (89).

Irradiación parcial de la mama

La irradiación parcial de la mama después de la cirugía conservadora permite integrar un volumen objetivo reducido limitado al lecho del tumor primario y la aceleración segura del tratamiento de radiación, generalmente en una semana o menos, para mejorar la comodidad de la atención. Por ello, también se ha evaluado en el CDIS.

El ensayo aleatorizado NSABP B-39/RTOG 0413 comparó la irradiación mamaria parcial acelerada con la irradiación mamaria fraccionada convencionalmente después de una cirugía conservadora de mama fue principalmente un ensayo de cáncer de mama invasivo, pero incluyó a 1031 pacientes (24 %) con CDIS. Aunque la irradiación mamaria parcial no cumplió con los criterios de equivalencia con la irradiación mamaria total en el control de las recurrencias locales, la diferencia absoluta en las tasas de recurrencia local a 10 años fue baja (4,6 % frente a 3,9 %) (101).

El ensayo RAPID asignó al azar a 2135 pacientes, incluidos 381 pacientes con CDIS, a irradiación mamaria parcial basada en haz externo adyuvante (38,5 Gy en 10 fracciones administradas dos veces al día durante 5 a 8 días) o irradiación mamaria total (31). Aunque los resultados mostraron que la irradiación parcial de la mama no era inferior a la irradiación total de la mama en la prevención de la recurrencia local; la irradiación parcial se asoció con un aumento de la toxicidad moderada y efectos cosméticos adversos.

Dado que los datos publicados que respaldan el uso de la irradiación mamaria parcial adyuvante en pacientes con DCIS de bajo riesgo son limitados, su aplicación fuera del estudio debe limitarse a pacientes de bajo riesgo definidos por las pautas internacionales y nacionales.

¿Se puede omitir la radioterapia?

Es posible que las pacientes de bajo riesgo no obtengan beneficios clínicamente significativos de la radioterapia y se están realizando investigaciones sobre perfiles moleculares para mejorar la precisión del pronóstico y guiar la omisión segura de la radioterapia después de la cirugía conservadora de la mama. Sin embargo, la definición de este subgrupo es controvertida.

El metanálisis del grupo EBCTCG definió un subgrupo potencialmente favorable en función del tamaño del tumor < 20 mm, grado nuclear bajo y márgenes quirúrgicos negativos, pero no identificó un subgrupo de pacientes de bajo riesgo. En este subgrupo de 291 pacientes, las tasas de eventos mamarios ipsilaterales a 10 años fueron del 30,1 % sin radioterapia adyuvante y del 12,1 % con irradiación mamaria total (102).

El ensayo E5194 del *Eastern Cooperative Oncology Group* (ECOG) evaluó de forma observacional la realización de cirugía conservadora sin radioterapia en dos cohortes de pacientes con CDIS. A pesar de la selección de pacientes con características favorable, las tasas de recurrencia local fueron del 14.4% en la primera cohorte y del 26.6% en la segunda, observando un incremento de las recurrencias durante los 12 años sin llegar a una meseta. Estos datos respaldan el uso rutinario de la radioterapia, en especial en pacientes de alto grado (103, 104).

Así, el estudio RTOG 9804 aleatorizó a 636 pacientes intervenidas de carcinoma *in situ*, de grado intermedio o bajo, con un tamaño menor a 2,5 cm, con márgenes negativos, a recibir radioterapia postoperatoria versus observación. Con un seguimiento de 7 años, el 6,7 % del grupo de observación presentó recidiva local, mientras que solo un 0,9 % del grupo de radioterapia (105). El estudio se cerró precozmente por la falta de reclutamiento. Con una mediana de seguimiento de 13,9 años, la incidencia acumulada de 15 años de recurrencia local, invasiva o *in situ*, fue del 7,1 % (IC del 95 %, 4,0-11,5) en todo el grupo de irradiación mamaria frente al 15,1 % (95 % IC, 10,8-20,2) en el grupo sin radiación (P=0,0007; HR=0,36; IC 95%, 0,20 a 0,66). La incidencia acumulada correspondiente de recidiva local invasiva fue del 5,4 % (IC del 95 %, 2,7-9,5) con radioterapia frente al 9,5 % (IC del 95 %, 6,0-13,9) sin radiación (P=0,027; HR=0,44; IC del 95 %, 0,21-0,91)(106).

Tras este estudio, el estudio de fase III de no inferioridad EORTC 1401/BOOG 2014-04, investiga la actitud frente al carcinoma *in situ* de bajo riesgo, comparando vigilancia frente a solo cirugía conservadora, y cirugía conservadora seguida de radioterapia frente a solo cirugía conservadora.

Diferentes ensayos aleatorios han demostrado una disminución de la tasa de recidiva local en un 50% con radioterapia después de la cirugía conservadora de la mama, pero ninguno de los ensayos ha demostrado un beneficio en términos de supervivencia. La siguiente tabla recoge los resultados de los estudios aleatorizados de primera generación que comparaban la tumorectomía con o sin radioterapia.

Tabla 18. Resultados comparativos de la tumorectomía con o sin radioterapia. ***Basada en Lebeau A. et al.*** **(107).**

Table 1. First-generation randomized trials comparing lumpectomy with and without radiation therapy

	NSABP B-17 [9, 15]		EORTC 10853 [10]		SweDCIS [11*, 26]		UK/ANZ DCIS [12, 27]	
Study period	1985-1990		1986-1996		1987-1999		1990-1998	
Follow-up	17.25		15.8		17.4		12.7	
Included patients	813		1010		1046		1030	
No RT	403		503		533		508	
RT	410		507		526		522	
Mammographic detection (%)	80.6		71.6		79		>90	
Central pathology review (%)	76.5 [15]		85.5		25.9		72.3	
Negative margins required	Yes		Yes		No		Yes	
Margins free (%)[a]	82.8		74.6		NR		69.1	
RT dose	50Gy/25fr		50Gy/25fr		50-54Gy/25-27fr		50Gy/25fr	
Boost	-		10Gy/5fr (5% of patients)		-		-	
	No RT	RT	No RT	RT	No RT	RT	No RT	RT
Local recurrences								
Total (%)	35	19.8	30	17	31.7	17.7	19.4	7
Invasive (%)	19.6	10.7	14.9	9.5	14.2	10.5	9.1	3.3
In situ (%)	15.4	9	15.1	7.5	17.5	7.2	9.7	3.8
Contralateral breast cancer (%)	7.9	9.3	7	10	9.2	12.7	4.1	3.3
Overall survival at 15 years (%)	84.2	82.9	87.8	87.6	73[b]	77.2[b]	90[c]	88.2[c]

EORTC, European Organisation for Research and Treatment of Cancer; NSABP, National Surgical Adjuvant Breast and Bowel Project; RT, postoperative radiotherapy; SweDCIS, Swedish Ductal Carcinoma *in Situ*; UK/ANZ DCIS, United Kingdom, Australia, and new Zealand Ductal Carcinoma *in Situ*.
[a]Confirmed by central pathology.
[b]At 20 years.
[c]At 12.7 years

9. Wapnir IL, Dignam JJ, Fisher B, Mamounas EP, Anderson SJ, Julian TB, et al. Long-term outcomes of invasive ipsilateral breast tumor recurrences after lumpectomy in NSABP B-17 and B-24 randomized clinical trials for DCIS. J Natl Cancer Inst. 2011;103(6):478-88.
10. Donker M, Litiere S, Werutsky G, Julien JP, Fentiman IS, Agresti R, et al. Breast-conserving treatment with or without radiotherapy in ductal carcinoma In Situ: 15-year recurrence rates and outcome after a recurrence, from the EORTC 10853 randomized phase III trial. J Clin Oncol. 2013;31(32):4054-9.
11. Wärnberg F, Garmo H, Emdin S, Hedberg V, Adwall L, Sandelin K, et al. Effect of radiotherapy after breast-conserving surgery for ductal carcinoma in situ: 20 years follow-up in the randomized SweDCIS Trial. J Clin Oncol. 2014;32(32):3613-8.
12. Cuzick J, Sestak I, Pinder SE, Ellis IO, Forsyth S, Bundred NJ, et al. Effect of tamoxifen and radiotherapy in women with locally excised ductal carcinoma in situ: long-term results from the UK/ANZ DCIS trial. Lancet Oncol. 2011;12(1):21-9.
15. Fisher ER, Dignam J, Tan-Chiu E, Costantino J, Fisher B, Paik S, et al. Pathologic findings from the National Surgical Adjuvant Breast Project (NSABP) eight-year update of Protocol B-17: intraductal carcinoma. Cancer. 1999;86(3):429-38.
26. Ringberg A, Nordgren H, Thorstensson S, Idvall I, Garmo H, Granstrand B, et al. Histopathological risk factors for ipsilateral breast events after breast conserving treatment for ductal carcinoma in situ of the breast--results from the Swedish randomised trial. Eur J Cancer. 2007;43(2):291-8.
27. Pinder SE, Duggan C, Ellis IO, Cuzick J, Forbes JF, Bishop H, et al. A new pathological system for grading DCIS with improved prediction of local recurrence: results from the UKCCCR/ANZ DCIS trial. Br J Cancer. 2010;103(1):94-100.

Por otra parte, el estudio RTOG 9804 incluyó a 636 pacientes con carcinoma *in situ* de buen pronóstico tratadas con tamoxifeno con o sin radioterapia. Nuevamente la radioterapia se asoció a una reducción del riesgo de recidiva (105).

Viani *et al.* publicaron un metaanálisis (108) donde se confirma que:

- La adición de la radioterapia reduce el riesgo de recidiva local en un 60 %.
- Las pacientes de alto grado y con márgenes positivos obtienen un mayor beneficio de la radioterapia.

En definitiva, los resultados a largo plazo de los estudio prospectivos, nos ayudan a la toma de decisiones individualizada considerando diversos aspectos como son: las preferencias del paciente, las causas de mortalidad, y los riesgos de la radioterapia.

Por otra parte, la individualización del tratamiento del CDIS podría venir guiada también por la información que nos aportan el perfil molecular utilizando ensayos de expresión multigénica para mejorar la precisión pronóstica del CDIS.

Así, la firma genética Oncotype DX® fue evaluada retrospectivamente en 327 pacientes del estudio ECOG E5194 como predictor del riesgo de recidiva en pacientes con carcinoma ductal *in situ* tratadas solo con cirugía sin radioterapia. La *DCIS score* predijo la recidiva local basada en tres niveles de riesgo (bajo, intermedio, alto). Así, esta firma podría ser útil para predecir qué pacientes deben ser irradiados (95). En un segundo estudio con mayor número de pacientes se obtuvieron resultados similares (95, 109). Sin embargo, el hecho de ser un estudio prospectivo y de tratarse de casos seleccionados no tratados con radioterapia, limita su aplicación en la práctica habitual en el contexto del carcinoma *in situ*.

Finalmente, otro grupo desarrolló una herramienta (decisión *Score*) derivada de genes relacionados con el cáncer y factores clínico-patológicos (edad, tamaño del tumor, estado de los márgenes, palpabilidad). Se demostró su valor pronóstico para el riesgo de recurrencia con un riesgo de cáncer de mama invasivo a 10 años del 4 % y un riesgo de evento mamario ipsilateral del 7 % en pacientes tratadas sin radioterapia. También se demostró que la puntuación predecía el beneficio de la radioterapia con un beneficio significativo para el grupo de riesgo elevado, pero no para el grupo de riesgo bajo (110).

Hormonoterapia

El tratamiento complementario con tamoxifeno durante cinco años en pacientes con carcinoma *in situ* tratado con tumorectomía ha demostrado disminuir tanto la recidiva local como la aparición de cáncer contralateral, en especial en forma de carcinoma infiltrante. La tasa de eventos a los cinco años era del 8,2 % vs. 13,4 % (p=0,0009), respectivamente. Las únicas pacientes que parecen beneficiarse de este tratamiento son aquellas con tumores hormonosensibles (111). Hay que tener en cuenta que se trata de un tratamiento asociado a efectos secundarios, y que no ha demostrado un beneficio en términos de supervivencia (112).

Los resultados de dos estudios de fase III comunicados recientemente no encontraron diferencias de eficacia entre el tamoxifeno y el anastrozol durante cinco años, administrados en pacientes posmenopáusicas tratadas con cirugía conservadora y radioterapia por un carcinoma *in situ* (113, 114).

CONCLUSIONES

En definitiva,

- El diagnóstico de carcinoma *in situ* aumenta en la era de la mamografía moderna.
- Ello genera nuevos retos en cuanto al sobretratamiento frente al infratratamiento en una enfermedad que es biológicamente heterogénea.
- El carcinoma ductal *in situ* no es una enfermedad uniforme. Algunos tienen una evolución indolente, mientras otros tienen potencial de evolucionar a una enfermedad agresiva.
- Los análisis anatomopatológicos convencionales no son suficientemente efectivos para identificar a aquellas pacientes en las que se podría evitar la radioterapia.
- El incremento de las mastectomías totales se debe, por una parte, a las preferencias de las pacientes y, por otra, a las mejoras de la cirugía reconstructiva.
- Son necesarios estudios que estratifiquen las diferentes poblaciones de pacientes y minimicen tratamientos si son innecesarios.
- Las nuevas firmas genéticas para estimar el riesgo (nomograma, 12-genes *DCIS score*) muestran resultados prometedores, pero requieren de validación prospectiva.

B. QUIMIOPREVENCIÓN

¿Qué es la quimioprevención?

¿En qué pacientes debemos considerar la quimioprevención?

¿Cuáles son los tratamientos en quimioprevención?

¿Qué es la quimioprevención?

INTRODUCCIÓN

La quimioprevención consiste en el uso de fármacos para prevenir la aparición de cáncer de mama. Pero ¿cómo seleccionar cuáles son las pacientes con más riesgo de padecer cáncer de mama?

Riesgo de padecer cáncer de mama

Se consideran factores de riesgo para desarrollar cáncer de mama:

- Edad avanzada
- Menarquia precoz y menopausia tardía
- Nuliparidad
- Edad avanzada para el primer embarazo a término
- Historia de tratamiento hormonal sustitutivo actual o pasado (conteniendo estrógenos y progestágenos)

Se consideran personas de alto riesgo:

- Personas con una historia familiar de cáncer de mama
- Historia personal de biopsia(s) de mama previa(s)
- Diagnóstico de enfermedad benigna de la mama de carácter proliferativo
- Historia personal de exposición a radiaciones
- Mujeres que tienen mutaciones genéticas específicas (BRCA1, BRCA2, p53 ó PTEN)

Modelos predictivos del riesgo

Existen algunos modelos predictivos de riesgo. Uno de los primeros desarrollados fue el de Gail, que fue modificado por científicos del NCI (*National Cancer Institute*) y del NSABP (*National Surgical Adjuvant Breast and Bowel Project*), para estimar el riesgo de las mujeres de desarrollar un cáncer de mama invasivo, generando el índice *"The NCI Breast Cancer Risk Assesment Tool"*. Este modelo estima el riesgo de desarrollar cáncer de mama a los cinco años, y lo compara con el riesgo medio de las mujeres de la misma edad. Una de las limitaciones de este modelo es que solo ha sido validado en mujeres de EE. UU. que son valoradas regularmente en el cribado de cáncer de mama.

Otro antiguo modelo es el de Claus, que puede proporcionar una estimación de riesgo de cáncer de mama futuro en mujeres con una fuerte historia familiar de cáncer de mama.

El modelo BRCAPRO fue desarrollado sobre las tasas de mutaciones de *BRCA* y su penetrancia, observados principalmente en mujeres judías askenazíes y de ascendencia europea. Estima la probabilidad de que una persona sea portadora de una mutación deletérea de *BRCA1* o *BRCA2*, así como su riesgo de desarrollar cáncer de mama u ovario (115). Se utiliza ampliamente en las unidades de consejo genético y está disponible gratuitamente a través de varios paquetes:

- BayesMendel R,
- CancerGene,
- HughesRiskApps,

Existe una versión simplificada llamada BRCAPROLYTE, útil en casos donde la información completa de los antecedentes familiares no esté disponible.

El algoritmo BOADICEA (*Breast and Ovarian Analysis of Disease Incidence and Carrier Estimation Algorithm*) es un software que se utiliza para calcular los riesgos de cáncer de mama y de ovario en las mujeres en función de su historia familiar. También se utiliza para calcular la probabilidad de ser portador de mutaciones en los genes *BRCA1* o *BRCA2* (116).

Lesiones benignas de la mama de alto riesgo

Diferentes lesiones benignas se asocian a un mayor riesgo de cáncer de mama:

- Las mujeres con atipia tienen un riesgo relativo de cáncer de mama de 4,2 sobre la población general.
- Las mujeres con cambios proliferativos sin atipia tienen un riesgo relativo de 1,88 de desarrollar cáncer de mama respecto a la población general.
- Las mujeres con lesiones no proliferativas tiene un riesgo relativo de 1,27.

¿En qué pacientes debemos considerar la quimioprevención?

PACIENTES CANDIDATAS

Las guías recomiendan que, en caso de mujeres con alto riesgo de cáncer de mama, hay que discutir los beneficios y riesgos de los tratamientos.

El tema de cuáles son las candidatas apropiadas para la prevención del cáncer de mama es controvertido. Los clásicos estudios de quimioprevención incluyen los siguientes grupos:

- Mujeres de más de 60 años
- Mujeres con biopsia mamaria con carcinoma lobular *in situ* o hiperplasia ductal atípica o hiperplasia lobular.
- Mujeres entre 35 y 59 años con riesgo absoluto proyectado a los cinco años ≥1,66 % (basado en la *National Cancer Institute Breast Cancer Risk Assessment Tool* o una medida equivalente)

Los datos preliminares sugieren que el tamoxifeno ayuda a reducir el riesgo de cáncer de mama en mujeres con mutaciones *BRCA*, pero el beneficio puede limitarse a ciertas mujeres que heredan estas mutaciones.

¿Cuáles son los tratamientos en quimioprevención?

FÁRMACOS EN QUIMIOPREVENCIÓN

Diferentes estudios han demostrado una disminución de la incidencia de cáncer de mama con diferentes tratamientos hormonales: tamoxifeno, raloxifeno, e inhibidores de la aromatasa (Tabla 17).

De 537 cánceres en el grupo de quimioprevención y 805 en el control, no hubo diferencias en la supervivencia. Sin embargo, la existencia de efectos secundarios de los fármacos, ha limitado su uso generalizado en quimioprevención.

Si evaluamos su eficacia por subgrupos, distinguiremos:

Moduladores selectivos del receptor de estrógenos (SERMS)

Tamoxifeno

Los estudios en pacientes de alto riesgo NSABP-P1 (85), IBIS-1 (117), Royal Marsden (118), y el estudio italiano (119) sugieren que administrado diariamente durante cinco años, puede prevenir los cánceres de mama hormonosensibles, reduciendo el riesgo de desarrollar cáncer de mama por lo menos en un tercio y siendo eficaz independientemente del estado de menopausia.

Este efecto no se ha relacionado con un incremento en la supervivencia, aumentando el riesgo de algunos efectos adversos como el cáncer uterino y de ETV, lo que hace que no se generalice su uso.

Recientemente se han publicado los resultados de un estudio aleatorizado que comparaba el tratamiento con bajas dosis de tamoxifeno 5 mg cada 24 horas versus placebo administrado durante 3 años tras la cirugía en mujeres con neoplasia intraepitelial incluyendo hiperplasia ductal y lobular atípica o carcinoma ductal *in situ*. El objetivo primario era la incidencia de carcinoma de mama invasivo o *in situ*. Tras 500 pacientes incluidas, con un seguimiento medio de 5,1 años; hubo 14 eventos neoplásicos con tamoxifeno y 28 con placebo (11,6 versus 23,9 por 1.000 años-persona; P = 0,02). El tamoxifeno disminuyó los eventos mamarios contralaterales en un 75%. Los efectos secundarios reportados por los pacientes no fueron diferentes entre los brazos de tratamiento, excepto por un ligero aumento en la frecuencia de los sofocos diarios con tamoxifeno (P = 0,02). Hubo 12 eventos adversos graves con tamoxifeno y 16 con placebo, incluida una trombosis venosa profunda y un cáncer de endometrio en estadio I con tamoxifeno y una embolia pulmonar con placebo. Los autores concluyeron que el tamoxifeno a dosis de 5 mg cada 24 horas puede ser una alternativa para resucir la recidiva del carcinoma intraepitelial de mama con limitada toxicidad (120).

Raloxifeno

El estudio STAR comparó el tamoxifeno y el raloxifeno, en pacientes posmenopáusicas de alto riesgo, siendo el raloxifeno ligeramente menos eficaz que el tamoxifeno en la prevención del cáncer de mama invasivo y con menos efectos secundarios (121).

Inhibidores de la aromatasa

El anastrozol y el exemestano muestran una reducción del riesgo de cáncer de mama en al menos un 50 % (86, 87) en posmenopáusicas.

Así, los inhibidores de la aromatasa constituyen una alternativa razonable a los SERMS en pacientes posmenopáusicas, aunque los síntomas articulares y musculares pueden limitar su aceptación en prevención.

Tabla 19. Estudios en quimioprevención. ***Basada en Narod S.A. et al. (122).***

Table. Characteristics of Incident Breast Cancers Detected in Antiestrogen Prevention Trials

Trial	Placebo, No.	Active Drug, No.
National Surgical Adjuvant Breast and Bowel Project (P-1) (7-y Follow-up), Tamoxifen		
Study participants: 13 207	6610	6597
Invasive breast cancer, total	250	145
ER positive	182	70
ER negative	42	56
Deaths from breast cancer	11	12
International Breast Cancer Intervention Study (IBIS-1) (16-y Follow-up), Tamoxifen		
Study participants: 7154	3575	3579
Invasive breast cancer, total	289	214
ER positive	238	160
ER negative	47	50
Deaths from breast cancer	26	31

Royal Marsden Trial (20-y Follow-up), Tamoxifen		
Study participants: 2494	1244	1250
Invasive breast cancer, total	104	82
ER positive	86	53
ER negative	17	24
Deaths from breast cancer	9	12
Italian Randomized Tamoxifen Prevention Trial (11-y Follow up), Tamoxifen		
Study participants: 5408	2708	2700
Invasive breast cancer, total	66	53
ER positive	52	40
ER negative	19	21
Deaths from breast cancer	2	2
Trial	**Placebo No.**	**Active Drug No.**
NCIC Clinical Trials Group Mammary Prevention (3-y Follow-up), Exemestane		
Study participants: 4560	2275	2285
Invasive breast cancer, total	32	11
ER positive	27	7
ER negative	5	4
Deaths from breast cancer	0	1
Internationak Breast Cancer Intervention Study (IBIS-II) (5-y Follow-up), Anastrazole		
Study participants: 3864	1920	1944
Invasive breast cancer, total	64	32
ER positive	47	20
ER negative	14	11
Deaths from breast cancer	0	2
All Chemoprevention Trials		
Study participants: 36 687	18 332	18 355
Invasive breast cancer, total	805	537
ER positive	632	350
ER negative	144	173
Deaths from breast cancer	48	60

RECOMENDACIONES

Según los datos disponibles, la Sociedad Americana de Oncología Clínica (ASCO) recomendaba en 2013 (123) que:

- En mujeres ≥ 35 años con riesgo incrementado de cáncer de mama, hay que ofrecer y discutir el tratamiento con tamoxifeno como una opción para reducir el riesgo de cáncer de mama con receptores estrogénicos positivos.
- En mujeres posmenopáusicas, el raloxifeno, el exemestano y el anastrozol también se asocian a una reducción del riesgo.

Las mujeres con mayor riesgo se definen como las que presentan un riesgo absoluto proyectado a los cinco años ≥ 1,66 % (basado en la *National Cancer Institute Breast Cancer Risk Assessment Tool* o una medida equivalente) o las mujeres diagnosticadas de un carcinoma lobulillar *in situ*.

Es importante explicar a las pacientes los riesgos y beneficios de cada opción terapéutica, y también tener en cuenta la edad y comorbilidades de cada mujer, sopesándolas con los potenciales efectos adversos de cada fármaco.

En definitiva, aunque serán candidatas a quimioprevención las mujeres con un mayor riesgo de cáncer de mama, es importante recordar que son mujeres sanas. Por ello, es importante que sean cuidadosamente informadas de los riesgos y beneficios de los fármacos potenciales antes de embarcarse en una estrategia de quimioprevención. Por tanto, en este escenario será fundamental una buena comunicación con las mujeres candidatas antes de tomar una decisión compartida, lo que será fundamental en el cumplimiento de la misma.

BIBLIOGRAFÍA

1. Moss SM, Wale C, Smith R, Evans A, Cuckle H, Duffy SW. Effect of mammographic screening from age 40 years on breast cancer mortality in the UK Age trial at 17 years' follow-up: a randomised controlled trial. Lancet Oncol. 2015;16(9):1123-32.
2. Canadian Task Force on Preventive Health C, Tonelli M, Connor Gorber S, Joffres M, Dickinson J, Singh H, et al. Recommendations on screening for breast cancer in average-risk women aged 40-74 years. CMAJ. 2011;183(17):1991-2001.
3. Gotzsche PC, Jorgensen KJ. Screening for breast cancer with mammography. Cochrane Database Syst Rev. 2013;6:CD001877.
4. Force USPST. Screening for breast cancer: U.S. Preventive Services Task Force recommendation statement. Ann Intern Med. 2009;151(10):716-26, W-236.
5. Independent UKPoBCS. The benefits and harms of breast cancer screening: an independent review. Lancet. 2012;380(9855):1778-86.
6. Kalager M, Zelen M, Langmark F, Adami HO. Effect of screening mammography on breast-cancer mortality in Norway. N Engl J Med. 2010;363(13):1203-10.
7. Rafferty EA, Park JM, Philpotts LE, Poplack SP, Sumkin JH, Halpern EF, et al. Assessing radiologist performance using combined digital mammography and breast tomosynthesis compared with digital mammography alone: results of a multicenter, multireader trial. Radiology. 2013;266(1):104-13.
8. Dang PA, Freer PE, Humphrey KL, Halpern EF, Rafferty EA. Addition of tomosynthesis to conventional digital mammography: effect on image interpretation time of screening examinations. Radiology. 2014;270(1):49-56.
9. Kriege M, Brekelmans CT, Boetes C, Besnard PE, Zonderland HM, Obdeijn IM, et al. Efficacy of MRI and mammography for breast-cancer screening in women with a familial or genetic predisposition. N Engl J Med. 2004;351(5):427-37.
10. Paluch-Shimon S, Cardoso F, Sessa C, Balmana J, Cardoso MJ, Gilbert F, et al. Prevention and screening in BRCA mutation carriers and other breast/ovarian hereditary cancer syndromes: ESMO Clinical Practice Guidelines for cancer prevention and screening. Annals of oncology : official journal of the European Society for Medical Oncology / ESMO. 2016;27(suppl 5):v103-v10.
11. Siu AL. Screening for Breast Cancer: U.S. Preventive Services Task Force Recommendation Statement. Ann Intern Med. 2016;164(4):279-96.
12. Cardoso F, Costa A, Senkus E, Aapro M, Andre F, Barrios CH, et al. 3rd ESO-ESMO International Consensus Guidelines for Advanced Breast Cancer (ABC 3). Ann Oncol. 2017;28(1):16-33.
13. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines). Breast Cancer Screening and Diagnosis Version 1.2016.
14. ASCO Perspective on Mammography Screening for Breast Cancer February 13, 2014. Available at: https://www.asco.org/advocacy-policy/asco-in-action/asco-perspective-mammography-screening-breast-cancer. Last accessed: Mar 2017.
15. Villaume K, Blanc M, Gouysse G, Walter T, Couderc C, Nejjari M, et al. VEGF secretion by neuroendocrine tumor cells is inhibited by octreotide and by inhibitors of the PI3K/AKT/mTOR pathway. Neuroendocrinology. 2010;91(3):268-78.
16. D'Orsi CJ, Sickles EA, Mendelson EB, Morris EA. ACR BI-RADS® Atlas, Breast Imaging Reporting and Data System. Reston, VA, American College of Radiology; 2013 [Available from: www.acr.org.
17. Sardanelli F, Boetes C, Borisch B, Decker T, Federico M, Gilbert FJ, et al. Magnetic resonance imaging of the breast: recommendations from the EUSOMA working group. Eur J Cancer. 2010;46(8):1296-316.
18. Caudle AS, Yang WT, Krishnamurthy S, Mittendorf EA, Black DM, Gilcrease MZ, et al. Improved Axillary Evaluation Following Neoadjuvant Therapy for Patients With Node-Positive Breast Cancer Using Selective Evaluation of Clipped Nodes: Implementation of Targeted Axillary Dissection. J Clin Oncol. 2016;34(10):1072-8.
19. Hammond ME, Hayes DF, Dowsett M, Allred DC, Hagerty KL, Badve S, et al. American Society of Clinical Oncology/College Of American Pathologists guideline recommendations for immunohistochemical testing of estrogen and progesterone receptors in breast cancer. J Clin Oncol. 2010;28(16):2784-95.
20. Senkus E, Kyriakides S, Penault-Llorca F, Poortmans P, Thompson A, Zackrisson S, et al. Primary breast cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Annals of oncology : official journal of the European Society for Medical Oncology / ESMO. 2013;24 Suppl 6:vi7-23.
21. Qureshi A, Pervez S. Allred scoring for ER reporting and it's impact in clearly distinguishing ER negative from ER positive breast cancers. JPMA The Journal of the Pakistan Medical Association. 2010;60(5):350-3.
22. Wolff AC, Hammond ME, Hicks DG, Dowsett M, McShane LM, Allison KH, et al. Recommendations for human epidermal growth factor receptor 2 testing in breast cancer: American Society of Clinical Oncology/College of American Pathologists clinical practice guideline update. J Clin Oncol. 2013;31(31):3997-4013.
23. Polley MY, Leung SC, McShane LM, Gao D, Hugh JC, Mastropasqua MG, et al. An international Ki67 reproducibility study. J Natl Cancer Inst. 2013;105(24):1897-906.
24. Polley MY, Leung SC, Gao D, Mastropasqua MG, Zabaglo LA, Bartlett JM, et al. An international study to increase concordance in Ki67 scoring. Modern pathology : an official journal of the United States and Canadian Academy of Pathology, Inc. 2015;28(6):778-86.

25. Loi S, Drubay D, Adams S, Pruneri G, Francis PA, Lacroix-Triki M, et al. Tumor-Infiltrating Lymphocytes and Prognosis: A Pooled Individual Patient Analysis of Early-Stage Triple-Negative Breast Cancers. J Clin Oncol. 2019;37(7):559-69.
26. Colomer R, Aranda-Lopez I, Albanell J, Garcia-Caballero T, Ciruelos E, Lopez-Garcia MA, et al. Biomarkers in breast cancer: A consensus statement by the Spanish Society of Medical Oncology and the Spanish Society of Pathology. Clin Transl Oncol. 2018;20(7):815-26.
27. Cardoso F, Kyriakides S, Ohno S, Penault-Llorca F, Poortmans P, Rubio IT, et al. Early breast cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-updagger. Annals of oncology : official journal of the European Society for Medical Oncology / ESMO. 2019;30(8):1194-220.
28. Sorlie T, Perou CM, Tibshirani R, Aas T, Geisler S, Johnsen H, et al. Gene expression patterns of breast carcinomas distinguish tumor subclasses with clinical implications. Proc Natl Acad Sci U S A. 2001;98(19):10869-74.
29. Hugh J, Hanson J, Cheang MC, Nielsen TO, Perou CM, Dumontet C, et al. Breast cancer subtypes and response to docetaxel in node-positive breast cancer: use of an immunohistochemical definition in the BCIRG 001 trial. J Clin Oncol. 2009;27(8):1168-76.
30. Garcia-Saenz JA, Bermejo B, Estevez LG, Palomo AG, Gonzalez-Farre X, Margeli M, et al. SEOM clinical guidelines in early-stage breast cancer 2015. Clin Transl Oncol. 2015;17(12):939-45.
31. Gianni L, Pienkowski T, Im YH, Roman L, Tseng LM, Liu MC, et al. Efficacy and safety of neoadjuvant pertuzumab and trastuzumab in women with locally advanced, inflammatory, or early HER2-positive breast cancer (NeoSphere): a randomised multicentre, open-label, phase 2 trial. Lancet Oncol. 2012;13(1):25-32.
32. O'Brien KM, Cole SR, Tse CK, Perou CM, Carey LA, Foulkes WD, et al. Intrinsic breast tumor subtypes, race, and long-term survival in the Carolina Breast Cancer Study. Clinical cancer research : an official journal of the American Association for Cancer Research. 2010;16(24):6100-10.
33. de Boer M, van Dijck JA, Bult P, Borm GF, Tjan-Heijnen VC. Breast cancer prognosis and occult lymph node metastases, isolated tumor cells, and micrometastases. J Natl Cancer Inst. 2010;102(6):410-25.
34. Fisher B, Bauer M, Wickerham DL, Redmond CK, Fisher ER, Cruz AB, et al. Relation of number of positive axillary nodes to the prognosis of patients with primary breast cancer. An NSABP update. Cancer. 1983;52(9):1551-7.
35. Sparano JA, Gray RJ, Makower DF, Pritchard KI, Albain KS, Hayes DF, et al. Adjuvant Chemotherapy Guided by a 21-Gene Expression Assay in Breast Cancer. N Engl J Med. 2018;379(2):111-21.
36. Piccart M, van 't Veer LJ, Poncet C, Lopes Cardozo JMN, Delaloge S, Pierga JY, et al. 70-gene signature as an aid for treatment decisions in early breast cancer: updated results of the phase 3 randomised MINDACT trial with an exploratory analysis by age. Lancet Oncol. 2021;22(4):476-88.
37. Andre F, Ismaila N, Henry NL, Somerfield MR, Bast RC, Barlow W, et al. Use of Biomarkers to Guide Decisions on Adjuvant Systemic Therapy for Women With Early-Stage Invasive Breast Cancer: ASCO Clinical Practice Guideline Update-Integration of Results From TAILORx. J Clin Oncol. 2019;37(22):1956-64.
38. Andre F, Ismaila N, Allison KH, Barlow WE, Collyar DE, Damodaran S, et al. Biomarkers for Adjuvant Endocrine and Chemotherapy in Early-Stage Breast Cancer: ASCO Guideline Update. J Clin Oncol. 2022;40(16):1816-37.
39. Puglisi F, Follador A, Minisini AM, Cardellino GG, Russo S, Andreetta C, et al. Baseline staging tests after a new diagnosis of breast cancer: further evidence of their limited indications. Annals of oncology : official journal of the European Society for Medical Oncology / ESMO. 2005;16(2):263-6.
40. Chen S, Parmigiani G. Meta-analysis of BRCA1 and BRCA2 penetrance. J Clin Oncol. 2007;25(11):1329-33.
41. Desmond A, Kurian AW, Gabree M, Mills MA, Anderson MJ, Kobayashi Y, et al. Clinical Actionability of Multigene Panel Testing for Hereditary Breast and Ovarian Cancer Risk Assessment. JAMA Oncol. 2015;1(7):943-51.
42. Walker LC, Fredericksen ZS, Wang X, Tarrell R, Pankratz VS, Lindor NM, et al. Evidence for SMAD3 as a modifier of breast cancer risk in BRCA2 mutation carriers. Breast cancer research : BCR. 2010;12(6):R102.
43. Jernstrom H, Lubinski J, Lynch HT, Ghadirian P, Neuhausen S, Isaacs C, et al. Breast-feeding and the risk of breast cancer in BRCA1 and BRCA2 mutation carriers. J Natl Cancer Inst. 2004;96(14):1094-8.
44. Kuhl CK, Schrading S, Leutner CC, Morakkabati-Spitz N, Wardelmann E, Fimmers R, et al. Mammography, breast ultrasound, and magnetic resonance imaging for surveillance of women at high familial risk for breast cancer. J Clin Oncol. 2005;23(33):8469-76.
45. Phillips KA, Milne RL, Rookus MA, Daly MB, Antoniou AC, Peock S, et al. Tamoxifen and risk of contralateral breast cancer for BRCA1 and BRCA2 mutation carriers. J Clin Oncol. 2013;31(25):3091-9.
46. Llort G, Chirivella I, Morales R, Serrano R, Sanchez AB, Teule A, et al. SEOM clinical guidelines in Hereditary Breast and ovarian cancer. Clin Transl Oncol. 2015;17(12):956-61.
47. Cibula D, Zikan M, Dusek L, Majek O. Oral contraceptives and risk of ovarian and breast cancers in BRCA mutation carriers: a meta-analysis. Expert Rev Anticancer Ther. 2011;11(8):1197-207.
48. Kotsopoulos J, Lubinski J, Moller P, Lynch HT, Singer CF, Eng C, et al. Timing of oral contraceptive use and the risk of breast cancer in BRCA1 mutation carriers. Breast cancer research and treatment. 2014;143(3):579-86.

49. Domchek SM, Friebel TM, Singer CF, Evans DG, Lynch HT, Isaacs C, et al. Association of risk-reducing surgery in BRCA1 or BRCA2 mutation carriers with cancer risk and mortality. JAMA. 2010;304(9):967-75.
50. Rebbeck TR, Kauff ND, Domchek SM. Meta-analysis of risk reduction estimates associated with risk-reducing salpingo-oophorectomy in BRCA1 or BRCA2 mutation carriers. J Natl Cancer Inst. 2009;101(2):80-7.
51. Fisher B, Jeong JH, Anderson S, Bryant J, Fisher ER, Wolmark N. Twenty-five-year follow-up of a randomized trial comparing radical mastectomy, total mastectomy, and total mastectomy followed by irradiation. N Engl J Med. 2002;347(8):567-75.
52. Krag DN, Anderson SJ, Julian TB, Brown AM, Harlow SP, Costantino JP, et al. Sentinel-lymph-node resection compared with conventional axillary-lymph-node dissection in clinically node-negative patients with breast cancer: overall survival findings from the NSABP B-32 randomised phase 3 trial. Lancet Oncol. 2010;11(10):927-33.
53. Bernet L, Piñero A, Vidal-Sicart S, Peg V, Giménez J, Algara M, et al. Consenso sobre la biopsia selectiva del ganglio centinela en el cáncer de mama. Revisión 2013 de la Sociedad Española de Senología y Patología Mamaria. Revista de Senología y Patología Mamaria. 2014;27(1):43-53.
54. Galimberti V, Cole BF, Zurrida S, Viale G, Luini A, Veronesi P, et al. Axillary dissection versus no axillary dissection in patients with sentinel-node micrometastases (IBCSG 23-01): a phase 3 randomised controlled trial. Lancet Oncol. 2013;14(4):297-305.
55. Giuliano AE, Hunt KK, Ballman KV, Beitsch PD, Whitworth PW, Blumencranz PW, et al. Axillary dissection vs no axillary dissection in women with invasive breast cancer and sentinel node metastasis: a randomized clinical trial. JAMA. 2011;305(6):569-75.
56. Donker M, van Tienhoven G, Straver ME, Meijnen P, van de Velde CJ, Mansel RE, et al. Radiotherapy or surgery of the axilla after a positive sentinel node in breast cancer (EORTC 10981-22023 AMAROS): a randomised, multicentre, open-label, phase 3 non-inferiority trial. Lancet Oncol. 2014;15(12):1303-10.
57. Román Guindo A, Martí Álvarez C, Hardisson Hernáez D, de Santiago García FJ, Sánchez Méndez JI. Evaluación de la respuesta patológica a la quimioterapia neoadyuvante en mama y axila según los fenotipos moleculares del cáncer de mama. Revista de Senología y Patología Mamaria - Journal of Breast Science. 2016;29(3):120-4.
58. Mamounas EP, Brown A, Anderson S, Smith R, Julian T, Miller B, et al. Sentinel node biopsy after neoadjuvant chemotherapy in breast cancer: results from National Surgical Adjuvant Breast and Bowel Project Protocol B-27. J Clin Oncol. 2005;23(12):2694-702.
59. Kelly AM, Dwamena B, Cronin P, Carlos RC. Breast cancer sentinel node identification and classification after neoadjuvant chemotherapy-systematic review and meta analysis. Academic radiology. 2009;16(5):551-63.
60. Pilewskie M, Morrow M. Axillary Nodal Management Following Neoadjuvant Chemotherapy: A Review. JAMA Oncol. 2017;3(4):549-55.
61. Boughey JC, Suman VJ, Mittendorf EA, Ahrendt GM, Wilke LG, Taback B, et al. Sentinel lymph node surgery after neoadjuvant chemotherapy in patients with node-positive breast cancer: the ACOSOG Z1071 (Alliance) clinical trial. JAMA. 2013;310(14):1455-61.
62. Kuehn T, Bauerfeind I, Fehm T, Fleige B, Hausschild M, Helms G, et al. Sentinel-lymph-node biopsy in patients with breast cancer before and after neoadjuvant chemotherapy (SENTINA): a prospective, multicentre cohort study. Lancet Oncol. 2013;14(7):609-18.
63. Boileau JF, Poirier B, Basik M, Holloway CM, Gaboury L, Sideris L, et al. Sentinel node biopsy after neoadjuvant chemotherapy in biopsy-proven node-positive breast cancer: the SN FNAC study. J Clin Oncol. 2015;33(3):258-64.
64. Favourable and unfavourable effects on long-term survival of radiotherapy for early breast cancer: an overview of the randomised trials. Early Breast Cancer Trialists' Collaborative Group. Lancet. 2000;355(9217):1757-70.
65. Obedian E, Haffty BG. Negative margin status improves local control in conservatively managed breast cancer patients. Cancer J Sci Am. 2000;6(1):28-33.
66. Buchholz TA, Somerfield MR, Griggs JJ, El-Eid S, Hammond ME, Lyman GH, et al. Margins for breast-conserving surgery with whole-breast irradiation in stage I and II invasive breast cancer: American Society of Clinical Oncology endorsement of the Society of Surgical Oncology/American Society for Radiation Oncology consensus guideline. J Clin Oncol. 2014;32(14):1502-6.
67. Houssami N, Macaskill P, Marinovich ML, Dixon JM, Irwig L, Brennan ME, et al. Meta-analysis of the impact of surgical margins on local recurrence in women with early-stage invasive breast cancer treated with breast-conserving therapy. Eur J Cancer. 2010;46(18):3219-32.
68. Moran MS, Schnitt SJ, Giuliano AE, Harris JR, Khan SA, Horton J, et al. Society of Surgical Oncology-American Society for Radiation Oncology consensus guideline on margins for breast-conserving surgery with whole-breast irradiation in stages I and II invasive breast cancer. Int J Radiat Oncol Biol Phys. 2014;88(3):553-64.
69. Morrow M, Van Zee KJ, Solin LJ, Houssami N, Chavez-MacGregor M, Harris JR, et al. Society of Surgical Oncology-American Society for Radiation Oncology-American Society of Clinical Oncology Consensus Guideline on Margins for Breast-Conserving Surgery With Whole-Breast Irradiation in Ductal Carcinoma in Situ. Practical radiation oncology. 2016;6(5):287-95.

70. De La Cruz L, Moody AM, Tappy EE, Blankenship SA, Hecht EM. Overall Survival, Disease-Free Survival, Local Recurrence, and Nipple-Areolar Recurrence in the Setting of Nipple-Sparing Mastectomy: A Meta-Analysis and Systematic Review. Ann Surg Oncol. 2015;22(10):3241-9.

71. Ebctcg, McGale P, Taylor C, Correa C, Cutter D, Duane F, et al. Effect of radiotherapy after mastectomy and axillary surgery on 10-year recurrence and 20-year breast cancer mortality: meta-analysis of individual patient data for 8135 women in 22 randomised trials. Lancet. 2014;383(9935):2127-35.

72. van de Water W, Bastiaannet E, Scholten AN, Kiderlen M, de Craen AJ, Westendorp RG, et al. Breast-conserving surgery with or without radiotherapy in older breast patients with early stage breast cancer: a systematic review and meta-analysis. Ann Surg Oncol. 2014;21(3):786-94.

73. Kunkler IH, Williams LJ, Jack WJ, Cameron DA, Dixon JM, investigators PI. Breast-conserving surgery with or without irradiation in women aged 65 years or older with early breast cancer (PRIME II): a randomised controlled trial. Lancet Oncol. 2015;16(3):266-73.

74. NSABP Foundation Inc. A Randomized Phase III Clinical Trial Evaluating Post-Mastectomy Chestwall and Regional Nodal XRT and Post-Lumpectomy Regional Nodal XRT in Patients With Positive Axillary Nodes Before Neoadjuvant Chemotherapy Who Convert to Pathologically Negative Axillary Nodes After Neoadjuvant Chemotherapy. ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). [cited 2017 Apr 1]. Available from: https://clinicaltrials.gov/ct2/show/NCT01872975.

75. Alliance for Clinical Trials in Oncology. A Randomized Phase III Trial Comparing Axillary Lymph Node Dissection to Axillary Radiation in Breast Cancer Patients (cT1-3 N1) Who Have Positive Sentinel Lymph Node Disease After Neoadjuvant Chemotherapy. ClinicalTrials.gov [Internet]: Bethesda (MD): National Library of Medicine (US); [cited 2017 Oct 11]. Available from: https://clinicaltrials.gov/ct2/show/NCT01901094.

76. Litiere S, Werutsky G, Fentiman IS, Rutgers E, Christiaens MR, Van Limbergen E, et al. Breast conserving therapy versus mastectomy for stage I-II breast cancer: 20 year follow-up of the EORTC 10801 phase 3 randomised trial. Lancet Oncol. 2012;13(4):412-9.

77. Bartelink H, Maingon P, Poortmans P, Weltens C, Fourquet A, Jager J, et al. Whole-breast irradiation with or without a boost for patients treated with breast-conserving surgery for early breast cancer: 20-year follow-up of a randomised phase 3 trial. Lancet Oncol. 2015;16(1):47-56.

78. Smith BD, Bellon JR, Blitzblau R, Freedman G, Haffty B, Hahn C, et al. Radiation therapy for the whole breast: Executive summary of an American Society for Radiation Oncology (ASTRO) evidence-based guideline. Practical radiation oncology. 2018;8(3):145-52.

79. Haviland JS, Owen JR, Dewar JA, Agrawal RK, Barrett J, Barrett-Lee PJ, et al. The UK Standardisation of Breast Radiotherapy (START) trials of radiotherapy hypofractionation for treatment of early breast cancer: 10-year follow-up results of two randomised controlled trials. Lancet Oncol. 2013;14(11):1086-94.

80. Valle LF, Agarwal S, Bickel KE, Herchek HA, Nalepinski DC, Kapadia NS. Hypofractionated whole breast radiotherapy in breast conservation for early-stage breast cancer: a systematic review and meta-analysis of randomized trials. Breast cancer research and treatment. 2017;162(3):409-17.

81. Zhou ZR, Mei X, Chen XX, Yang ZZ, Hou J, Zhang L, et al. Systematic review and meta-analysis comparing hypofractionated with conventional fraction radiotherapy in treatment of early breast cancer. Surgical oncology. 2015;24(3):200-11.

82. Marta GN, Macedo CR, Carvalho Hde A, Hanna SA, da Silva JL, Riera R. Accelerated partial irradiation for breast cancer: systematic review and meta-analysis of 8653 women in eight randomized trials. Radiother Oncol. 2015;114(1):42-9.

83. Haagensen CD, Bodian C, Haagensen DE. Breast carcinoma. Risk and detection. Philadelphia, PA: WB Saunders; 1989.

84. Fisher B, Costantino JP, Wickerham DL, Redmond CK, Kavanah M, Cronin WM, et al. Tamoxifen for prevention of breast cancer: report of the National Surgical Adjuvant Breast and Bowel Project P-1 Study. J Natl Cancer Inst. 1998;90(18):1371-88.

85. Fisher B, Costantino JP, Wickerham DL, Cecchini RS, Cronin WM, Robidoux A, et al. Tamoxifen for the prevention of breast cancer: current status of the National Surgical Adjuvant Breast and Bowel Project P-1 study. J Natl Cancer Inst. 2005;97(22):1652-62.

86. Goss PE, Ingle JN, Ales-Martinez JE, Cheung AM, Chlebowski RT, Wactawski-Wende J, et al. Exemestane for breast-cancer prevention in postmenopausal women. N Engl J Med. 2011;364(25):2381-91.

87. Cuzick J, Sestak I, Forbes JF, Dowsett M, Knox J, Cawthorn S, et al. Anastrozole for prevention of breast cancer in high-risk postmenopausal women (IBIS-II): an international, double-blind, randomised placebo-controlled trial. Lancet. 2014;383(9922):1041-8.

88. Pieri A, Harvey J, Bundred N. Pleomorphic lobular carcinoma in situ of the breast: Can the evidence guide practice? World J Clin Oncol. 2014;5(3):546-53.

89. Silverstein MJ. The University of Southern California/Van Nuys prognostic index for ductal carcinoma in situ of the breast. American journal of surgery. 2003;186(4):337-43.

90. Bartlett JM, Nofech-Moses S, Rakovitch E. Ductal carcinoma in situ of the breast: can biomarkers improve current management? Clinical chemistry. 2014;60(1):60-7.

91. Lari SA, Kuerer HM. Biological Markers in DCIS and Risk of Breast Recurrence: A Systematic Review. Journal of Cancer. 2011;2:232-61.
92. Kerlikowske K, Molinaro AM, Gauthier ML, Berman HK, Waldman F, Bennington J, et al. Biomarker expression and risk of subsequent tumors after initial ductal carcinoma in situ diagnosis. J Natl Cancer Inst. 2010;102(9):627-37.
93. Molinaro AM, Sison JD, Ljung BM, Tlsty TD, Kerlikowske K. Risk prediction for local versus regional/metastatic tumors after initial ductal carcinoma in situ diagnosis treated by lumpectomy. Breast cancer research and treatment. 2016;157(2):351-61.
94. Rakovitch E, Nofech-Mozes S, Hanna W, Narod S, Thiruchelvam D, Saskin R, et al. HER2/neu and Ki-67 expression predict non-invasive recurrence following breast-conserving therapy for ductal carcinoma in situ. Br J Cancer. 2012;106(6):1160-5.
95. Solin LJ, Gray R, Baehner FL, Butler SM, Hughes LL, Yoshizawa C, et al. A multigene expression assay to predict local recurrence risk for ductal carcinoma in situ of the breast. J Natl Cancer Inst. 2013;105(10):701-10.
96. Rutter CE, Park HS, Killelea BK, Evans SB. Growing Use of Mastectomy for Ductal Carcinoma-In Situ of the Breast Among Young Women in the United States. Ann Surg Oncol. 2015;22(7):2378-86.
97. Ashfaq A, McGhan LJ, Pockaj BA, Gray RJ, Bagaria SP, McLaughlin SA, et al. Impact of breast reconstruction on the decision to undergo contralateral prophylactic mastectomy. Ann Surg Oncol. 2014;21(9):2934-40.
98. Esposito A, Criscitiello C, Curigliano G. Highlights from the 14(th) St Gallen International Breast Cancer Conference 2015 in Vienna: Dealing with classification, prognostication, and prediction refinement to personalize the treatment of patients with early breast cancer. Ecancermedicalscience. 2015;9:518.
99. Francis AM, Haugen CE, Grimes LM, Crow JR, Yi M, Mittendorf EA, et al. Is Sentinel Lymph Node Dissection Warranted for Patients with a Diagnosis of Ductal Carcinoma In Situ? Ann Surg Oncol. 2015;22(13):4270-9.
100. King MT, Link EK, Whelan TJ, Olivotto IA, Kunkler I, Westenberg AH, et al. Quality of life after breast-conserving therapy and adjuvant radiotherapy for non-low-risk ductal carcinoma in situ (BIG 3-07/TROG 07.01): 2-year results of a randomised, controlled, phase 3 trial. Lancet Oncol. 2020;21(5):685-98.
101. Vicini FA, Cecchini RS, White JR, Arthur DW, Julian TB, Rabinovitch RA, et al. Long-term primary results of accelerated partial breast irradiation after breast-conserving surgery for early-stage breast cancer: a randomised, phase 3, equivalence trial. Lancet. 2019;394(10215):2155-64.
102. Correa C, McGale P, Taylor C, Wang Y, Clarke M, Davies C, et al. Overview of the randomized trials of radiotherapy in ductal carcinoma in situ of the breast. Journal of the National Cancer Institute Monographs. 2010;2010(41):162-77.
103. Hughes LL, Wang M, Page DL, Gray R, Solin LJ, Davidson NE, et al. Local excision alone without irradiation for ductal carcinoma in situ of the breast: a trial of the Eastern Cooperative Oncology Group. J Clin Oncol. 2009;27(32):5319-24.
104. Solin LJ, Gray R, Hughes LL, Wood WC, Lowen MA, Badve SS, et al. Surgical Excision Without Radiation for Ductal Carcinoma in Situ of the Breast: 12-Year Results From the ECOG-ACRIN E5194 Study. J Clin Oncol. 2015;33(33):3938-44.
105. McCormick B, Winter K, Hudis C, Kuerer HM, Rakovitch E, Smith BL, et al. RTOG 9804: a prospective randomized trial for good-risk ductal carcinoma in situ comparing radiotherapy with observation. J Clin Oncol. 2015;33(7):709-15.
106. McCormick B, Winter KA, Woodward W, Kuerer HM, Sneige N, Rakovitch E, et al. Randomized Phase III Trial Evaluating Radiation Following Surgical Excision for Good-Risk Ductal Carcinoma In Situ: Long-Term Report From NRG Oncology/RTOG 9804. J Clin Oncol. 2021;39(32):3574-82.
107. Lebeau A, Kühn T. Updates in the treatment of ductal carcinoma in situ of the breast. Curr Opin Obstet Gynecol. 2016;28(1):49-58.
108. Viani GA, Stefano EJ, Afonso SL, De Fendi LI, Soares FV, Leon PG, et al. Breast-conserving surgery with or without radiotherapy in women with ductal carcinoma in situ: a meta-analysis of randomized trials. Radiation oncology. 2007;2:28.
109. Group EBCC, Group ER, Bijker N, Meijnen P, Peterse JL, Bogaerts J, et al. Breast-conserving treatment with or without radiotherapy in ductal carcinoma-in-situ: ten-year results of European Organisation for Research and Treatment of Cancer randomized phase III trial 10853--a study by the EORTC Breast Cancer Cooperative Group and EORTC Radiotherapy Group. J Clin Oncol. 2006;24(21):3381-7.
110. Bremer T, Whitworth PW, Patel R, Savala J, Barry T, Lyle S, et al. A Biological Signature for Breast Ductal Carcinoma In Situ to Predict Radiotherapy Benefit and Assess Recurrence Risk. Clinical cancer research : an official journal of the American Association for Cancer Research. 2018;24(23):5895-901.
111. Allred DC, Anderson SJ, Paik S, Wickerham DL, Nagtegaal ID, Swain SM, et al. Adjuvant tamoxifen reduces subsequent breast cancer in women with estrogen receptor-positive ductal carcinoma in situ: a study based on NSABP protocol B-24. J Clin Oncol. 2012;30(12):1268-73.
112. Fisher B, Dignam J, Wolmark N, Wickerham DL, Fisher ER, Mamounas E, et al. Tamoxifen in treatment of intraductal breast cancer: National Surgical Adjuvant Breast and Bowel Project B-24 randomised controlled trial. Lancet. 1999;353(9169):1993-2000.
113. Margolese RG, Cecchini RS, Julian TB. Primary results, NRG Oncology/NSABP B-35. 2015 ASCO Annual Meeting. Abstract LBA500. Presented May 30, 2015.

114. Forbes JF, Sestak I, Howell A, Bonanni B, Bundred N, Levy C, et al. Anastrozole versus tamoxifen for the prevention of locoregional and contralateral breast cancer in postmenopausal women with locally excised ductal carcinoma in situ (IBIS-II DCIS): a double-blind, randomised controlled trial. Lancet. 2016;387(10021):866-73.

115. Berry DA, Iversen ES, Gudbjartsson DF, Hiller EH, Garber JE, Peshkin BN, et al. BRCAPRO validation, sensitivity of genetic testing of BRCA1/BRCA2, and prevalence of other breast cancer susceptibility genes. J Clin Oncol. 2002;20(11):2701-12.

116. Lee AJ, Cunningham AP, Kuchenbaecker KB, Mavaddat N, Easton DF, Antoniou AC, et al. BOADICEA breast cancer risk prediction model: updates to cancer incidences, tumour pathology and web interface. Br J Cancer. 2014;110(2):535-45.

117. Cuzick J, Sestak I, Cawthorn S, Hamed H, Holli K, Howell A, et al. Tamoxifen for prevention of breast cancer: extended long-term follow-up of the IBIS-I breast cancer prevention trial. Lancet Oncol. 2015;16(1):67-75.

118. Powles TJ, Ashley S, Tidy A, Smith IE, Dowsett M. Twenty-year follow-up of the Royal Marsden randomized, double-blinded tamoxifen breast cancer prevention trial. J Natl Cancer Inst. 2007;99(4):283-90.

119. Veronesi U, Maisonneuve P, Rotmensz N, Bonanni B, Boyle P, Viale G, et al. Tamoxifen for the prevention of breast cancer: late results of the Italian Randomized Tamoxifen Prevention Trial among women with hysterectomy. J Natl Cancer Inst. 2007;99(9):727-37.

120. DeCensi A, Puntoni M, Guerrieri-Gonzaga A, Caviglia S, Avino F, Cortesi L, et al. Randomized Placebo Controlled Trial of Low-Dose Tamoxifen to Prevent Local and Contralateral Recurrence in Breast Intraepithelial Neoplasia. J Clin Oncol. 2019;37(19):1629-37.

121. Vogel VG, Costantino JP, Wickerham DL, Cronin WM, Cecchini RS, Atkins JN, et al. Update of the National Surgical Adjuvant Breast and Bowel Project Study of Tamoxifen and Raloxifene (STAR) P-2 Trial: Preventing breast cancer. Cancer prevention research. 2010;3(6):696-706.

122. Narod SA. Tamoxifen Chemoprevention--End of the Road? JAMA Oncol. 2015;1(8):1033-4.

123. Visvanathan K, Hurley P, Bantug E, Brown P, Col NF, Cuzick J, et al. Use of pharmacologic interventions for breast cancer risk reduction: American Society of Clinical Oncology clinical practice guideline. J Clin Oncol. 2013;31(23):2942-62.

124. Kaufmann M, von Minckwitz G, Mamounas EP, Cameron D, Carey LA, Cristofanilli M, et al. Recommendations from an international consensus conference on the current status and future of neoadjuvant systemic therapy in primary breast cancer. Ann Surg Oncol. 2012;19(5):1508-16.

125. Rastogi P, Anderson SJ, Bear HD, Geyer CE, Kahlenberg MS, Robidoux A, et al. Preoperative chemotherapy: updates of National Surgical Adjuvant Breast and Bowel Project Protocols B-18 and B-27. J Clin Oncol. 2008;26(5):778-85.

126. Azim HA, Jr., Michiels S, Zagouri F, Delaloge S, Filipits M, Namer M, et al. Utility of prognostic genomic tests in breast cancer practice: The IMPAKT 2012 Working Group Consensus Statement. Annals of oncology : official journal of the European Society for Medical Oncology / ESMO. 2013;24(3):647-54.

127. Sormani MP. Modeling the distribution of new MRI cortical lesions in multiple sclerosis longitudinal studies by Sormani MP, Calabrese M, Signori A, Giorgio A, Gallo P, De Stefano N [PLoS One 2011;6(10):e26712. Epub 2011 October 20]. Mult Scler Relat Disord. 2012;1(3):108.

128. Cortazar P, Zhang L, Untch M, Mehta K, Costantino JP, Wolmark N, et al. Pathological complete response and long-term clinical benefit in breast cancer: the CTNeoBC pooled analysis. Lancet. 2014;384(9938):164-72.

129. Wang-Lopez Q, Chalabi N, Abrial C, Radosevic-Robin N, Durando X, Mouret-Reynier MA, et al. Can pathologic complete response (pCR) be used as a surrogate marker of survival after neoadjuvant therapy for breast cancer? Critical reviews in oncology/hematology. 2015;95(1):88-104.

130. Fei F, Messina C, Slaets L, Chakiba C, Cameron D, Bogaerts J, et al. Tumour size is the only predictive factor of distant recurrence after pathological complete response to neoadjuvant chemotherapy in patients with large operable or locally advanced breast cancers: a sub-study of EORTC 10994/BIG 1-00 phase III trial. Eur J Cancer. 2015;51(3):301-9.

131. Zhao Y, Dong X, Li R, Ma X, Song J, Li Y, et al. Evaluation of the pathological response and prognosis following neoadjuvant chemotherapy in molecular subtypes of breast cancer. Onco Targets Ther. 2015;8:1511-21.

132. Sparano JA, Gray RJ, Makower DF, Pritchard KI, Albain KS, Hayes DF, et al. Prospective Validation of a 21-Gene Expression Assay in Breast Cancer. N Engl J Med. 2015;373(21):2005-14.

133. Geisler J, Smith I, Miller W. Presurgical (neoadjuvant) endocrine therapy is a useful model to predict response and outcome to endocrine treatment in breast cancer patients. The Journal of steroid biochemistry and molecular biology. 2012;131(3-5):93-100.

134. Alba E, Calvo L, Albanell J, De la Haba JR, Arcusa Lanza A, Chacon JI, et al. Chemotherapy (CT) and hormonotherapy (HT) as neoadjuvant treatment in luminal breast cancer patients: results from the GEICAM/2006-03, a multicenter, randomized, phase-II study. Annals of oncology : official journal of the European Society for Medical Oncology / ESMO. 2012;23(12):3069-74.

135. Cortazar P, Zhang L, Untch M, Mehta K, Costantino J, Wolmark N, et al. Abstract S1-11: Meta-analysis Results from the Collaborative Trials in Neoadjuvant Breast Cancer (CTNeoBC). Cancer research2012. p. S1-11-S1-.

136. Early Breast Cancer Trialists' Collaborative G, Clarke M, Coates AS, Darby SC, Davies C, Gelber RD, et al. Adjuvant chemotherapy in oestrogen-receptor-poor breast cancer: patient-level meta-analysis of randomised trials. Lancet. 2008;371(9606):29-40.

137. Opdam M, van der Noort V, Kleijn M, Glas A, Mandjes I, Kruger D, et al. Avoid systemic overtreatment of postmenopausal breast cancer patients with ultralow MammaPrint result. ESMO Virtual Congress 20202020.

138. Michalides R, van Tinteren H, Balkenende A, Vermorken JB, Benraadt J, Huldij J, et al. Cyclin A is a prognostic indicator in early stage breast cancer with and without tamoxifen treatment. Br J Cancer. 2002;86(3):402-8.

139. Lopes Cardozo J, Drukker C, Schmidt M, van 't Veer L, Glas A, Witteveen A, et al. Outcome of patients with an ultralow risk 70-gene signature in the MINDACT trial. J Clin Oncol. 2021;39(15_suppl):500-.

140. Cardoso F, van 't Veer L, Poncet C, Lopes Cardozo J, Delaloge S, Pierga J-Y, et al. MINDACT: Long-term results of the large prospective trial testing the 70-gene signature MammaPrint as guidance for adjuvant chemotherapy in breast cancer patients. Journal of Clinical Oncology. 2020;38(15_suppl):506-.

141. Cardoso F. MINDACT (EORTC 10041/BIG3-04): Long-term results of the large prospective trial testing the 70-gene signature MammaPrint as guidance for adjuvant chemotherapy in breast cancer patients. Breast Cancer Group News. 2020.

142. Postmenopausal Women with HR+/HER2- Early Breast Cancer, 1-3 Positive Nodes, and a Low Risk of Recurrence Can Safely Forego Chemotherapy. The oncologist. 2021;26 Suppl 2:S11-S2.

143. Johnston SRD, Harbeck N, Hegg R, Toi M, Martin M, Shao ZM, et al. Abemaciclib Combined With Endocrine Therapy for the Adjuvant Treatment of HR+, HER2-, Node-Positive, High-Risk, Early Breast Cancer (monarchE). J Clin Oncol. 2020;38(34):3987-98.

144. Early Breast Cancer Trialists' Collaborative G, Davies C, Godwin J, Gray R, Clarke M, Cutter D, et al. Relevance of breast cancer hormone receptors and other factors to the efficacy of adjuvant tamoxifen: patient-level meta-analysis of randomised trials. Lancet. 2011;378(9793):771-84.

145. Francis PA, Regan MM, Fleming GF, Lang I, Ciruelos E, Bellet M, et al. Adjuvant ovarian suppression in premenopausal breast cancer. N Engl J Med. 2015;372(5):436-46.

146. Pagani O, Regan MM, Walley BA, Fleming GF, Colleoni M, Lang I, et al. Adjuvant exemestane with ovarian suppression in premenopausal breast cancer. N Engl J Med. 2014;371(2):107-18.

147. Francis PA, Pagani O, Fleming GF, Walley BA, Colleoni M, Lang I, et al. Tailoring Adjuvant Endocrine Therapy for Premenopausal Breast Cancer. N Engl J Med. 2018;379(2):122-37.

148. Al-Mubarak M, Tibau A, Templeton AJ, Cescon DW, Ocana A, Seruga B, et al. Extended adjuvant tamoxifen for early breast cancer: a meta-analysis. PloS one. 2014;9(2):e88238.

149. Burstein HJ, Temin S, Anderson H, Buchholz TA, Davidson NE, Gelmon KE, et al. Adjuvant endocrine therapy for women with hormone receptor-positive breast cancer: american society of clinical oncology clinical practice guideline focused update. J Clin Oncol. 2014;32(21):2255-69.

150. Noordhoek I, Treuner K, Putter H, Zhang Y, Wong J, Meershoek-Klein Kranenbarg E, et al. Breast Cancer Index Predicts Extended Endocrine Benefit to Individualize Selection of Patients with HR(+) Early-stage Breast Cancer for 10 Years of Endocrine Therapy. Clinical cancer research : an official journal of the American Association for Cancer Research. 2021;27(1):311-9.

151. Goss PE, Ingle JN, Martino S, Robert NJ, Muss HB, Livingston RB, et al. Impact of premenopausal status at breast cancer diagnosis in women entered on the placebo-controlled NCIC CTG MA17 trial of extended adjuvant letrozole. Annals of oncology : official journal of the European Society for Medical Oncology / ESMO. 2013;24(2):355-61.

152. Controlled trial of tamoxifen as a single adjuvant agent in the management of early breast cancer. 'Nolvadex' Adjuvant Trial Organisation. Br J Cancer. 1988;57(6):608-11.

153. (EBCTCG) EBCTCG. Effects of chemotherapy and hormonal therapy for early breast cancer on recurrence and 15-year survival: an overview of the randomised trials. Lancet. 2005;365(9472):1687-717.

154. Early Breast Cancer Trialists' Collaborative G, Dowsett M, Forbes JF, Bradley R, Ingle J, Aihara T, et al. Aromatase inhibitors versus tamoxifen in early breast cancer: patient-level meta-analysis of the randomised trials. Lancet. 2015;386(10001):1341-52.

155. Dowsett M, Cuzick J, Ingle J, Coates A, Forbes J, Bliss J, et al. Meta-analysis of breast cancer outcomes in adjuvant trials of aromatase inhibitors versus tamoxifen. J Clin Oncol. 2010;28(3):509-18.

156. Howell A, Cuzick J, Baum M, Buzdar A, Dowsett M, Forbes JF, et al. Results of the ATAC (Arimidex, Tamoxifen, Alone or in Combination) trial after completion of 5 years' adjuvant treatment for breast cancer. Lancet. 2005;365(9453):60-2.

157. Breast International Group 1-98 Collaborative G, Thurlimann B, Keshaviah A, Coates AS, Mouridsen H, Mauriac L, et al. A comparison of letrozole and tamoxifen in postmenopausal women with early breast cancer. N Engl J Med. 2005;353(26):2747-57.

158. van de Velde CJ, Rea D, Seynaeve C, Putter H, Hasenburg A, Vannetzel JM, et al. Adjuvant tamoxifen and exemestane in early breast cancer (TEAM): a randomised phase 3 trial. Lancet. 2011;377(9762):321-31.

159. Jonat W, Gnant M, Boccardo F, Kaufmann M, Rubagotti A, Zuna I, et al. Effectiveness of switching from adjuvant tamoxifen to anastrozole in postmenopausal women with hormone-sensitive early-stage breast cancer: a meta-analysis. Lancet Oncol. 2006;7(12):991-6.

160. Goss PE, Ingle JN, Martino S, Robert NJ, Muss HB, Piccart MJ, et al. A randomized trial of letrozole in postmenopausal women after five years of tamoxifen therapy for early-stage breast cancer. N Engl J Med. 2003;349(19):1793-802.

161. Goss PE, Ingle JN, Martino S, Robert NJ, Muss HB, Piccart MJ, et al. Randomized trial of letrozole following tamoxifen as extended adjuvant therapy in receptor-positive breast cancer: updated findings from NCIC CTG MA.17. J Natl Cancer Inst. 2005;97(17):1262-71.

162. Jakesz R, Greil R, Gnant M, Schmid M, Kwasny W, Kubista E, et al. Extended adjuvant therapy with anastrozole among postmenopausal breast cancer patients: results from the randomized Austrian Breast and Colorectal Cancer Study Group Trial 6a. J Natl Cancer Inst. 2007;99(24):1845-53.

163. Mamounas EP, Jeong JH, Wickerham DL, Smith RE, Ganz PA, Land SR, et al. Benefit from exemestane as extended adjuvant therapy after 5 years of adjuvant tamoxifen: intention-to-treat analysis of the National Surgical Adjuvant Breast And Bowel Project B-33 trial. J Clin Oncol. 2008;26(12):1965-71.

164. Davies C, Pan H, Godwin J, Gray R, Arriagada R, Raina V, et al. Long-term effects of continuing adjuvant tamoxifen to 10 years versus stopping at 5 years after diagnosis of oestrogen receptor-positive breast cancer: ATLAS, a randomised trial. Lancet. 2013;381(9869):805-16.

165. Davis C, Pan H, Godwin J, Gray R, Peto R. 10 v 5 years of adjuvant tamoxifen (TAM) in ER+ disease. Effects on outcome in the first and in the second decade after diagnosis. San Antonio Breast Cancer Conference: S1-2. 2012.

166. Gray R, Rea D, Handley K, Bowden S, Perry P, Earl H, et al. aTTom: Long-term effects of continuing adjuvant tamoxifen to 10 years versus stopping at 5 years in 6,953 women with early breast cancer. 2013 ASCO Annual Meeting. J Clin Oncol 31, 2013 (suppl; abstr 5).

167. Metzger Filho O, Giobbie-Hurder A, Mallon E, Gusterson B, Viale G, Winer EP, et al. Relative Effectiveness of Letrozole Compared With Tamoxifen for Patients With Lobular Carcinoma in the BIG 1-98 Trial. J Clin Oncol. 2015;33(25):2772-9.

168. Early Breast Cancer Trialists' Collaborative G, Peto R, Davies C, Godwin J, Gray R, Pan HC, et al. Comparisons between different polychemotherapy regimens for early breast cancer: meta-analyses of long-term outcome among 100,000 women in 123 randomised trials. Lancet. 2012;379(9814):432-44.

169. Coates AS, Winer EP, Goldhirsch A, Gelber RD, Gnant M, Piccart-Gebhart M, et al. -Tailoring therapies-improving the management of early breast cancer: St Gallen International Expert Consensus on the Primary Therapy of Early Breast Cancer 2015. Annals of oncology : official journal of the European Society for Medical Oncology / ESMO. 2015;26(8):1533-46.

170. Albain KS, Barlow WE, Shak S, Hortobagyi GN, Livingston RB, Yeh IT, et al. Prognostic and predictive value of the 21-gene recurrence score assay in postmenopausal women with node-positive, oestrogen-receptor-positive breast cancer on chemotherapy: a retrospective analysis of a randomised trial. Lancet Oncol. 2010;11(1):55-65.

171. Harris LN, Ismaila N, McShane LM, Andre F, Collyar DE, Gonzalez-Angulo AM, et al. Use of Biomarkers to Guide Decisions on Adjuvant Systemic Therapy for Women With Early-Stage Invasive Breast Cancer: American Society of Clinical Oncology Clinical Practice Guideline. J Clin Oncol. 2016.

172. De Laurentiis M, Cancello G, D'Agostino D, Giuliano M, Giordano A, Montagna E, et al. Taxane-based combinations as adjuvant chemotherapy of early breast cancer: a meta-analysis of randomized trials. J Clin Oncol. 2008;26(1):44-53.

173. Fujii T, Le Du F, Xiao L, Kogawa T, Barcenas CH, Alvarez RH, et al. Effectiveness of an Adjuvant Chemotherapy Regimen for Early-Stage Breast Cancer: A Systematic Review and Network Meta-analysis. JAMA Oncol. 2015;1(9):1311-8.

174. Hart CD, Sanna G, Siclari O, Biganzoli L, Di Leo A. Defining optimal duration and predicting benefit from chemotherapy in patients with luminal-like subtypes. Breast. 2015;24 Suppl 2:S136-42.

175. Gandhi S, Fletcher GG, Eisen A, Mates M, Freedman OC, Dent SF, et al. Adjuvant chemotherapy for early female breast cancer: a systematic review of the evidence for the 2014 Cancer Care Ontario systemic therapy guideline. Curr Oncol. 2015;22(Suppl 1):S82-94.

176. Dent R, Trudeau M, Pritchard KI, Hanna WM, Kahn HK, Sawka CA, et al. Triple-negative breast cancer: clinical features and patterns of recurrence. Clinical cancer research : an official journal of the American Association for Cancer Research. 2007;13(15 Pt 1):4429-34.

177. Berry DA, Cirrincione C, Henderson IC, Citron ML, Budman DR, Goldstein LJ, et al. Estrogen-receptor status and outcomes of modern chemotherapy for patients with node-positive breast cancer. JAMA. 2006;295(14):1658-67.

178. Vaz-Luis I, Ottesen RA, Hughes ME, Mamet R, Burstein HJ, Edge SB, et al. Outcomes by tumor subtype and treatment pattern in women with small, node-negative breast cancer: a multi-institutional study. J Clin Oncol. 2014;32(20):2142-50.

179. Jones S, Holmes FA, O'Shaughnessy J, Blum JL, Vukelja SJ, McIntyre KJ, et al. Docetaxel With Cyclophosphamide Is Associated With an Overall Survival Benefit Compared With Doxorubicin and Cyclophosphamide: 7-Year Follow-Up of US Oncology Research Trial 9735. J Clin Oncol. 2009;27(8):1177-83.

180. Kim HA, Seong MK, Kim EK, Kang E, Park S, Hur MH, et al. Evaluation of the Survival Benefit of Different Chemotherapy Regimens in Patients with T1-2N0 Triple-Negative Breast Cancer. J Breast Cancer. 2015;18(3):271-8.

181. Lim S, Park SH, Park HK, Hur MH, Oh SJ, Suh YJ. Prognostic Role of Adjuvant Chemotherapy in Node-Negative (N0), Triple-Negative (TN), Medullary Breast Cancer (MBC) in the Korean Population. PloS one. 2015;10(11):e0140208.

182. Petrelli F, Cabiddu M, Coinu A, Borgonovo K, Ghilardi M, Lonati V, et al. Adjuvant dose-dense chemotherapy in breast cancer: a systematic review and meta-analysis of randomized trials. Breast cancer research and treatment. 2015;151(2):251-9.

183. Swain SM, Tang G, Geyer CE, Jr., Rastogi P, Atkins JN, Donnellan PP, et al. Definitive results of a phase III adjuvant trial comparing three chemotherapy regimens in women with operable, node-positive breast cancer: the NSABP B-38 trial. J Clin Oncol. 2013;31(26):3197-204.

184. Perez EA, Romond EH, Suman VJ, Jeong JH, Davidson NE, Geyer CE, Jr., et al. Four-year follow-up of trastuzumab plus adjuvant chemotherapy for operable human epidermal growth factor receptor 2-positive breast cancer: joint analysis of data from NCCTG N9831 and NSABP B-31. J Clin Oncol. 2011;29(25):3366-73.

185. Goldhirsch A, Gelber RD, Piccart-Gebhart MJ, de Azambuja E, Procter M, Suter TM, et al. 2 years versus 1 year of adjuvant trastuzumab for HER2-positive breast cancer (HERA): an open-label, randomised controlled trial. Lancet. 2013;382(9897):1021-8.

186. Slamon D, Eiermann W, Robert N, Pienkowski T, Martin M, Press M, et al. Adjuvant trastuzumab in HER2-positive breast cancer. N Engl J Med. 2011;365(14):1273-83.

187. Perez EA, Suman VJ, Davidson NE, Gralow JR, Kaufman PA, Visscher DW, et al. Sequential versus concurrent trastuzumab in adjuvant chemotherapy for breast cancer. J Clin Oncol. 2011;29(34):4491-7.

188. Romond EH, Perez EA, Bryant J, Suman VJ, Geyer CE, Davidson NE, et al. Trastuzumab plus adjuvant chemotherapy for operable HER2-positive breast cancer. N Engl J Med. 2005;353(16):1673-84.

189. Perez EA, Romond EH, Suman VJ, Jeong JH, Sledge G, Geyer CE, et al. Trastuzumab plus adjuvant chemotherapy for human epidermal growth factor receptor 2-positive breast cancer: planned joint analysis of overall survival from NSABP B-31 and NCCTG N9831. J Clin Oncol. 2014;32(33):3744-52.

190. Joensuu H, Bono P, Kataja V, Alanko T, Kokko R, Asola R, et al. Fluorouracil, epirubicin, and cyclophosphamide with either docetaxel or vinorelbine, with or without trastuzumab, as adjuvant treatments of breast cancer: final results of the FinHer Trial. J Clin Oncol. 2009;27(34):5685-92.

191. Spielmann M, Roché H, Delozier T, Canon JL, Romieu G, Bourgeois H, et al. Trastuzumab for patients with axillary-node-positive breast cancer: results of the FNCLCC-PACS 04 trial. J Clin Oncol. 2009;27(36):6129-34.

192. Chan A, Moy B, Mansi J, Ejlertsen B, Holmes FA, Chia S, et al. Final Efficacy Results of Neratinib in HER2-positive Hormone Receptor-positive Early-stage Breast Cancer From the Phase III ExteNET Trial. Clinical breast cancer. 2021;21(1):80-91 e7.

193. Tanaka K, Kawaguchi H, Nakamura Y, Taguchi K, Nishiyama K, Ohno S. Effect of HER2 status on risk of recurrence in women with small, node-negative breast tumours. Br J Surg. 2011;98(11):1561-5.

194. Gonzalez-Angulo AM, Litton JK, Broglio KR, Meric-Bernstam F, Rakkhit R, Cardoso F, et al. High risk of recurrence for patients with breast cancer who have human epidermal growth factor receptor 2-positive, node-negative tumors 1 cm or smaller. J Clin Oncol. 2009;27(34):5700-6.

195. Zhou Q, Yin W, Du Y, Lu J. For or against adjuvant trastuzumab for pT1a-bN0M0 breast cancer patients with HER2-positive tumors: a meta-analysis of published literatures. PloS one. 2014;9(1):e83646.

196. Joerger M, Thurlimann B, Huober J. Small HER2-positive, node-negative breast cancer: who should receive systemic adjuvant treatment? Annals of oncology : official journal of the European Society for Medical Oncology / ESMO. 2011;22(1):17-23.

197. Tolaney SM, Barry WT, Dang CT, Yardley DA, Moy B, Marcom PK, et al. Adjuvant paclitaxel and trastuzumab for node-negative, HER2-positive breast cancer. N Engl J Med. 2015;372(2):134-41.

198. Tutt ANJ, Garber JE, Kaufman B, Viale G, Fumagalli D, Rastogi P, et al. Adjuvant Olaparib for Patients with BRCA1- or BRCA2-Mutated Breast Cancer. N Engl J Med. 2021;384(25):2394-405.

199. Kramar A, Bachelot T, Madrange N, Pierga JY, Kerbrat P, Espié M, et al. Trastuzumab duration effects within patient prognostic subgroups in the PHARE trial. Annals of oncology : official journal of the European Society for Medical Oncology / ESMO. 2014;25(8):1563-70.

200. Pivot X, Romieu G, Bonnefori H. PHARE trial results comparing 6 to 12 months of adjuvant trastuzumab in early breast cancer. 2012 ESMO Congress. Abstract LBA5. Presented October 1, 2012.

201. Gelber R, Goldhirsch A, Piccart M. HERA Trial: 2 years versus 1 year of trastuzumab after adjuvant chemotherapy in women with HER2-positive early breast cancer at 8 years of median follow up. 2012 ESMO Congress. Abstract LBA6. Presented October 1, 2012.

202. Gonzalez-Angulo AM, Parinyanitikul N, Lei X, Mittendorf EA, Zhang H, Valero V, et al. Effect of adjuvant trastuzumab among patients treated with anti-HER2-based neoadjuvant therapy. Br J Cancer. 2015;112(4):630-5.

203. Slamon D, Eiermann W, Robert N, Giermek J, Martin M, Jasiowka M, et al. Ten-year follow-up of BCIRG-006 comparing doxorubicin plus cyclophosphamide followed by docetaxel with doxorubicin plus cyclophosphamide followed by docetaxel and trastuzumab with docetaxel, carboplatin and trastuzumab in HER2-positive early breast cancer patients. Presented at the 38th Annual San Antonio Breast Cancer Symposium, December 8-12, 2015; Abstract S5-04.

204. Cortes J, Ciruelos E, Perez-Garcia J, Albanell J, Garcia-Estevez L, Ruiz-Borrego M, et al. Contextualizing pertuzumab approval in the treatment of HER2-positive breast cancer patients. Cancer Treat Rev. 2020;83:101944.

205. Piccart M, Procter M, Fumagalli D, de Azambuja E, Clark E, Ewer MS, et al. Interim overall survival analysis of APHINITY (BIG 4-11): A randomized multicenter, double-blind, placebo-controlled trial comparing chemotherapy plus trastuzumab plus pertuzumab versus chemotherapy plus trastuzumab plus placebo as adjuvant therapy in patients with operable HER2-positive early breast cancer. San Antonio Breast Cancer Symposium. 2020;80(4):Suppl.

206. Jackisch C, Kim SB, Semiglazov V, Melichar B, Pivot X, Hillenbach C, et al. Subcutaneous versus intravenous formulation of trastuzumab for HER2-positive early breast cancer: updated results from the phase III HannaH study. Annals of oncology : official journal of the European Society for Medical Oncology / ESMO. 2015;26(2):320-5.

207. Pivot X, Gligorov J, Muller V, Curigliano G, Knoop A, Verma S, et al. Patients' preferences for subcutaneous trastuzumab versus conventional intravenous infusion for the adjuvant treatment of HER2-positive early breast cancer: final analysis of 488 patients in the international, randomized, two-cohort PrefHer study. Annals of oncology : official journal of the European Society for Medical Oncology / ESMO. 2014;25(10):1979-87.

208. Slamon DJ, Leyland-Jones B, Shak S, Fuchs H, Paton V, Bajamonde A, et al. Use of chemotherapy plus a monoclonal antibody against HER2 for metastatic breast cancer that overexpresses HER2. N Engl J Med. 2001;344(11):783-92.

209. Perez EA, Suman VJ, Davidson NE, Sledge GW, Kaufman PA, Hudis CA, et al. Cardiac safety analysis of doxorubicin and cyclophosphamide followed by paclitaxel with or without trastuzumab in the North Central Cancer Treatment Group N9831 adjuvant breast cancer trial. J Clin Oncol. 2008;26(8):1231-8.

210. Mauri D, Pavlidis N, Ioannidis JP. Neoadjuvant versus adjuvant systemic treatment in breast cancer: a meta-analysis. J Natl Cancer Inst. 2005;97(3):188-94.

211. von Minckwitz G. Preoperative therapy: what, when and for whom? Annals of oncology : official journal of the European Society for Medical Oncology / ESMO. 2008;19 Suppl 5:v113-6.

212. Early Breast Cancer Trialists' Collaborative Group (EBCTCG). Long-term outcomes for neoadjuvant versus adjuvant chemotherapy in early breast cancer: meta-analysis of individual patient data from ten randomised trials. Lancet Oncol. 2018;19(1):27-39.

213. Schott AF, Hayes DF. Defining the benefits of neoadjuvant chemotherapy for breast cancer. J Clin Oncol. 2012;30(15):1747-9.

214. De Mattos-Arruda L, Shen R, Reis-Filho JS, Cortés J. Translating neoadjuvant therapy into survival benefits: one size does not fit all. Nat Rev Clin Oncol. 2016;13(9):566-79.

215. Mueller V. Prospective monitoring of circulating tumor cells in breast cancer patients treated with primary systemic therapy—A translational project of the German Breast Group study GeparQuattro. ASCO 2007. Abs 21085: http://ascopubs.org/doi/abs/10.1200/jco.2007.25.18_suppl.21085.

216. van der Hage JA, van de Velde CJ, Julien JP, Tubiana-Hulin M, Vandervelden C, Duchateau L. Preoperative chemotherapy in primary operable breast cancer: results from the European Organization for Research and Treatment of Cancer trial 10902. J Clin Oncol. 2001;19(22):4224-37.

217. Scholl SM, Fourquet A, Asselain B, Pierga JY, Vilcoq JR, Durand JC, et al. Neoadjuvant versus adjuvant chemotherapy in premenopausal patients with tumours considered too large for breast conserving surgery: preliminary results of a randomised trial: S6. Eur J Cancer. 1994;30A(5):645-52.

218. Gradishar WJ, Anderson BO, Abraham J, Aft R, Agnese D, Allison KH, et al. Breast Cancer, Version 3.2020, NCCN Clinical Practice Guidelines in Oncology. Journal of the National Comprehensive Cancer Network : JNCCN. 2020;18(4):452-78.

219. Cortazar P, Zhang L, Untch M, Mehta K, Costantino JP, Wolmark N, et al. Pathological complete response and long-term clinical benefit in breast cancer: the CTNeoBC pooled analysis. The Lancet. 2014;384(9938):164-72.

220. Ameztoy K, Baslam M, Sanchez-Lopez AM, Munoz FJ, Bahaji A, Almagro G, et al. Plant responses to fungal volatiles involve global posttranslational thiol redox proteome changes that affect photosynthesis. Plant, cell & environment. 2019;42(9):2627-44.

221. Kuerer HM, Newman LA, Buzdar AU, Hunt KK, Dhingra K, Buchholz TA, et al. Residual metastatic axillary lymph nodes following neoadjuvant chemotherapy predict disease-free survival in patients with locally advanced breast cancer. American journal of surgery. 1998;176(6):502-9.

222. Ogston KN, Miller ID, Payne S, Hutcheon AW, Sarkar TK, Smith I, et al. A new histological grading system to assess response of breast cancers to primary chemotherapy: prognostic significance and survival. Breast. 2003;12(5):320-7.

223. Symmans WF, Peintinger F, Hatzis C, Rajan R, Kuerer H, Valero V, et al. Measurement of residual breast cancer burden to predict survival after neoadjuvant chemotherapy. J Clin Oncol. 2007;25(28):4414-22.

224. Loibl S, Poortmans P, Morrow M, Denkert C, Curigliano G. Breast cancer. Lancet. 2021;397(10286):1750-69.

225. Asano Y. Prediction of survival after neoadjuvant chemotherapy for breast cancer by evaluation of tumor-infiltrating lymphocytes and residual cancer burden. BMC cancer. 2017;17:888

226. Denkert C, von Minckwitz G, Darb-Esfahani S, Lederer B, Heppner BI, Weber KE, et al. Tumour-infiltrating lymphocytes and prognosis in different subtypes of breast cancer: a pooled analysis of 3771 patients treated with neoadjuvant therapy. Lancet Oncol. 2018;19(1):40-50.

227. Korn EL, Sachs MC, McShane LM. Statistical controversies in clinical research: assessing pathologic complete response as a trial-level surrogate end point for early-stage breast cancer. Annals of oncology : official journal of the European Society for Medical Oncology / ESMO. 2016;27(1):10-5.

228. von Minckwitz G, Untch M, Blohmer JU, Costa SD, Eidtmann H, Fasching PA, et al. Definition and impact of pathologic complete response on prognosis after neoadjuvant chemotherapy in various intrinsic breast cancer subtypes. J Clin Oncol. 2012;30(15):1796-804.

229. US Department of Health and Human Services. Guidance for Industry. Pathological Complete Response in Neoadjuvant Treatment of High-Risk Early-Stage Breast Cancer: Use as an Endpoint to Support Accelerated Approval. 2014.

230. Abdel-Fatah TM, Ball G, Lee AH, Pinder S, MacMilan RD, Cornford E, et al. Nottingham Clinico-Pathological Response Index (NPRI) after neoadjuvant chemotherapy (Neo-ACT) accurately predicts clinical outcome in locally advanced breast cancer. Clinical cancer research : an official journal of the American Association for Cancer Research. 2015;21(5):1052-62.

231. Jebbink M, van Werkhoven E, Mandjes IA, Wesseling J, Lips EH, Vrancken Peeters MJ, et al. The prognostic value of the neoadjuvant response index in triple-negative breast cancer: validation and comparison with pathological complete response as outcome measure. Breast cancer research and treatment. 2015;153(1):145-52.

232. Salgado R, Denkert C, Campbell C, Savas P, Nuciforo P, Nucifero P, et al. Tumor-Infiltrating Lymphocytes and Associations With Pathological Complete Response and Event-Free Survival in HER2-Positive Early-Stage Breast Cancer Treated With Lapatinib and Trastuzumab: A Secondary Analysis of the NeoALTTO Trial. JAMA Oncol. 2015;1(4):448-54.

233. Majewski IJ, Nuciforo P, Mittempergher L, Bosma AJ, Eidtmann H, Holmes E, et al. PIK3CA mutations are associated with decreased benefit to neoadjuvant human epidermal growth factor receptor 2-targeted therapies in breast cancer. J Clin Oncol. 2015;33(12):1334-9.

234. Zardavas D, Phillips WA, Loi S. PIK3CA mutations in breast cancer: reconciling findings from preclinical and clinical data. Breast cancer research : BCR. 2014;16(1):201.

235. Lerebours F, Pulido M, Fourme E, Debled M, Becette V, Bonnefoi H, et al. Predictive factors of 5-year relapse-free survival in HR+/HER2- breast cancer patients treated with neoadjuvant endocrine therapy: pooled analysis of two phase 2 trials. Br J Cancer. 2020;122(6):759-65.

236. Mao Y, Qu Q, Zhang Y, Liu J, Chen X, Shen K. The value of tumor infiltrating lymphocytes (TILs) for predicting response to neoadjuvant chemotherapy in breast cancer: a systematic review and meta-analysis. PloS one. 2014;9(12):e115103.

237. Hirata T, Shimizu C, Yonemori K, Hirakawa A, Kouno T, Tamura K, et al. Change in the hormone receptor status following administration of neoadjuvant chemotherapy and its impact on the long-term outcome in patients with primary breast cancer. Br J Cancer. 2009;101(9):1529-36.

238. Banys-Paluchowski M, Gruber IV, Hartkopf A, Paluchowski P, Krawczyk N, Marx M, et al. Axillary ultrasound for prediction of response to neoadjuvant therapy in the context of surgical strategies to axillary dissection in primary breast cancer: a systematic review of the current literature. Archives of gynecology and obstetrics. 2020;301(2):341-53.

239. Fowler AM, Mankoff DA, Joe BN. Imaging Neoadjuvant Therapy Response in Breast Cancer. Radiology. 2017;285(2):358-75.

240. King TA, Morrow M. Surgical issues in patients with breast cancer receiving neoadjuvant chemotherapy. Nat Rev Clin Oncol. 2015;12(6):335-43.

241. Marinovich ML, Houssami N, Macaskill P, Sardanelli F, Irwig L, Mamounas EP, et al. Meta-analysis of magnetic resonance imaging in detecting residual breast cancer after neoadjuvant therapy. J Natl Cancer Inst. 2013;105(5):321-33.

242. De Los Santos JF, Cantor A, Amos KD, Forero A, Golshan M, Horton JK, et al. Magnetic resonance imaging as a predictor of pathologic response in patients treated with neoadjuvant systemic treatment for operable breast cancer. Translational Breast Cancer Research Consortium trial 017. Cancer. 2013;119(10):1776-83.

243. Weiss A, Lee KC, Romero Y, Ward E, Kim Y, Ojeda-Fournier H, et al. Calcifications on mammogram do not correlate with tumor size after neoadjuvant chemotherapy. Ann Surg Oncol. 2014;21(10):3310-6.

244. Heil J, Kuerer HM, Pfob A, Rauch G, Sinn HP, Golatta M, et al. Eliminating the breast cancer surgery paradigm after neoadjuvant systemic therapy: current evidence and future challenges. Annals of oncology : official journal of the European Society for Medical Oncology / ESMO. 2020;31(1):61-71.

245. Franceschini G. Sentinel node biopsy after neoadjuvant chemotherapy for breast cancer in patients with pre-treatment node-positive: Recommendations to optimize the performance. Eur J Surg Oncol. 2020;46(1):216-7.

246. Gradishar WJ, Anderson BO, Blair SL, Burstein HJ, Cyr A, Elias AD, et al. Breast cancer version 3.2014. Journal of the National Comprehensive Cancer Network : JNCCN. 2014;12(4):542-90.

247. Mamounas EP, Anderson SJ, Dignam JJ, Bear HD, Julian TB, Geyer CE, Jr., et al. Predictors of locoregional recurrence after neoadjuvant chemotherapy: results from combined analysis of National Surgical Adjuvant Breast and Bowel Project B-18 and B-27. J Clin Oncol. 2012;30(32):3960-6.

248. El Hage Chehade H, Headon H, El Tokhy O, Heeney J, Kasem A, Mokbel K. Is sentinel lymph node biopsy a viable alternative to complete axillary dissection following neoadjuvant chemotherapy in women with node-positive breast cancer at diagnosis? An updated meta-analysis involving 3,398 patients. American journal of surgery. 2016;212(5):969-81.

249. Balic M, Thomssen C, Wurstlein R, Gnant M, Harbeck N. St. Gallen/Vienna 2019: A Brief Summary of the Consensus Discussion on the Optimal Primary Breast Cancer Treatment. Breast Care (Basel). 2019;14(2):103-10.

250. NetworK NCC. NCCN Clinical Practice Guidelines in Oncology: Breast cancer. Version 2.2020. 2020.

251. Mamounas EP, White JR, Bandos H, Julian TB, Khan AJ, Shaitelman SF, et al. NSABP B-51/RTOG 1304: Randomized phase III clinical trial evaluating the role of postmastectomy chest wall and regional nodal XRT (CWRNRT) and post-lumpectomy RNRT in patients (pts) with documented positive axillary (Ax) nodes before neoadjuvant chemotherapy (NC) who convert to pathologically negative Ax nodes after NC. 2014 ASCO Annual Meeting. J Clin Oncol 32:5s, 2014 (suppl; abstr TPS1141).

252. Chen AM, Meric-Bernstam F, Hunt KK, Thames HD, Oswald MJ, Outlaw ED, et al. Breast conservation after neoadjuvant chemotherapy: the MD Anderson cancer center experience. J Clin Oncol. 2004;22(12):2303-12.

253. Suleman K, Almalik O, Haque E, Mushtaq A, Badran A, Alsayed A, et al. Does the Timing of Surgery after Neoadjuvant Therapy in Breast Cancer Patients Affect the Outcome? Oncology. 2020;98(3):168-73.

254. Recht A, Comen EA, Fine RE, Fleming GF, Hardenbergh PH, Ho AY, et al. Postmastectomy Radiotherapy: An American Society of Clinical Oncology, American Society for Radiation Oncology, and Society of Surgical Oncology Focused Guideline Update. J Clin Oncol. 2016.

255. Bellon JR, Wong JS, Burstein HJ. Should response to preoperative chemotherapy affect radiotherapy recommendations after mastectomy for stage II breast cancer? J Clin Oncol. 2012;30(32):3916-20.

256. von Minckwitz G, Untch M, Nuesch E, Loibl S, Kaufmann M, Kummel S, et al. Impact of treatment characteristics on response of different breast cancer phenotypes: pooled analysis of the German neo-adjuvant chemotherapy trials. Breast cancer research and treatment. 2011;125(1):145-56.

257. Kim HS, Yoo TK, Park WC, Chae BJ. Potential Benefits of Neoadjuvant Chemotherapy in Clinically Node-Positive Luminal Subtype(-) Breast Cancer. J Breast Cancer. 2019;22(3):412-24.

258. Purushotham A, Pinder S, Cariati M, Harries M, Goldhirsch A. Neoadjuvant chemotherapy: not the best option in estrogen receptor-positive, HER2-negative, invasive classical lobular carcinoma of the breast? J Clin Oncol. 2010;28(22):3552-4.

259. Ellis MJ, Tao Y, Luo J, A'Hern R, Evans DB, Bhatnagar AS, et al. Outcome prediction for estrogen receptor-positive breast cancer based on postneoadjuvant endocrine therapy tumor characteristics. J Natl Cancer Inst. 2008;100(19):1380-8.

260. Smith I, Robertson J, Kilburn L, Wilcox M, Evans A, Holcombe C, et al. Long-term outcome and prognostic value of Ki67 after perioperative endocrine therapy in postmenopausal women with hormone-sensitive early breast cancer (POETIC): an open-label, multicentre, parallel-group, randomised, phase 3 trial. Lancet Oncol. 2020;21(11):1443-54.

261. Barchiesi G, Mazzotta M, Krasniqi E, Pizzuti L, Marinelli D, Capomolla E, et al. Neoadjuvant Endocrine Therapy in Breast Cancer: Current Knowledge and Future Perspectives. International journal of molecular sciences. 2020;21(10).

262. Gradishar WJ, Anderson BO, Balassanian R, Blair SL, Burstein HJ, Cyr A, et al. Breast Cancer, Version 1.2016. J Natl Compr Canc Netw. 2015;13(12):1475-85.

263. Semiglazov VF, Semiglazov VV, Dashyan GA, Ziltsova EK, Ivanov VG, Bozhok AA, et al. Phase 2 randomized trial of primary endocrine therapy versus chemotherapy in postmenopausal patients with estrogen receptor-positive breast cancer. Cancer. 2007;110(2):244-54.

264. Sartor O, de Bono JS. Metastatic Prostate Cancer. N Engl J Med. 2018;378(7):645-57.

265. Bear HD, Anderson S, Smith RE, Geyer CE, Mamounas EP, Fisher B, et al. Sequential preoperative or postoperative docetaxel added to preoperative doxorubicin plus cyclophosphamide for operable breast cancer:National Surgical Adjuvant Breast and Bowel Project Protocol B-27. J Clin Oncol. 2006;24(13):2019-27.

266. Bonnefoi H, Piccart M, Bogaerts J, Mauriac L, Fumoleau P, Brain E. Phase III trial (EORTC 10994/BIG 1-00) assessing the value of p53 using a functional assay to predict sensitivity to a taxane versus non taxane primary chemotherapy in breast cancer: final analysis. The Lancet Oncology. 2011;12(6):529-39.

267. Bonnefoi H, Litière S, Piccart M, MacGrogan G, Fumoleau P, Brain E, et al. Pathological complete response after neoadjuvant chemotherapy is an independent predictive factor irrespective of simplified breast cancer intrinsic subtypes: a landmark and two-step approach analyses from the EORTC 10994/BIG 1-00 phase III trial. Annals of oncology : official journal of the European Society for Medical Oncology / ESMO. 2014;25(6):1128-36.

268. Gianni L, Baselga J, Eiermann W, Porta VG, Semiglazov V, Lluch A, et al. Phase III trial evaluating the addition of paclitaxel to doxorubicin followed by cyclophosphamide, methotrexate, and fluorouracil, as adjuvant or primary systemic therapy: European Cooperative Trial in Operable Breast Cancer. J Clin Oncol. 2009;27(15):2474-81.

269. Bines J, Earl H, Buzaid AC, Saad ED. Anthracyclines and taxanes in the neo/adjuvant treatment of breast cancer: does the sequence matter? Annals of oncology : official journal of the European Society for Medical Oncology / ESMO. 2014;25(6):1079-85.

270. Martinez-Lopez J, Teixeira H, Morgado M, Almagro M, Sousa AI, Villa F, et al. Participatory coastal management through elicitation of ecosystem service preferences and modelling driven by "coastal squeeze". The Science of the total environment. 2019;652:1113-28.

271. Gradishar WJ, Moran MS, Abraham J, Aft R, Agnese D, Allison KH, et al. Breast Cancer, Version 3.2022, NCCN Clinical Practice Guidelines in Oncology. Journal of the National Comprehensive Cancer Network. 2022;20(6):691-722.

272. Heys SD, Hutcheon AW, Sarkar TK, Ogston KN, Miller ID, Payne S, et al. Neoadjuvant docetaxel in breast cancer: 3-year survival results from the Aberdeen trial. Clinical breast cancer. 2002;3 Suppl 2:S69-74.

273. Smith IC, Heys SD, Hutcheon AW, Miller ID, Payne S, Gilbert FJ, et al. Neoadjuvant chemotherapy in breast cancer: significantly enhanced response with docetaxel. J Clin Oncol. 2002;20(6):1456-66.

274. Harbeck N, Gluz O, Christgen M, Braun M, Kuemmel S, Schumacher C, et al. Final analysis of WSG-ADAPT HER2+/HR+ phase II trial: Efficacy, safety, and predictive markers for 12-weeks of neoadjuvant TDM1 with or without endocrine therapy versus trastuzumab+endocrine therapy in HER2-positive hormone-receptor-positive early breast cancer [abstract]. Abstracts from the 38th Annual SABCS. Dec. 8-12, 2015. S5-03.

275. Hofmann D, Nitz U, Gluz O, Kates RE, Schinkoethe T, Staib P, et al. WSG ADAPT - adjuvant dynamic marker-adjusted personalized therapy trial optimizing risk assessment and therapy response prediction in early breast cancer: study protocol for a prospective, multi-center, controlled, non-blinded, randomized, investigator initiated phase II/III trial. Trials. 2013;14:261.

276. von Minckwitz G, Kummel S, Vogel P, Hanusch C, Eidtmann H, Hilfrich J, et al. Intensified neoadjuvant chemotherapy in early-responding breast cancer: phase III randomized GeparTrio study. J Natl Cancer Inst. 2008;100(8):552-62.

277. Dowsett M, Ellis MJ, Dixon JM, Gluz O, Robertson J, Kates R, et al. Evidence-based guidelines for managing patients with primary ER+ HER2– breast cancer deferred from surgery due to the COVID-19 pandemic. npj Breast Cancer. 2020;6(1):21.

278. Heil J, Pfob A, Sinn HP, Rauch G, Bach P, Schaefgen B, et al. SABCS 2019. Abstract GS5-03: Diagnosing residual disease and pathologic complete response after neoadjuvant chemotherapy in breast cancer patients by image-guided vacuum-assisted breast biopsy: Results of a prospective multicenter trial. Cancer research. 2020;80(4):Suppl.

279. Tasoulis MK, Lee H, Yang W, Pope R, Krishnamurthy S, Kim S, et al. SABCS 2019. Abstract GS5-04: Accuracy of post-neoadjuvant chemotherapy image-guided breast biopsy to predict the presence of residual cancer: A multi-institutional pooled analysis. Cancer research. 2020;80(4):Suppl.

280. Basik M, Cecchini RS, De Los Santos JF, Umphrey HR, Julian TB, Mamounas EP, et al. SABCS 2019. Abstract GS5-05: Primary analysis of NRG-BR005, a phase II trial assessing accuracy of tumor bed biopsies in predicting pathologic complete response (pCR) in patients with clinical/radiological complete response after neoadjuvant chemotherapy (NCT) to explore the feasibility of breast-conserving treatment without surgery. Cancer research. 2020;80(4):Suppl.

281. Vrancken Peeters MJTFD, van Loevezijn A, van der Noordaa MEM, van Duijnhoven FH, Loo CE, van Werkhoven E, et al. SABCS 2019. Abstract GS5-06: Towards omitting breast surgery in patients with a pathologic complete response after neoadjuvant systemic treatment: interim analysis of the MICRA trial (Minimally Invasive Complete Response Assessment). Cancer research. 2020;80(4):Suppl.

282. Toi M, Lee S-J, Lee ES, Ohtani S, Im Y-H, Im S-A, et al. A phase III trial of adjuvant capecitabine in breast cancer patients with HER2-negative pathologic residual invasive disease after neoadjuvant chemotherapy (CREATE-X, JBCRG-04) [abstract]. Presented at the 38th Annual San Antonio Breast Cancer Symposium, December 8-12, 2015; Abstr S1-07.

283. Symmans WF, Wei C, Gould R, Yu X, Zhang Y, Liu M, et al. Long-Term Prognostic Risk After Neoadjuvant Chemotherapy Associated With Residual Cancer Burden and Breast Cancer Subtype. J Clin Oncol. 2017;35(10):1049-60.

284. Golshan M, Loibl S, Wong SM, Houber JB, O'Shaughnessy J, Rugo HS, et al. Breast Conservation After Neoadjuvant Chemotherapy for Triple-Negative Breast Cancer: Surgical Results From the BrighTNess Randomized Clinical Trial. JAMA surgery. 2020:e195410.

285. Biswas T, Efird JT, Prasad S, Jindal C, Walker PR. The survival benefit of neoadjuvant chemotherapy and pCR among patients with advanced stage triple negative breast cancer. Oncotarget. 2017;8(68):112712-9.

286. Untch M, Jackisch C, Schneeweis A, Conrad B, Aktas B, Denkert C, et al. A randomized phase III trial comparing neoadjuvant chemotherapy with weekly nanoparticle-based paclitaxel with solvent-based paclitaxel followed by anthracyline/cyclophosphamide for patients with early breast cancer (GeparSepto); GBG 69 [abstract]. Abstracts from the 37th Annual SABCS Dec. 9-13, 2014. S2-07.

287. Colleoni M. Neoadjuvant nab-paclitaxel in breast cancer: trial results and patient care. Lancet Oncol. 2016;17(3):265-6.

288. Gianni L, Mansutti M, Anton A, Calvo L, Bisagni G, Bermejo B, et al. ETNA (Evaluating Treatment with Neoadjuvant Abraxane) randomized phase III study comparing neoadjuvant nab-paclitaxel (nab-P) versus paclitaxel (P) both followed by anthracycline regimens in women with HER2-negative high-risk breast cancer: A MICHELANGO study. 2016 ASCO Annual Meeting. J Clin Oncol 34, 2016 (suppl; abstr 502).

289. von Minckwitz G, Schneeweiss A, Loibl S, Salat C, Denkert C, Rezai M, et al. Neoadjuvant carboplatin in patients with triple-negative and HER2-positive early breast cancer (GeparSixto; GBG 66): a randomised phase 2 trial. Lancet Oncol. 2014;15(7):747-56.

290. Hahnen E, Lederer B, Hauke J, Loibl S, Krober S, Schneeweiss A, et al. Germline Mutation Status, Pathological Complete Response, and Disease-Free Survival in Triple-Negative Breast Cancer: Secondary Analysis of the GeparSixto Randomized Clinical Trial. JAMA Oncol. 2017;3(10):1378-85.

291. Sikov WM, Berry DA, Perou CM, Singh B, Cirrincione CT, Tolaney SM, et al. Impact of the addition of carboplatin and/or bevacizumab to neoadjuvant once-per-week paclitaxel followed by dose-dense doxorubicin and cyclophosphamide on pathologic complete response rates in stage II to III triple-negative breast cancer: CALGB 40603 (Alliance). J Clin Oncol. 2015;33(1):13-21.

292. Untch M, Jackisch C, Schneeweiß A, Conrad B, Aktas B, Denkert C, et al. Abstract S2-07: A randomized phase III trial comparing neoadjuvant chemotherapy with weekly nanoparticle-based paclitaxel with solvent-based paclitaxel followed by anthracyline/cyclophosphamide for patients with early breast cancer (GeparSepto); GBG 69. Cancer research. 2015;75(9 Supplement):S2-07-S2-.

293. Schneeweiss A, Jackisch C, Schmatloch S, Aktas B, Denkert C, Schem C, et al. Survival analysis of the prospectively randomized phase III GeparSepto trial comparing neoadjuvant chemotherapy with weekly nab-paclitaxel with solvent-based paclitaxel followed by anthracycline/cyclophosphamide for patients with early breast cancer – GBG69. Presented at the 40th Annual San Antonio Breast Cancer Symposium,San Antonio, USA. December 5-9, 2017. Available from: http://www.gbg.de/wAssets/docs/press/2017-GeparSepto-Presentation-SABCS.pdf.

294. Byrski T, Gronwald J, Huzarski T, Grzybowska E, Budryk M, Stawicka M, et al. Pathologic complete response rates in young women with BRCA1-positive breast cancers after neoadjuvant chemotherapy. J Clin Oncol. 2010;28(3):375-9.

295. Valero V. Carboplatin for early triple-negative breast cancer? Lancet Oncol. 2014;15(7):676-8.

296. Petrelli F, Coinu A, Borgonovo K, Cabiddu M, Ghilardi M, Lonati V, et al. The value of platinum agents as neoadjuvant chemotherapy in triple-negative breast cancers: a systematic review and meta-analysis. Breast cancer research and treatment. 2014;144(2):223-32.

297. Poggio F, Bruzzone M, Ceppi M, Ponde NF, La Valle G, Del Mastro L, et al. Platinum-based neoadjuvant chemotherapy in triple-negative breast cancer: a systematic review and meta-analysis. Annals of oncology : official journal of the European Society for Medical Oncology / ESMO. 2018;29(7):1497-508.

298. Nahleh Z, Botrus G, Dwivedi A, Jennings M, Nagy S, Tfayli A. Bevacizumab in the neoadjuvant treatment of human epidermal growth factor receptor 2-negative breast cancer: A meta-analysis of randomized controlled trials. Mol Clin Oncol. 2019;10(3):357-65.

299. Schmid P, Cortés J, Dent R, Pusztai L, McArthur HL, Kuemmel S, et al. KEYNOTE-522: Phase 3 study of pembrolizumab (pembro) + chemotherapy (chemo) vs placebo (pbo) + chemo as neoadjuvant treatment, followed by pembro vs pbo as adjuvant treatment for early triple-negative breast cancer (TNBC). Presentado en: ESMO Presidential Symposium II. Annals of Oncology. 2019;30(Suppl. 5).

300. Schmid P, Cortes J, Pusztai L, McArthur H, Kummel S, Bergh J, et al. Pembrolizumab for Early Triple-Negative Breast Cancer. N Engl J Med. 2020;382(9):810-21.

301. Nanda R, Liu MC, Yau C, Shatsky R, Pusztai L, Wallace A, et al. Effect of Pembrolizumab Plus Neoadjuvant Chemotherapy on Pathologic Complete Response in Women With Early-Stage Breast Cancer: An Analysis of the Ongoing Phase 2 Adaptively Randomized I-SPY2 Trial. JAMA Oncol. 2020;6(5):676-84.

302. Schmid P, Adams S, Rugo HS, Schneeweiss A, Barrios CH, Iwata H, et al. Atezolizumab and Nab-Paclitaxel in Advanced Triple-Negative Breast Cancer. N Engl J Med. 2018;379(22):2108-21.

303. Schmid P, Rugo HS, Adams S, Schneeweiss A, Barrios CH, Iwata H, et al. Atezolizumab plus nab-paclitaxel as first-line treatment for unresectable, locally advanced or metastatic triple-negative breast cancer (IMpassion130): updated efficacy results from a randomised, double-blind, placebo-controlled, phase 3 trial. Lancet Oncol. 2020;21(1):44-59.

304. Mittendorf EA, Harbeck N, Zhang H, Saji S, Jung KH, Patel S, et al. Abstract GS3-02: Patient-reported outcomes (PROs) from the Ph 3 IMpassion031 trial of neoadjuvant (NA) atezolizumab + chemo in early triple-negative breast cancer (eTNBC). Cancer research. 2021;81(4 Supplement):GS3-02.

305. Hoeijmakers JH. Genome maintenance mechanisms for preventing cancer. Nature. 2001;411(6835):366-74.

306. Cardoso F, Costa A, Senkus E, Aapro M, Andre F, Barrios CH, et al. 3rd ESO-ESMO International Consensus Guidelines for Advanced Breast Cancer (ABC 3). Ann Oncol. 2017;28(1):16-33.

307. Tung N, Arun B, Hacker MR, Hofstatter E, Toppmeyer DL, Isakoff SJ, et al. TBCRC 031: Randomized Phase II Study of Neoadjuvant Cisplatin Versus Doxorubicin-Cyclophosphamide in Germline BRCA Carriers With HER2-Negative Breast Cancer (the INFORM trial). J Clin Oncol. 2020:Jco1903292.

308. Loibl S, O'Shaughnessy J, Untch M, Sikov WM, Rugo HS, McKee MD, et al. Addition of the PARP inhibitor veliparib plus carboplatin or carboplatin alone to standard neoadjuvant chemotherapy in triple-negative breast cancer (BrighTNess): a randomised, phase 3 trial. Lancet Oncol. 2018;19(4):497-509.

309. Litton JK, Scoggins ME, Hess KR, Adrada BE, Murthy RK, Damodaran S, et al. Neoadjuvant Talazoparib for Patients With Operable Breast Cancer With a Germline BRCA Pathogenic Variant. J Clin Oncol. 2020;38(5):388-94.

310. van Mackelenbergh M, Seither F, Möbus V, O'Shaugnessy J, Martin M, Joenssuu H, et al. SABCS 2019. Abstract GS1-07. Effects of capecitabine as part of neo-/adjuvant chemotherapy. A meta-analysis of individual patient data from 12 randomized trials including 15,457 patients. 2019.

311. Mayer IA, Zhao F, Arteaga CL, Symmans WF, Park BH, Burnette BL, et al. Randomized Phase III Postoperative Trial of Platinum-Based Chemotherapy Versus Capecitabine in Patients With Residual Triple-Negative Breast Cancer Following Neoadjuvant Chemotherapy: ECOG-ACRIN EA1131. J Clin Oncol. 2021;39(23):2539-51.

312. Buzdar AU, Suman VJ, Meric-Bernstam F, Leitch AM, Ellis MJ, Boughey JC, et al. Fluorouracil, epirubicin, and cyclophosphamide (FEC-75) followed by paclitaxel plus trastuzumab versus paclitaxel plus trastuzumab followed by FEC-75 plus trastuzumab as neoadjuvant treatment for patients with HER2-positive breast cancer (Z1041): a randomised, controlled, phase 3 trial. Lancet Oncol. 2013;14(13):1317-25.

313. Schneeweiss A, Chia S, Hickish T, Harvey V, Eniu A, Hegg R, et al. Pertuzumab plus trastuzumab in combination with standard neoadjuvant anthracycline-containing and anthracycline-free chemotherapy regimens in patients with HER2-positive early breast cancer: a randomized phase II cardiac safety study (TRYPHAENA). Annals of oncology : official journal of the European Society for Medical Oncology / ESMO. 2013;24(9):2278-84.

314. Hoffmann-La Roche. A Multicenter, Multinational, Phase II Study to Evaluate Perjeta in Combination With Herceptin and Standard Neoadjuvant Anthracycline-Based Chemotherapy in Patients With HER2-Positive, Locally Advanced, Inflammatory, or Early-Stage Breast Cancer. ClinicalTrials.gov [Internet]: Bethesda (MD): National Library of Medicine (US); [cited 2016 Oct 11]. Available from: https://clinicaltrials.gov/ct2/show/NCT02132949.

315. Swain SM, Ewer MS, Viale G, Delaloge S, Ferrero JM, Verrill M, et al. Pertuzumab, trastuzumab, and standard anthracycline- and taxane-based chemotherapy for the neoadjuvant treatment of patients with HER2-positive localized breast cancer (BERENICE): a phase II, open-label, multicenter, multinational cardiac safety study. Annals of oncology : official journal of the European Society for Medical Oncology / ESMO. 2018;29(3):646-53.

316. Hoffmann-La Roche. A Multicenter, Open-label, Single-arm Study of a Pertuzumab in Combination With Trastuzumab and a Taxane in First Line Treatment of Patients With HER2- Positive Advanced (Metastatic or Locally Recurrent) Breast Cancer. ClinicalTrials.gov [Internet]: Bethesda (MD): National Library of Medicine (US); [cited 2016 Oct 11]. Available from: https://clinicaltrials.gov/ct2/show/NCT01572038

317. Datko F, D'Andrea G, Dickler M, Goldfarb S, Theodoulou M, Lake D, et al. Phase II study of pertuzumab, trastuzumab, and weekly paclitaxel in patients with HER2-overexpressing metastatic breast cancer (MBC).2013 ASCO Annual Meeting. J Clin Oncol 31, 2013 (suppl; abstr 606).

318. Hurvitz SA, Martin M, Symmans WF, Jung KH, Huang CS, Thompson AM, et al. Neoadjuvant trastuzumab, pertuzumab, and chemotherapy versus trastuzumab emtansine plus pertuzumab in patients with HER2-positive breast cancer (KRISTINE): a randomised, open-label, multicentre, phase 3 trial. Lancet Oncol. 2018;19(1):115-26.

319. Hurvitz SA, Martin M, Jung KH, Huang CS, Harbeck N, Valero V, et al. Neoadjuvant Trastuzumab Emtansine and Pertuzumab in Human Epidermal Growth Factor Receptor 2-Positive Breast Cancer: Three-Year Outcomes From the Phase III KRISTINE Study. J Clin Oncol. 2019;37(25):2206-16.

320. Hoffmann-La Roche. A Randomized Multicenter, Double-Blind, Placebo-Controlled Comparison of Chemotherapy Plus Trastuzumab Plus Placebo Versus Chemotherapy Plus Trastuzumab Plus Pertuzumab as Adjuvant Therapy in Patients With Operable HER2-Positive Primary Breast Cancer. ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US); [cited 2016 Oct 11]. Available from: https://clinicaltrials.gov/ct2/show/NCT01358877.

321. Shao Z, Pang D, Yang H, Li W, Wang S, Cui S, et al. Efficacy, Safety, and Tolerability of Pertuzumab, Trastuzumab, and Docetaxel for Patients With Early or Locally Advanced ERBB2-Positive Breast Cancer in Asia: The PEONY Phase 3 Randomized Clinical Trial. JAMA Oncol. 2019.

322. Diaz-Redondo T, Lavado-Valenzuela R, Jimenez B, Pascual T, Galvez F, Falcon A, et al. Different Pathological Complete Response Rates According to PAM50 Subtype in HER2+ Breast Cancer Patients Treated With Neoadjuvant Pertuzumab/Trastuzumab vs. Trastuzumab Plus Standard Chemotherapy: An Analysis of Real-World Data. Frontiers in oncology. 2019;9:1178.

323. van Ramshorst MS, van der Voort A, van Werkhoven ED, Mandjes IA, Kemper I, Dezentje VO, et al. Neoadjuvant chemotherapy with or without anthracyclines in the presence of dual HER2 blockade for HER2-positive breast cancer (TRAIN-2): a multicentre, open-label, randomised, phase 3 trial. Lancet Oncol. 2018;19(12):1630-40.

324. van der Voort A, van Ramshorst MS, van Werkhoven ED, Mandjes IA, Kemper I, Vulink AJ, et al. Three-Year Follow-up of Neoadjuvant Chemotherapy With or Without Anthracyclines in the Presence of Dual ERBB2 Blockade in Patients With ERBB2-Positive Breast Cancer: A Secondary Analysis of the TRAIN-2 Randomized, Phase 3 Trial. JAMA Oncol. 2021;7(7):978-84.

325. Cortes J, Gebhart G, Ruiz Borrego M, Stradella A, Bermejo B, Escrivá S, et al. Chemotherapy (CT) de-escalation using an FDG-PET/CT (F-PET) and pathological response-adapted strategy in HER2[+] early breast cancer (EBC): PHERGain Trial. Journal of Clinical Oncology. 2020;38(15_suppl):503-.

326. Harbeck N, Gluz O, Christgen M, Kates RE, Braun M, Kuemmel S, et al. De-Escalation Strategies in Human Epidermal Growth Factor Receptor 2 (HER2)-Positive Early Breast Cancer (BC): Final Analysis of the West German Study Group Adjuvant Dynamic Marker-Adjusted Personalized Therapy Trial Optimizing Risk Assessment and Therapy Response Prediction in Early BC HER2- and Hormone Receptor-Positive Phase II Randomized Trial-Efficacy, Safety, and Predictive Markers for 12 Weeks of Neoadjuvant Trastuzumab Emtansine With or Without Endocrine Therapy (ET) Versus Trastuzumab Plus ET. J Clin Oncol. 2017;35(26):3046-54.

327. Buzdar AU, Valero V, Ibrahim NK, Francis D, Broglio KR, Theriault RL, et al. Neoadjuvant therapy with paclitaxel followed by 5-fluorouracil, epirubicin, and cyclophosphamide chemotherapy and concurrent trastuzumab in human epidermal growth factor receptor 2-positive operable breast cancer: an update of the initial randomized study population and data of additional patients treated with the same regimen. Clinical cancer research : an official journal of the American Association for Cancer Research. 2007;13(1):228-33.

328. Buzdar AU, Ibrahim NK, Francis D, Booser DJ, Thomas ES, Theriault RL, et al. Significantly higher pathologic complete remission rate after neoadjuvant therapy with trastuzumab, paclitaxel, and epirubicin chemotherapy: results of a randomized trial in human epidermal growth factor receptor 2-positive operable breast cancer. J Clin Oncol. 2005;23(16):3676-85.

329. Gianni L, Eiermann W, Semiglazov V, Manikhas A, Lluch A, Tjulandin S, et al. Neoadjuvant chemotherapy with trastuzumab followed by adjuvant trastuzumab versus neoadjuvant chemotherapy alone, in patients with HER2-positive locally advanced breast cancer (the NOAH trial): a randomised controlled superiority trial with a parallel HER2-negative cohort. Lancet. 2010;375(9712):377-84.

330. Untch M, Rezai M, Loibl S, Fasching PA, Huober J, Tesch H, et al. Neoadjuvant treatment with trastuzumab in HER2-positive breast cancer: results from the GeparQuattro study. J Clin Oncol. 2010;28(12):2024-31.

331. Nitz U, Gluz O, Christgen M, Grischke E, Augustin D, Kümmel S, et al. Final analysis of WSG-ADAPT HER2+/HR- trial: Efficacy, safety, and predictive markers for 12-weeks of neoadjuvant dual blockade with trastuzumab + pertuzumab ± weekly paclitaxel in HER2+/HR- early breast cancer (EBC). 2016 ASCO Annual Meeting. J Clin Oncol 34, 2016 (suppl; abstr 518).

332. Nitz UA, Gluz O, Christgen M, Grischke EM, Augustin D, Kuemmel S, et al. De-escalation strategies in HER2-positive early breast cancer (EBC): final analysis of the WSG-ADAPT HER2+/HR− phase II trial: efficacy, safety, and predictive markers for 12 weeks of neoadjuvant dual blockade with trastuzumab and pertuzumab ± weekly paclitaxel. Annals of Oncology. 2017;28(11):2768-72.

333. von Minckwitz G, Huang CS, Mano MS, Loibl S, Mamounas EP, Untch M, et al. Trastuzumab Emtansine for Residual Invasive HER2-Positive Breast Cancer. N Engl J Med. 2019;380(7):617-28.

334. Allemani C, Sant M, Weir HK, Richardson LC, Baili P, Storm H, et al. Breast cancer survival in the US and Europe: a CONCORD high-resolution study. Int J Cancer. 2013;132(5):1170-81.

335. Hortobagyi G, Buzdar A. Locally advanced breast cancer: a review including the MD Anderson experience. In: Ragaz J, Ariel I, editors. High-Risk Breast Cancer. Berlin: Springer-Verlag; 1991. p. 382-415.

336. GEICAM (Grupo Español De Investivación En Cancer de Mama). Proyecto El Álamo III. Madrid2014. Available from: https://www.geicam.org/wp-content/uploads/2017/04/Lib_El_AlamoIII_Anexo_I.pdf.

337. Haagensen CD, Stout AP. Carcinoma of the Breast: Ii. Criteria of Operability. Annals of surgery. 1943;118(5):859-70.

338. Giordano SH. Update on locally advanced breast cancer. The oncologist. 2003;8(6):521-30.

339. Woodward WA. Inflammatory breast cancer: unique biological and therapeutic considerations. Lancet Oncol. 2015;16(15):e568-76.

340. Hance KW, Anderson WF, Devesa SS, Young HA, Levine PH. Trends in inflammatory breast carcinoma incidence and survival: the surveillance, epidemiology, and end results program at the National Cancer Institute. J Natl Cancer Inst. 2005;97(13):966-75.

341. van Golen KL, Cristofanilli M. The Third International Inflammatory Breast Cancer Conference. Breast cancer research : BCR. 2013;15(6):318.

342. Dawood S, Merajver SD, Viens P, Vermeulen PB, Swain SM, Buchholz TA, et al. International expert panel on inflammatory breast cancer: consensus statement for standardized diagnosis and treatment. Annals of oncology : official journal of the European Society for Medical Oncology / ESMO. 2011;22(3):515-23.

343. Edge SB, Compton CC. The American Joint Committee on Cancer: the 7th edition of the AJCC cancer staging manual and the future of TNM. Ann Surg Oncol. 2010;17(6):1471-4.

344. Zell JA, Tsang WY, Taylor TH, Mehta RS, Anton-Culver H. Prognostic impact of human epidermal growth factor-like receptor 2 and hormone receptor status in inflammatory breast cancer (IBC): analysis of 2,014 IBC patient cases from the California Cancer Registry. Breast cancer research : BCR. 2009;11(1):R9.

345. van Uden DJ, van Laarhoven HW, Westenberg AH, de Wilt JH, Blanken-Peeters CF. Inflammatory breast cancer: an overview. Critical reviews in oncology/hematology. 2015;93(2):116-26.

346. Abraham HG, Xia Y, Mukherjee B, Merajver SD. Incidence and survival of inflammatory breast cancer between 1973 and 2015 in the SEER database. Breast Cancer Res Treat. 2021;185(1):229-38.

347. Rosenbluth JM, Overmoyer BA. Inflammatory Breast Cancer: a Separate Entity. Curr Oncol Rep. 2019;21(10):86.

348. Ueno NT, Buzdar AU, Singletary SE, Ames FC, McNeese MD, Holmes FA, et al. Combined-modality treatment of inflammatory breast carcinoma: twenty years of experience at M. D. Anderson Cancer Center. Cancer chemotherapy and pharmacology. 1997;40(4):321-9.

349. Harris EE, Schultz D, Bertsch H, Fox K, Glick J, Solin LJ. Ten-year outcome after combined modality therapy for inflammatory breast cancer. Int J Radiat Oncol Biol Phys. 2003;55(5):1200-8.

350. Baldini E, Gardin G, Evagelista G, Prochilo T, Collecchi P, Lionetto R. Long-term results of combined-modality therapy for inflammatory breast carcinoma. Clinical breast cancer. 2004;5(5):358-63.

351. Low JA, Berman AW, Steinberg SM, Danforth DN, Lippman ME, Swain SM. Long-term follow-up for locally advanced and inflammatory breast cancer patients treated with multimodality therapy. J Clin Oncol. 2004;22(20):4067-74.

352. Cristofanilli M, Gonzalez-Angulo AM, Buzdar AU, Kau SW, Frye DK, Hortobagyi GN. Paclitaxel improves the prognosis in estrogen receptor negative inflammatory breast cancer: the M. D. Anderson Cancer Center experience. Clinical breast cancer. 2004;4(6):415-9.

353. Hurley J, Doliny P, Reis I, Silva O, Gomez-Fernandez C, Velez P, et al. Docetaxel, cisplatin, and trastuzumab as primary systemic therapy for human epidermal growth factor receptor 2-positive locally advanced breast cancer. J Clin Oncol. 2006;24(12):1831-8.

354. Boussen H, Cristofanilli M, Zaks T, DeSilvio M, Salazar V, Spector N. Phase II study to evaluate the efficacy and safety of neoadjuvant lapatinib plus paclitaxel in patients with inflammatory breast cancer. J Clin Oncol. 2010;28(20):3248-55.

355. Van Pelt AE, Mohsin S, Elledge RM, Hilsenbeck SG, Gutierrez MC, Lucci A, Jr., et al. Neoadjuvant trastuzumab and docetaxel in breast cancer: preliminary results. Clinical breast cancer. 2003;4(5):348-53.

356. Veyret C, Levy C, Chollet P, Merrouche Y, Roche H, Kerbrat P, et al. Inflammatory breast cancer outcome with epirubicin-based induction and maintenance chemotherapy: ten-year results from the French Adjuvant Study Group GETIS 02 Trial. Cancer. 2006;107(11):2535-44.

357. Cheng YC, Rondon G, Yang Y, Smith TL, Gajewski JL, Donato ML, et al. The use of high-dose cyclophosphamide, carmustine, and thiotepa plus autologous hematopoietic stem cell transplantation as consolidation therapy for high-risk primary breast cancer after primary surgery or neoadjuvant chemotherapy. Biology of blood and marrow transplantation : journal of the American Society for Blood and Marrow Transplantation. 2004;10(11):794-804.

358. Viens P, Palangie T, Janvier M, Fabbro M, Roche H, Delozier T, et al. First-line high-dose sequential chemotherapy with rG-CSF and repeated blood stem cell transplantation in untreated inflammatory breast cancer: toxicity and response (PEGASE 02 trial). Br J Cancer. 1999;81(3):449-56.

359. Kaufmann M, von Minckwitz G, Bear HD, Buzdar A, McGale P, Bonnefoi H, et al. Recommendations from an international expert panel on the use of neoadjuvant (primary) systemic treatment of operable breast cancer: new perspectives 2006. Annals of oncology : official journal of the European Society for Medical Oncology / ESMO. 2007;18(12):1927-34.

360. Hortobagyi G, Singletary S, Strom E. Treatment of Locally Advanced and Inflammatory Breast Cancer. Philadelphia, PA: Lippincott, Williams & Wilkins; 2000.

361. Stearns V, Ewing CA, Slack R, Penannen MF, Hayes DF, Tsangaris TN. Sentinel lymphadenectomy after neoadjuvant chemotherapy for breast cancer may reliably represent the axilla except for inflammatory breast cancer. Ann Surg Oncol. 2002;9(3):235-42.

362. Hidar S, Bibi M, Gharbi O, Tebra S, Trabelsi A, Korbi S, et al. Sentinel lymph node biopsy after neoadjuvant chemotherapy in inflammatory breast cancer. International journal of surgery. 2009;7(3):272-5.

363. Panades M, Olivotto IA, Speers CH, Shenkier T, Olivotto TA, Weir L, et al. Evolving treatment strategies for inflammatory breast cancer: a population-based survival analysis. J Clin Oncol. 2005;23(9):1941-50.

364. Bristol IJ, Woodward WA, Strom EA, Cristofanilli M, Domain D, Singletary SE, et al. Locoregional treatment outcomes after multimodality management of inflammatory breast cancer. Int J Radiat Oncol Biol Phys. 2008;72(2):474-84.

365. Antón A, Solà I, Alba E, Barnadas A, Barrajón E, Blancas I, et al. Guía GEICAM de práctica Clínica para el diagnóstico y tratamiento del Cáncer de Mama Metastásico. 2015. Disponible en: https://www.geicam.org/wp-content/uploads/2016/06/GUIA-GEICAM-COMPLETA.pdf.

366. Carlson RW, Allred DC, Anderson BO, Burstein HJ, Edge SB, Farrar WB, et al. Metastatic breast cancer, version 1.2012: featured updates to the NCCN guidelines. Journal of the National Comprehensive Cancer Network : JNCCN. 2012;10(7):821-9.

367. de Duenas EM, Hernandez AL, Zotano AG, Carrion RM, Lopez-Muniz JI, Novoa SA, et al. Prospective evaluation of the conversion rate in the receptor status between primary breast cancer and metastasis: results from the GEICAM 2009-03 ConvertHER study. Breast cancer research and treatment. 2014;143(3):507-15.

368. Harris L, Fritsche H, Mennel R, Norton L, Ravdin P, Taube S, et al. American Society of Clinical Oncology 2007 update of recommendations for the use of tumor markers in breast cancer. J Clin Oncol. 2007;25(33):5287-312.

369. Van Poznak C, Somerfield MR, Bast RC, Cristofanilli M, Goetz MP, Gonzalez-Angulo AM, et al. Use of Biomarkers to Guide Decisions on Systemic Therapy for Women With Metastatic Breast Cancer: American Society of Clinical Oncology Clinical Practice Guideline. J Clin Oncol. 2015;33(24):2695-704.

370. Eisenhauer EA, Therasse P, Bogaerts J, Schwartz LH, Sargent D, Ford R, et al. New response evaluation criteria in solid tumours: revised RECIST guideline (version 1.1). Eur J Cancer. 2009;45(2):228-47.

371. Schwartz LH, Bogaerts J, Ford R, Shankar L, Therasse P, Gwyther S, et al. Evaluation of lymph nodes with RECIST 1.1. Eur J Cancer. 2009;45(2):261-7.

372. Twelves C, Cortes J, Vahdat L, Olivo M, He Y, Kaufman PA, et al. Erratum to: Efficacy of eribulin in women with metastatic breast cancer: a pooled analysis of two phase 3 studies. Breast cancer research and treatment. 2015;149(1):313.

373. Ellis M, Naughton M, Ma C. Treatment approach to metastatic hormone receptor-positive breast cancer: endocrine therapy UpToDate: Waltham, MA: UpToDate Inc; 2005 [cited 2016 Mar 1]. Available from: http://www.uptodate.com/contents/treatment-approach-to-metastatic-hormone-receptor-positive-breast-cancer-endocrine-therapy.

374. Partridge AH, Rumble RB, Carey LA, Come SE, Davidson NE, Di Leo A, et al. Chemotherapy and targeted therapy for women with human epidermal growth factor receptor 2-negative (or unknown) advanced breast cancer: American Society of Clinical Oncology Clinical Practice Guideline. J Clin Oncol. 2014;32(29):3307-29.

375. Cardoso F, Costa A, Norton L, Senkus E, Aapro M, Andre F, et al. ESO-ESMO 2nd international consensus guidelines for advanced breast cancer (ABC2)dagger. Annals of oncology : official journal of the European Society for Medical Oncology / ESMO. 2014;25(10):1871-88.

376. Gennari A, André F, Barrios CH, Cortés J, de Azambuja E, DeMichele A, et al. ESMO Clinical Practice Guideline for the diagnosis, staging and treatment of patients with metastatic breast cancer[☆]. Annals of Oncology. 2021;32(12):1475-95.

377. Gradishar WJ, Anderson BO, Balassanian R, Blair SL, Burstein HJ, Cyr A, et al. Breast Cancer, Version 2.2016: NCCN Clinical Practice Guidelines in Oncology; 2016. Available from: https://www.nccn.org/store/login/login.aspx?ReturnURL=http://www.nccn.org/professionals/physician_gls/pdf/breast.pdf.

378. Baselga J, Campone M, Piccart M, Burris HA, 3rd, Rugo HS, Sahmoud T, et al. Everolimus in postmenopausal hormone-receptor-positive advanced breast cancer. N Engl J Med. 2012;366(6):520-9.

379. Turner NC, Ro J, Andre F, Loi S, Verma S, Iwata H, et al. Palbociclib in Hormone-Receptor-Positive Advanced Breast Cancer. N Engl J Med. 2015;373(3):209-19.

380. Finn RS, Crown JP, Lang I, Boer K, Bondarenko IM, Kulyk SO, et al. The cyclin-dependent kinase 4/6 inhibitor palbociclib in combination with letrozole versus letrozole alone as first-line treatment of oestrogen receptor-positive, HER2-negative, advanced breast cancer (PALOMA-1/TRIO-18): a randomised phase 2 study. Lancet Oncol. 2015;16(1):25-35.

381. Tripathy D, Im SA, Colleoni M, Franke F, Bardia A, Harbeck N, et al. Ribociclib plus endocrine therapy for premenopausal women with hormone-receptor-positive, advanced breast cancer (MONALEESA-7): a randomised phase 3 trial. Lancet Oncol. 2018;19(7):904-15.

382. Im SA, Lu YS, Bardia A, Harbeck N, Colleoni M, Franke F, et al. Overall Survival with Ribociclib plus Endocrine Therapy in Breast Cancer. N Engl J Med. 2019;381(4):307-16.

383. Tripathy D, Im S-A, Colleoni M, Franke F, Bardia A, Harbeck N, et al. Abstract PD2-04: Updated overall survival (OS) results from the phase III MONALEESA-7 trial of pre- or perimenopausal patients with hormone receptor positive/human epidermal growth factor receptor 2 negative (HR+/HER2−) advanced breast cancer (ABC) treated with endocrine therapy (ET) ± ribociclib. Cancer research. 2021;81(4 Supplement):PD2-04-PD2-.

384. Sledge GW, Jr., Toi M, Neven P, Sohn J, Inoue K, Pivot X, et al. MONARCH 2: Abemaciclib in Combination With Fulvestrant in Women With HR+/HER2- Advanced Breast Cancer Who Had Progressed While Receiving Endocrine Therapy. J Clin Oncol. 2017;35(25):2875-84.

385. Sledge GW, Jr., Toi M, Neven P, Sohn J, Inoue K, Pivot X, et al. The Effect of Abemaciclib Plus Fulvestrant on Overall Survival in Hormone Receptor-Positive, ERBB2-Negative Breast Cancer That Progressed on Endocrine Therapy-MONARCH 2: A Randomized Clinical Trial. JAMA Oncol. 2019.

386. Bonneterre J, Buzdar A, Nabholtz JM, Robertson JF, Thurlimann B, von Euler M, et al. Anastrozole is superior to tamoxifen as first-line therapy in hormone receptor positive advanced breast carcinoma. Cancer. 2001;92(9):2247-58.

387. Bonneterre J, Thurlimann B, Robertson JF, Krzakowski M, Mauriac L, Koralewski P, et al. Anastrozole versus tamoxifen as first-line therapy for advanced breast cancer in 668 postmenopausal women: results of the Tamoxifen or Arimidex Randomized Group Efficacy and Tolerability study. J Clin Oncol. 2000;18(22):3748-57.

388. Ellis MJ, Llombart-Cussac A, Feltl D, Dewar JA, Jasiowka M, Hewson N, et al. Fulvestrant 500 mg Versus Anastrozole 1 mg for the First-Line Treatment of Advanced Breast Cancer: Overall Survival Analysis From the Phase II FIRST Study. J Clin Oncol. 2015;33(32):3781-7.

389. Rugo HS, Finn RS, Diéras V, Ettl J, Lipatov O, Joy AA, et al. Palbociclib plus letrozole as first-line therapy in estrogen receptor-positive/human epidermal growth factor receptor 2-negative advanced breast cancer with extended follow-up. Breast cancer research and treatment. 2019;174(3):719-29.

390. Hortobagyi GN, Stemmer SM, Burris HA, Yap YS, Sonke GS, Paluch-Shimon S, et al. Ribociclib as First-Line Therapy for HR-Positive, Advanced Breast Cancer. N Engl J Med. 2016.

391. Goetz MP, Toi M, Campone M, Sohn J, Paluch-Shimon S, Huober J, et al. MONARCH 3: Abemaciclib As Initial Therapy for Advanced Breast Cancer. J Clin Oncol. 2017;35(32):3638-46.

392. Johnston S, Martin M, Di Leo A, Im SA, Awada A, Forrester T, et al. MONARCH 3 final PFS: a randomized study of abemaciclib as initial therapy for advanced breast cancer. NPJ Breast Cancer. 2019;5:5.

393. Slamon DJ, Neven P, Chia S, Fasching PA, De Laurentiis M, Im SA, et al. Phase III Randomized Study of Ribociclib and Fulvestrant in Hormone Receptor-Positive, Human Epidermal Growth Factor Receptor 2-Negative Advanced Breast Cancer: MONALEESA-3. J Clin Oncol. 2018;36(24):2465-72.

394. Slamon DJ, Neven P, Chia S, Fasching PA, De Laurentiis M, Im SA, et al. Overall Survival with Ribociclib plus Fulvestrant in Advanced Breast Cancer. N Engl J Med. 2020;382(6):514-24.

395. Neven P, Fasching PA, Chia S, Jesuralem G, Im S, Petrakova K, et al., editors. LBA4 - Updated overall survival (OS) results from the first-line (1L) population in the Phase III MONALEESA-3 trial of postmenopausal patients (pts) with HR+/HER2? advanced breast cancer (ABC) treated with ribociclib (RIB) + fulvestrant (FUL). ESMO Breast Cancer congress; 2022: Annals or Oncology.

396. Slamon DJ, Neven P, Chia SKL, Jerusalem GHM, De Laurentiis M, Im S-A, et al. Updated overall survival (OS) results from the phase III MONALEESA-3 trial of postmenopausal patients (pts) with HR+/HER2- advanced breast cancer (ABC) treated with fulvestrant (FUL) ± ribociclib (RIB). Journal of Clinical Oncology. 2021;39(15_suppl):1001-.

397. Cristofanilli M, Turner NC, Bondarenko I, Ro J, Im SA, Masuda N, et al. Fulvestrant plus palbociclib versus fulvestrant plus placebo for treatment of hormone-receptor-positive, HER2-negative metastatic breast cancer that progressed on previous endocrine therapy (PALOMA-3): final analysis of the multicentre, double-blind, phase 3 randomised controlled trial. Lancet Oncol. 2016;17(4):425-39.

398. Cristofanilli M, Rugo H, Im S-A, Slamon D, Harbeck N, Bondarenko I, et al. Overall survival (OS) with palbociclib (PAL) + fulvestrant (FUL) in women with hormone receptor–positive (HR+), human epidermal growth factor receptor 2–negative (HER2–) advanced breast cancer (ABC): Updated analyses from PALOMA-3. Journal of Clinical Oncology. 2021;39:1000-.

399. Cristofanilli M, Rugo HS, Im S-A, Slamon DJ, Harbeck N, Bondarenko I, et al. Overall Survival with Palbociclib and Fulvestrant in Women with HR+/HER2– ABC: Updated Exploratory Analyses of PALOMA-3, a Double-blind, Phase III Randomized Study. Clinical Cancer Research. 2022:OF1-OF10.

400. André F, Ciruelos E, Rubovszky G, Campone M, Loibl S, Rugo HS, et al. Alpelisib for PIK3CA-Mutated, Hormone Receptor–Positive Advanced Breast Cancer. The New England Journal of Medicine. 2019;380:1929 - 40.

401. Cristofanilli M, Turner NC, Bondarenko I, Ro J, Im S-A, Masuda N, et al. Fulvestrant plus palbociclib versus fulvestrant plus placebo for treatment of hormone-receptor-positive, HER2-negative metastatic breast cancer that progressed on previous endocrine therapy (PALOMA-3): final analysis of the multicentre, double-blind, phase 3 randomised controlled trial. The Lancet Oncology. 2016;17(4):425-39.

402. Chia S, Gradishar W, Mauriac L, Bines J, Amant F, Federico M, et al. Double-blind, randomized placebo controlled trial of fulvestrant compared with exemestane after prior nonsteroidal aromatase inhibitor therapy in postmenopausal women with hormone receptor-positive, advanced breast cancer: results from EFECT. J Clin Oncol. 2008;26(10):1664-70.

403. Di Leo A, Jerusalem G, Petruzelka L, Torres R, Bondarenko IN, Khasanov R, et al. Results of the CONFIRM phase III trial comparing fulvestrant 250 mg with fulvestrant 500 mg in postmenopausal women with estrogen receptor-positive advanced breast cancer. J Clin Oncol. 2010;28(30):4594-600.

404. Barrios C, Forbes JF, Jonat W, Conte P, Gradishar W, Buzdar A, et al. The sequential use of endocrine treatment for advanced breast cancer: where are we? Annals of oncology : official journal of the European Society for Medical Oncology / ESMO. 2012;23(6):1378-86.

405. Zamora P, Servitja S, Santaballa A, García J, de Paz L, Plata Y, et al. CASCADE study: Treatment and clinical outcomes of metastatic breast cancer by tumor immunophenotypes. Póster presentado en San Antonio Breast Cancer Symposium. San Antonio, USA. P3-07-39. December 10.

406. Dear RF, McGeechan K, Jenkins MC, Barratt A, Tattersall MH, Wilcken N. Combination versus sequential single agent chemotherapy for metastatic breast cancer. Cochrane Database Syst Rev. 2013;12:CD008792.

407. Piccart-Gebhart MJ, Burzykowski T, Buyse M, Sledge G, Carmichael J, Luck HJ, et al. Taxanes alone or in combination with anthracyclines as first-line therapy of patients with metastatic breast cancer. J Clin Oncol. 2008;26(12):1980-6.

408. Xu YC, Wang HX, Tang L, Ma Y, Zhang FC. A systematic review of vinorelbine for the treatment of breast cancer. The breast journal. 2013;19(2):180-8.

409. Aapro M, Finek J. Oral vinorelbine in metastatic breast cancer: a review of current clinical trial results. Cancer Treat Rev. 2012;38(2):120-6.

410. Chan A, Verrill M. Capecitabine and vinorelbine in metastatic breast cancer. Eur J Cancer. 2009;45(13):2253-65.

411. Gennari A, Stockler M, Puntoni M, Sormani M, Nanni O, Amadori D, et al. Duration of chemotherapy for metastatic breast cancer: a systematic review and meta-analysis of randomized clinical trials. J Clin Oncol. 2011;29(16):2144-9.

412. Tutt A, Ellis P, Kilburn L, Gilett C, Pinder S, Abraham J, et al. The TNT trial: A randomized phase III trial of carboplatin (C) compared with docetaxel (D) for patients with metastatic or recurrent locally advanced triple negative or BRCA1/2 breast cancer (CRUK/07/012). Cancer research. 2015;75:S3-0.

413. Robson ME, Tung N, Conte P, Im SA, Senkus E, Xu B, et al. OlympiAD final overall survival and tolerability results: Olaparib versus chemotherapy treatment of physician's choice in patients with a germline BRCA mutation and HER2-negative metastatic breast cancer. Annals of oncology : official journal of the European Society for Medical Oncology / ESMO. 2019;30(4):558-66.

414. Litton JK, Rugo HS, Ettl J, Hurvitz SA, Goncalves A, Lee KH, et al. Talazoparib in Patients with Advanced Breast Cancer and a Germline BRCA Mutation. N Engl J Med. 2018;379(8):753-63.

415. Miles DW, Chan A, Dirix LY, Cortes J, Pivot X, Tomczak P, et al. Phase III study of bevacizumab plus docetaxel compared with placebo plus docetaxel for the first-line treatment of human epidermal growth factor receptor 2-negative metastatic breast cancer. J Clin Oncol. 2010;28(20):3239-47.

416. Miller K, Wang M, Gralow J, Dickler M, Cobleigh M, Perez EA, et al. Paclitaxel plus bevacizumab versus paclitaxel alone for metastatic breast cancer. N Engl J Med. 2007;357(26):2666-76.

417. Robert NJ, Dieras V, Glaspy J, Brufsky AM, Bondarenko I, Lipatov ON, et al. RIBBON-1: randomized, double-blind, placebo-controlled, phase III trial of chemotherapy with or without bevacizumab for first-line treatment of human epidermal growth factor receptor 2-negative, locally recurrent or metastatic breast cancer. J Clin Oncol. 2011;29(10):1252-60.

418. Miles DW, Dieras V, Cortes J, Duenne AA, Yi J, O'Shaughnessy J. First-line bevacizumab in combination with chemotherapy for HER2-negative metastatic breast cancer: pooled and subgroup analyses of data from 2447 patients. Annals of oncology : official journal of the European Society for Medical Oncology / ESMO. 2013;24(11):2773-80.

419. Gligorov J, Doval D, Bines J, Alba E, Cortes P, Pierga JY, et al. Maintenance capecitabine and bevacizumab versus bevacizumab alone after initial first-line bevacizumab and docetaxel for patients with HER2-negative metastatic breast cancer (IMELDA): a randomised, open-label, phase 3 trial. Lancet Oncol. 2014;15(12):1351-60.

420. Schmid P, Adams S, Rugo HS, Schneeweiss A, Barrios CH, Iwata H, et al. ASCO 2019. Abstract 1003: IMpassion130: updated overall survival (OS) from a global, randomized, double-blind, placebo-controlled, Phase III study of atezolizumab (atezo) + nab-paclitaxel (nP) in previously untreated locally advanced or metastatic triple-negative breast cancer (mTNBC). Journal of Clinical Oncology. 2019;37:1003-.

421. Montero AJ, Adams B, Diaz-Montero CM, Gluck S. Nab-paclitaxel in the treatment of metastatic breast cancer: a comprehensive review. Expert review of clinical pharmacology. 2011;4(3):329-34.

422. Cortes J, O'Shaughnessy J, Loesch D, Blum JL, Vahdat LT, Petrakova K, et al. Eribulin monotherapy versus treatment of physician's choice in patients with metastatic breast cancer (EMBRACE): a phase 3 open-label randomised study. Lancet. 2011;377(9769):914-23.

423. Kaufman PA, Awada A, Twelves C, Yelle L, Perez EA, Velikova G, et al. Phase III open-label randomized study of eribulin mesylate versus capecitabine in patients with locally advanced or metastatic breast cancer previously treated with an anthracycline and a taxane. J Clin Oncol. 2015;33(6):594-601.

424. Blum JL, Jones SE, Buzdar AU, LoRusso PM, Kuter I, Vogel C, et al. Multicenter phase II study of capecitabine in paclitaxel-refractory metastatic breast cancer. J Clin Oncol. 1999;17(2):485-93.

425. Batist G, Ramakrishnan G, Rao CS, Chandrasekharan A, Gutheil J, Guthrie T, et al. Reduced cardiotoxicity and preserved antitumor efficacy of liposome-encapsulated doxorubicin and cyclophosphamide compared with conventional doxorubicin and cyclophosphamide in a randomized, multicenter trial of metastatic breast cancer. J Clin Oncol. 2001;19(5):1444-54.

426. Rom J, Bechstein S, Domschke C, Golatta M, Mayer C, Heil J, et al. Efficacy and toxicity profile of pegylated liposomal doxorubicin (Caelyx) in patients with advanced breast cancer. Anti-cancer drugs. 2014;25(2):219-24.

427. Blum JL, Savin MA, Edelman G, Pippen JE, Robert NJ, Geister BV, et al. Phase II study of weekly albumin-bound paclitaxel for patients with metastatic breast cancer heavily pretreated with taxanes. Clinical breast cancer. 2007;7(11):850-6.

428. Gradishar WJ, Tjulandin S, Davidson N, Shaw H, Desai N, Bhar P, et al. Phase III trial of nanoparticle albumin-bound paclitaxel compared with polyethylated castor oil-based paclitaxel in women with breast cancer. J Clin Oncol. 2005;23(31):7794-803.

429. Colleoni M, Rocca A, Sandri MT, Zorzino L, Masci G, Nole F, et al. Low-dose oral methotrexate and cyclophosphamide in metastatic breast cancer: antitumor activity and correlation with vascular endothelial growth factor levels. Annals of oncology : official journal of the European Society for Medical Oncology / ESMO. 2002;13(1):73-80.

430. Bardia A, Hurvitz SA, Tolaney SM, Loirat D, Punie K, Oliveira M, et al. Sacituzumab Govitecan in Metastatic Triple-Negative Breast Cancer. N Engl J Med. 2021;384(16):1529-41.

431. Koshy N, Quispe D, Shi R, Mansour R, Burton GV. Cisplatin-gemcitabine therapy in metastatic breast cancer: Improved outcome in triple negative breast cancer patients compared to non-triple negative patients. Breast. 2010;19(3):246-8.

432. Swain SM, Baselga J, Kim SB, Ro J, Semiglazov V, Campone M, et al. Pertuzumab, trastuzumab, and docetaxel in HER2-positive metastatic breast cancer. N Engl J Med. 2015;372(8):724-34.

433. Swain SM, Miles D, Kim SB, Im YH, Im SA, Semiglazov V, et al. Pertuzumab, trastuzumab, and docetaxel for HER2-positive metastatic breast cancer (CLEOPATRA): end-of-study results from a double-blind, randomised, placebo-controlled, phase 3 study. Lancet Oncol. 2020;21(4):519-30.

434. Verma S, Miles D, Gianni L, Krop IE, Welslau M, Baselga J, et al. Trastuzumab emtansine for HER2-positive advanced breast cancer. N Engl J Med. 2012;367(19):1783-91.

435. Huober J, Fasching PA, Barsoum M, Petruzelka L, Wallwiener D, Thomssen C, et al. Higher efficacy of letrozole in combination with trastuzumab compared to letrozole monotherapy as first-line treatment in patients with HER2-positive, hormone-receptor-positive metastatic breast cancer - results of the eLEcTRA trial. Breast. 2012;21(1):27-33.

436. Kaufman B, Mackey JR, Clemens MR, Bapsy PP, Vaid A, Wardley A, et al. Trastuzumab plus anastrozole versus anastrozole alone for the treatment of postmenopausal women with human epidermal growth factor receptor 2-positive, hormone receptor-positive metastatic breast cancer: results from the randomized phase III TAnDEM study. J Clin Oncol. 2009;27(33):5529-37.

437. Rimawi M, Ferrero JM, de la Haba-Rodriguez J, Poole C, De Placido S, Osborne CK, et al. First-Line Trastuzumab Plus an Aromatase Inhibitor, With or Without Pertuzumab, in Human Epidermal Growth Factor Receptor 2-Positive and Hormone Receptor-Positive Metastatic or Locally Advanced Breast Cancer (PERTAIN): A Randomized, Open-Label Phase II Trial. J Clin Oncol. 2018;36(28):2826-35.

438. Geyer CE, Forster J, Lindquist D, Chan S, Romieu CG, Pienkowski T, et al. Lapatinib plus capecitabine for HER2-positive advanced breast cancer. N Engl J Med. 2006;355(26):2733-43.

439. von Minckwitz G, du Bois A, Schmidt M, Maass N, Cufer T, de Jongh FE, et al. Trastuzumab beyond progression in human epidermal growth factor receptor 2-positive advanced breast cancer: a german breast group 26/breast international group 03-05 study. J Clin Oncol. 2009;27(12):1999-2006.

440. Blackwell KL, Burstein HJ, Storniolo AM, Rugo HS, Sledge G, Aktan G, et al. Overall survival benefit with lapatinib in combination with trastuzumab for patients with human epidermal growth factor receptor 2-positive metastatic breast cancer: final results from the EGF104900 Study. J Clin Oncol. 2012;30(21):2585-92.

441. Gavila J, Lopez-Tarruella S, Saura C, Munoz M, Oliveira M, De la Cruz-Merino L, et al. SEOM clinical guidelines in metastatic breast cancer 2015. Clin Transl Oncol. 2015;17(12):946-55.

442. Baselga J, Gelmon KA, Verma S, Wardley A, Conte P, Miles D, et al. Phase II trial of pertuzumab and trastuzumab in patients with human epidermal growth factor receptor 2-positive metastatic breast cancer that progressed during prior trastuzumab therapy. J Clin Oncol. 2010;28(7):1138-44.

443. Urruticoechea A, Rizwanullah M, Im S, Sánchez-Ruiz A, Lang I, Tomasello G, et al. PHEREXA: A phase III study of trastuzumab (H) + capecitabine (X) ± pertuzumab (P) for patients (pts) who progressed during/after one line of H-based therapy in the HER2-positive metastatic breast cancer (MBC) setting. 2016 ASCO Annual Meeting. J Clin Oncol 34, 2016 (suppl; abstr 504).

444. Bachelot T, Romieu G, Campone M, Dieras V, Cropet C, Dalenc F, et al. Lapatinib plus capecitabine in patients with previously untreated brain metastases from HER2-positive metastatic breast cancer (LANDSCAPE): a single-group phase 2 study. Lancet Oncol. 2013;14(1):64-71.

445. Krop IE, Kim SB, Gonzalez-Martin A, LoRusso PM, Ferrero JM, Smitt M, et al. Trastuzumab emtansine versus treatment of physician's choice for pretreated HER2-positive advanced breast cancer (TH3RESA): a randomised, open-label, phase 3 trial. Lancet Oncol. 2014;15(7):689-99.

446. SEOM. Informe de evaluación de Trastuzumab deruxtecan (Enhertu®) en el tratamiento de pacientes con cáncer de mama no resecable o metastásico HER2 positivo 2021 [Available from: https://seom.org/seomcms/images/stories/Informes_SEOM/IEV_SEOM_trastuzumab_deruxtecan_mama_her2_positivo.pdf.

447. Cortés J, Kim S-B, Chung W-P, Im S-A, Park YH, Hegg R, et al. Trastuzumab Deruxtecan versus Trastuzumab Emtansine for Breast Cancer. The New England Journal of Medicine. 2022;386:1143 - 54.

448. Murthy RK, Loi S, Okines A, Paplomata E, Hamilton E, Hurvitz SA, et al. Tucatinib, Trastuzumab, and Capecitabine for HER2-Positive Metastatic Breast Cancer. N Engl J Med. 2020;382(7):597-609.

449. Seah DS, Luis IV, Macrae E, Sohl J, Litsas G, Winer EP, et al. Use and duration of chemotherapy in patients with metastatic breast cancer according to tumor subtype and line of therapy. Journal of the National Comprehensive Cancer Network : JNCCN. 2014;12(1):71-80.

450. Gavilá J, Lopez-Tarruella S, Saura C, Muñoz M, Oliveira M, De la Cruz-Merino L, et al. SEOM clinical guidelines in metastatic breast cancer 2015. Clinical & Translational Oncology. 2015;17:946-55.

451. Martin M, Mahillo E, Llombart-Cussac A, Lluch A, Munarriz B, Pastor M, et al. The "El Alamo" project (1990-1997): two consecutive hospital-based studies of breast cancer outcomes in Spain. Clin Transl Oncol. 2006;8(7):508-18.

452. Dawood S, Broglio K, Ensor J, Hortobagyi GN, Giordano SH. Survival differences among women with de novo stage IV and relapsed breast cancer. Annals of oncology : official journal of the European Society for Medical Oncology / ESMO. 2010;21(11):2169-74.

453. Lobbezoo DJ, van Kampen RJ, Voogd AC, Dercksen MW, van den Berkmortel F, Smilde TJ, et al. Prognosis of metastatic breast cancer: are there differences between patients with de novo and recurrent metastatic breast cancer? Br J Cancer. 2015;112(9):1445-51.

454. Servitja S, Zamora P, Santaballa A, García J, De-Paz L, Plata Y, et al. Longer overall survival in de novo versus recidivant patients with locally advanced/metastatic breast cancer. . Cancer Res. 2015;San Antonio Breast Cancer Symposium 2015.

455. Khan SA, Stewart AK, Morrow M. Does aggressive local therapy improve survival in metastatic breast cancer? Surgery. 2002;132(4):620-6; discussion 6-7.

456. Gnerlich J, Jeffe DB, Deshpande AD, Beers C, Zander C, Margenthaler JA. Surgical removal of the primary tumor increases overall survival in patients with metastatic breast cancer: analysis of the 1988-2003 SEER data. Ann Surg Oncol. 2007;14(8):2187-94.

457. Fields RC, Jeffe DB, Trinkaus K, Zhang Q, Arthur C, Aft R, et al. Surgical resection of the primary tumor is associated with increased long-term survival in patients with stage IV breast cancer after controlling for site of metastasis. Ann Surg Oncol. 2007;14(12):3345-51.

458. Ruiterkamp J, Ernst MF, van de Poll-Franse LV, Bosscha K, Tjan-Heijnen VC, Voogd AC. Surgical resection of the primary tumour is associated with improved survival in patients with distant metastatic breast cancer at diagnosis. Eur J Surg Oncol. 2009;35(11):1146-51.

459. Perez-Fidalgo JA, Pimentel P, Caballero A, Bermejo B, Barrera JA, Burgues O, et al. Removal of primary tumor improves survival in metastatic breast cancer. Does timing of surgery influence outcomes? Breast. 2011;20(6):548-54.

460. Babiera GV, Rao R, Feng L, Meric-Bernstam F, Kuerer HM, Singletary SE, et al. Effect of primary tumor extirpation in breast cancer patients who present with stage IV disease and an intact primary tumor. Ann Surg Oncol. 2006;13(6):776-82.

461. Blanchard DK, Shetty PB, Hilsenbeck SG, Elledge RM. Association of surgery with improved survival in stage IV breast cancer patients. Annals of surgery. 2008;247(5):732-8.

462. Rapiti E, Verkooijen HM, Vlastos G, Fioretta G, Neyroud-Caspar I, Sappino AP, et al. Complete excision of primary breast tumor improves survival of patients with metastatic breast cancer at diagnosis. J Clin Oncol. 2006;24(18):2743-9.

463. Ruiterkamp J, Voogd AC, Bosscha K, Tjan-Heijnen VC, Ernst MF. Impact of breast surgery on survival in patients with distant metastases at initial presentation: a systematic review of the literature. Breast cancer research and treatment. 2010;120(1):9-16.

464. Petrelli F, Barni S. Surgery of primary tumors in stage IV breast cancer: an updated meta-analysis of published studies with meta-regression. Med Oncol. 2012;29(5):3282-90.

465. Harris E, Barry M, Kell MR. Meta-analysis to determine if surgical resection of the primary tumour in the setting of stage IV breast cancer impacts on survival. Ann Surg Oncol. 2013;20(9):2828-34.

466. Nguyen DH, Truong PT, Alexander C, Walter CV, Hayashi E, Christie J, et al. Can locoregional treatment of the primary tumor improve outcomes for women with stage IV breast cancer at diagnosis? Int J Radiat Oncol Biol Phys. 2012;84(1):39-45.

467. King T, Lyman J, Gonen M, Reyes S, Hwang ES, Rugo H, et al. A prospective analysis of surgery and survival in stage IV breast cancer (TBCRC 013). 2016 ASCO Annual Meeting. J Clin Oncol 34, 2016 (suppl; abstr 1006).

468. Badwe R, Hawaldar R, Nair N, Kaushik R, Parmar V, Siddique S, et al. Locoregional treatment versus no treatment of the primary tumour in metastatic breast cancer: an open-label randomised controlled trial. Lancet Oncol. 2015;16(13):1380-8.

469. Soran A, Ozbas S, Kelsey SF, Gulluoglu BM. Randomized trial comparing locoregional resection of primary tumor with no surgery in stage IV breast cancer at the presentation (Protocol MF07-01): a study of Turkish Federation of the National Societies for Breast Diseases. The breast journal. 2009;15(4):399-403.

470. Soran A, Ozmen V, Ozbas S, et al. Early follow up of a randomized trial evaluating resection of the primary breast tumor in women presenting with de novo stage IV breast cancer; Turkish study (protocol MF07-01) [abstract]. San Antonio Breast Cancer Symposium 2013.Cancer Res, 73 (24 suppl): Abstract S2-03.

471. Soran A, Ozmen V, Ozbas A, Karanlik H, Muslumanoglu M, Igci A, et al. A randomized controlled trial evaluating resection of the primary breast tumor in women presenting with de novo stage IV breast cancer: Turkish Study (Protocol MF07-01).2016 ASCO Annual Meeting. J Clin Oncol 34, 2016 (suppl; abstr 1005).

472. Ruiterkamp J, Voogd AC, Tjan-Heijnen VC, Bosscha K, van der Linden YM, Rutgers EJ, et al. SUBMIT: Systemic therapy with or without up front surgery of the primary tumor in breast cancer patients with distant metastases at initial presentation. BMC Surg. 2012;12:5.

473. Eastern Cooperative Oncology Group. A Randomized Phase III Trial of the Value of Early Local Therapy for the Intact Primary Tumor in Patients With Metastatic Breast Cancer. ClinicalTrials.gov [Internet]: Bethesda (MD): National Library of Medicine (US); [cited 2016 Oct 25]. Available from: https://clinicaltrials.gov/ct2/show/NCT01242800.

474. Shien T, Nakamura K, Shibata T, Kinoshita T, Aogi K, Fujisawa T, et al. A randomized controlled trial comparing primary tumour resection plus systemic therapy with systemic therapy alone in metastatic breast cancer (PRIM-BC): Japan Clinical Oncology Group Study JCOG1017. Jpn J Clin Oncol. 2012;42(10):970-3.

475. Austrian Breast & Colorectal Cancer Study Group. Primary Operation in SYnchronous meTastasized InVasivE Breast Cancer, a Multicenter Prospective Randomized Study to Evaluate the Use of Local Therapy. ClinicalTrials.gov [Internet]: Bethesda (MD): National Library of Medicine (US); [cited 2016 Oct 25]. Available from: https://clinicaltrials.gov/ct2/show/NCT01015625.

476. Soran A, Ozmen V, Ozbas S, Karanlik H, Muslumanoglu M, Igci A, et al. Randomized Trial Comparing Resection of Primary Tumor with No Surgery in Stage IV Breast Cancer at Presentation: Protocol MF07-01. Ann Surg Oncol. 2018;25(11):3141-9.

477. Ozmen V, Ozbas S, Karanlik H, Muslumanoglu M, Igci A, Canturk Z, et al. ESMO 2019. The importance of primary surgery in patients with de novo stage IV BC survived at least 5-year; Protocol MF07-01 randomized clinical trial. Annals of Oncology. 2019;30(Suppl. 5):104-42.

478. Khan SA, Zhao F, Solin LJ, Goldstein LJ, Cella D, Basik M, et al. A randomized phase III trial of systemic therapy plus early local therapy versus systemic therapy alone in women with de novo stage IV breast cancer: A trial of the ECOG-ACRIN Research Group (E2108). Journal of Clinical Oncology. 2020;38(18_suppl):LBA2-LBA.

479. Fitzal F, Bjelic-Radisic V, Knauer M, Steger G, Hubalek M, Balic M, et al. Impact of Breast Surgery in Primary Metastasized Breast Cancer: Outcomes of the Prospective Randomized Phase III ABCSG-28 POSYTIVE Trial. Annals of surgery. 2019;269(6):1163-9.

480. Reinhorn D, Mutai R, Yerushalmi R, Moore A, Amir E, Goldvaser H. Locoregional therapy in de novo metastatic breast cancer: Systemic review and meta-analysis. Breast. 2021;58:173-81.

481. Le Scodan R, Stevens D, Brain E, Floiras JL, Cohen-Solal C, De La Lande B, et al. Breast cancer with synchronous metastases: survival impact of exclusive locoregional radiotherapy. J Clin Oncol. 2009;27(9):1375-81.

482. Bourgier C, Khodari W, Vataire AL, Pessoa EL, Dunant A, Delaloge S, et al. Breast radiotherapy as part of loco-regional treatments in stage IV breast cancer patients with oligometastatic disease. Radiother Oncol. 2010;96(2):199-203.

483. Ly BH, Nguyen NP, Vinh-Hung V, Rapiti E, Vlastos G. Loco-regional treatment in metastatic breast cancer patients: is there a survival benefit? Breast cancer research and treatment. 2010;119(3):537-45.

484. Pagani O, Senkus E, Wood W, Colleoni M, Cufer T, Kyriakides S, et al. International guidelines for management of metastatic breast cancer: can metastatic breast cancer be cured? J Natl Cancer Inst. 2010;102(7):456-63.

485. Planchard D, Soria JC, Michiels S, Grunenwald D, Validire P, Caliandro R, et al. Uncertain benefit from surgery in patients with lung metastases from breast carcinoma. Cancer. 2004;100(1):28-35.

486. Lee MY, Chang WJ, Kim HS, Lee JY, Lim SH, Lee JE, et al. Clinicopathological Features and Prognostic Factors Affecting Survival Outcomes in Isolated Locoregional Recurrence of Breast Cancer: Single-Institutional Series. PloS one. 2016;11(9):e0163254.

487. Wadasadawala T, Vadgaonkar R, Bajpai J. Management of Isolated Locoregional Recurrences in Breast Cancer: A Review of Local and Systemic Modalities. Clinical breast cancer. 2017;17(7):493-502.

488. Amir E, Clemons M, Purdie CA, Miller N, Quinlan P, Geddie W, et al. Tissue confirmation of disease recurrence in breast cancer patients: pooled analysis of multi-centre, multi-disciplinary prospective studies. Cancer Treat Rev. 2012;38(6):708-14.

489. Hoe AL, Royle GT, Taylor I. Breast liver metastases--incidence, diagnosis and outcome. J R Soc Med. 1991;84(12):714-6.

490. Maksan SM, Lehnert T, Bastert G, Herfarth C. Curative liver resection for metastatic breast cancer. Eur J Surg Oncol. 2000;26(3):209-12.

491. Chua TC, Saxena A, Liauw W, Chu F, Morris DL. Hepatic resection for metastatic breast cancer: a systematic review. Eur J Cancer. 2011;47(15):2282-90.

492. Bortolotto C, Macchi S, Veronese L, Dore R, Draghi F, Rossi S. Radiofrequency ablation of metastatic lesions from breast cancer. J Ultrasound. 2012;15(3):199-205.

493. Milano MT, Katz AW, Zhang H, Okunieff P. Oligometastases treated with stereotactic body radiotherapy: long-term follow-up of prospective study. Int J Radiat Oncol Biol Phys. 2012;83(3):878-86.

494. Palma DA, Olson R, Harrow S, Gaede S, Louie AV, Haasbeek C, et al. Stereotactic ablative radiotherapy versus standard of care palliative treatment in patients with oligometastatic cancers (SABR-COMET): a randomised, phase 2, open-label trial. Lancet. 2019;393(10185):2051-8.

495. Palma DA, Olson R, Harrow S, Correa RJM, Schneiders F, Haasbeek CJA, et al. Stereotactic ablative radiotherapy for the comprehensive treatment of 4-10 oligometastatic tumors (SABR-COMET-10): study protocol for a randomized phase III trial. BMC cancer. 2019;19(1):816.

496. Camacho LH, Kurzrock R, Cheung A, Barber DF, Gupta S, Madoff DC, et al. Pilot study of regional, hepatic intra-arterial paclitaxel in patients with breast carcinoma metastatic to the liver. Cancer. 2007;109(11):2190-6.

497. Friedel G, Pastorino U, Ginsberg RJ, Goldstraw P, Johnston M, Pass H, et al. Results of lung metastasectomy from breast cancer: prognostic criteria on the basis of 467 cases of the International Registry of Lung Metastases. European journal of cardio-thoracic surgery : official journal of the European Association for Cardio-thoracic Surgery. 2002;22(3):335-44.

498. Milano MT, Katz AW, Schell MC, Philip A, Okunieff P. Descriptive analysis of oligometastatic lesions treated with curative-intent stereotactic body radiotherapy. Int J Radiat Oncol Biol Phys. 2008;72(5):1516-22.

499. Dupuy DE, Zagoria RJ, Akerley W, Mayo-Smith WW, Kavanagh PV, Safran H. Percutaneous radiofrequency ablation of malignancies in the lung. AJR American journal of roentgenology. 2000;174(1):57-9.

500. Boxer DI, Todd CE, Coleman R, Fogelman I. Bone secondaries in breast cancer: the solitary metastasis. J Nucl Med. 1989;30(8):1318-20.

501. Wegener B, Schlemmer M, Stemmler J, Jansson V, Durr HR, Pietschmann MF. Analysis of orthopedic surgery of bone metastases in breast cancer patients. BMC musculoskeletal disorders. 2012;13:232.

502. Noble J, Sirohi B, Ashley S, Ladas G, Smith I. Sternal/para-sternal resection for parasternal local recurrence in breast cancer. Breast. 2010;19(5):350-4.

503. Koizumi M, Yoshimoto M, Kasumi F, Ogata E. Comparison between solitary and multiple skeletal metastatic lesions of breast cancer patients. Annals of oncology : official journal of the European Society for Medical Oncology / ESMO. 2003;14(8):1234-40.

504. Aebi S, Gelber S, Láng I, Anderson S, Robidoux A, Martín M, et al. Chemotherapy prolongs survival for isolated local or regional recurrence of breast cancer: The CALOR trial (Chemotherapy as Adjuvant for Locally Recurrent breast cancer; IBCSG 27-02, NSABP B-37, BIG 1-02). Presented at: CTRC-AACR San Antonio Breast Cancer Symposium, December 4–8, 2012; San Antonio, Texas. Abstract S3-2.

505. Aebi S, Gelber S, Anderson SJ, Lang I, Robidoux A, Martin M, et al. Chemotherapy for isolated locoregional recurrence of breast cancer (CALOR): a randomised trial. Lancet Oncol. 2014;15(2):156-63.

506. Wapnir I, Price KN, Anderson SJ, Robidoux A, Martin M, Nortier JWR, et al. Chemotherapy (CT) for isolated locoregional recurrence (ILRR) of breast cancer in ER-positive (ER+) and ER-negative (ER-) cohorts: Final analysis of the CALOR trial. Journal of Clinical Oncology. 2017;35(15_suppl):513-.

507. Waeber M, Castiglione-Gertsch M, Dietrich D, Thurlimann B, Goldhirsch A, Brunner KW, et al. Adjuvant therapy after excision and radiation of isolated postmastectomy locoregional breast cancer recurrence: definitive results of a phase III randomized trial (SAKK 23/82) comparing tamoxifen with observation. Annals of oncology : official journal of the European Society for Medical Oncology / ESMO. 2003;14(8):1215-21.

508. Jemal A, Siegel R, Ward E, Murray T, Xu J, Smigal C, et al. Cancer statistics, 2006. CA Cancer J Clin. 2006;56(2):106-30.

509. Stalsberg H, Thomas DB, Rosenblatt KA, Jimenez LM, McTiernan A, Stemhagen A, et al. Histologic types and hormone receptors in breast cancer in men: a population-based study in 282 United States men. Cancer Causes Control. 1993;4(2):143-51.

510. Wang-Rodriguez J, Cross K, Gallagher S, Djahanban M, Armstrong JM, Wiedner N, et al. Male breast carcinoma: correlation of ER, PR, Ki-67, Her2-Neu, and p53 with treatment and survival, a study of 65 cases. Modern pathology : an official journal of the United States and Canadian Academy of Pathology, Inc. 2002;15(8):853-61.

511. Cardoso F, Bartlett JMS, Slaets L, van Deurzen CHM, van Leeuwen-Stok E, Porter P, et al. Characterization of male breast cancer: results of the EORTC 10085/TBCRC/BIG/NABCG International Male Breast Cancer Program. Annals of oncology : official journal of the European Society for Medical Oncology / ESMO. 2018;29(2):405-17.

512. Masci G, Caruso M, Caruso F, Salvini P, Carnaghi C, Giordano L, et al. Clinicopathological and Immunohistochemical Characteristics in Male Breast Cancer: A Retrospective Case Series. The oncologist. 2015;20(6):586-92.

513. Gentilini O, Chagas E, Zurrida S, Intra M, De Cicco C, Gatti G, et al. Sentinel lymph node biopsy in male patients with early breast cancer. The oncologist. 2007;12(5):512-5.

514. Ruddy KJ, Winer EP. Male breast cancer: risk factors, biology, diagnosis, treatment, and survivorship. Annals of oncology : official journal of the European Society for Medical Oncology / ESMO. 2013;24(6):1434-43.

515. Atalay C, Kanlioz M, Altinok M. Prognostic factors affecting survival in male breast cancer. Journal of experimental & clinical cancer research : CR. 2003;22(1):29-33.

516. Stranzl H, Mayer R, Quehenberger F, Prettenhofer U, Willfurth P, Stoger H, et al. Adjuvant radiotherapy in male breast cancer. Radiother Oncol. 1999;53(1):29-35.

517. Ribeiro G, Swindell R. Adjuvant tamoxifen for male breast cancer (MBC). Br J Cancer. 1992;65(2):252-4.

518. Zhou FF, Xia LP, Wang X, Guo GF, Rong YM, Qiu HJ, et al. Analysis of prognostic factors in male breast cancer: a report of 72 cases from a single institution. Chin J Cancer. 2010;29(2):184-8.

519. Fogh S, Hirsch AE, Langmead JP, Goldberg SI, Rosenberg CL, Taghian AG, et al. Use of tamoxifen with postsurgical irradiation may improve survival in estrogen and progesterone receptor-positive male breast cancer. Clinical breast cancer. 2011;11(1):39-45.

520. Xu S, Yang Y, Tao W, Song Y, Chen Y, Ren Y, et al. Tamoxifen adherence and its relationship to mortality in 116 men with breast cancer. Breast cancer research and treatment. 2012;136(2):495-502.

521. Mauras N, O'Brien KO, Klein KO, Hayes V. Estrogen suppression in males: metabolic effects. The Journal of clinical endocrinology and metabolism. 2000;85(7):2370-7.

522. Giordano SH, Valero V, Buzdar AU, Hortobagyi GN. Efficacy of anastrozole in male breast cancer. American journal of clinical oncology. 2002;25(3):235-7.

523. Masci G, Gandini C, Zuradelli M, Pedrazzoli P, Torrisi R, Lutman FR, et al. Fulvestrant for advanced male breast cancer patients: a case series. Annals of oncology : official journal of the European Society for Medical Oncology / ESMO. 2011;22(4):985.

524. Hassett MJ, Somerfield MR, Baker ER, Cardoso F, Kansal KJ, Kwait DC, et al. Management of Male Breast Cancer: ASCO Guideline. https://doiorg/101200/JCO1903120. 2020.

525. Telli ML, Horst KC, Guardino AE, Dirbas FM, Carlson RW. Phyllodes tumors of the breast: natural history, diagnosis, and treatment. Journal of the National Comprehensive Cancer Network : JNCCN. 2007;5(3):324-30.

526. Salvadori B, Cusumano F, Del Bo R, Delledonne V, Grassi M, Rovini D, et al. Surgical treatment of phyllodes tumors of the breast. Cancer. 1989;63(12):2532-6.

527. Birch JM, Alston RD, McNally RJ, Evans DG, Kelsey AM, Harris M, et al. Relative frequency and morphology of cancers in carriers of germline TP53 mutations. Oncogene. 2001;20(34):4621-8.

528. Chaney AW, Pollack A, McNeese MD, Zagars GK, Pisters PW, Pollock RE, et al. Primary treatment of cystosarcoma phyllodes of the breast. Cancer. 2000;89(7):1502-11.

529. Mangi AA, Smith BL, Gadd MA, Tanabe KK, Ott MJ, Souba WW. Surgical management of phyllodes tumors. Archives of surgery. 1999;134(5):487-92; discussion 92-3.

530. Pandey M, Mathew A, Kattoor J, Abraham EK, Mathew BS, Rajan B, et al. Malignant phyllodes tumor. The breast journal. 2001;7(6):411-6.

531. Tse GM, Lee CS, Kung FY, Scolyer RA, Law BK, Lau TS, et al. Hormonal receptors expression in epithelial cells of mammary phyllodes tumors correlates with pathologic grade of the tumor: a multicenter study of 143 cases. American journal of clinical pathology. 2002;118(4):522-6.

532. Stensheim H, Møller B, van Dijk T, Fosså SD. Cause-specific survival for women diagnosed with cancer during pregnancy or lactation: a registry-based cohort study. J Clin Oncol. 2009;27(1):45-51.

533. Lee YY, Roberts CL, Dobbins T, Stavrou E, Black K, Morris J, et al. Incidence and outcomes of pregnancy-associated cancer in Australia, 1994-2008: a population-based linkage study. BJOG : an international journal of obstetrics and gynaecology. 2012;119(13):1572-82.

534. Gwyn K, Theriault R. Breast cancer during pregnancy. Oncology (Williston Park). 2001;15(1):39-46; discussion , 9-51.

535. Middleton LP, Amin M, Gwyn K, Theriault R, Sahin A. Breast carcinoma in pregnant women: assessment of clinicopathologic and immunohistochemical features. Cancer. 2003;98(5):1055-60.

536. Kuerer HM, Gwyn K, Ames FC, Theriault RL. Conservative surgery and chemotherapy for breast carcinoma during pregnancy. Surgery. 2002;131(1):108-10.

537. Annane K, Bellocq JP, Brettes JP, Mathelin C. Infiltrative breast cancer during pregnancy and conservative surgery. Fetal diagnosis and therapy. 2005;20(5):442-4.

538. Khera SY, Kiluk JV, Hasson DM, Meade TL, Meyers MP, Dupont EL, et al. Pregnancy-associated breast cancer patients can safely undergo lymphatic mapping. The breast journal. 2008;14(3):250-4.

539. Mondi MM, Cuenca RE, Ollila DW, Stewart JHt, Levine EA. Sentinel lymph node biopsy during pregnancy: initial clinical experience. Ann Surg Oncol. 2007;14(1):218-21.

540. Johnson PH, Gwyn K, Gordon N. The treatment of pregnant women with breast cancer and the outcomes of the children exposed to chemotherapy in utero [abstract]. J Clin Oncol. 2005;23(Suppl 16):Abstract 540.

541. Hahn KM, Johnson PH, Gordon N, Kuerer H, Middleton L, Ramirez M, et al. Treatment of pregnant breast cancer patients and outcomes of children exposed to chemotherapy in utero. Cancer. 2006;107(6):1219-26.

542. Gainford MC, Clemons M. Breast cancer in pregnancy: are taxanes safe? Clin Oncol (R Coll Radiol). 2006;18(2):159.

543. Mir O, Berveiller P, Ropert S, Goffinet F, Pons G, Treluyer JM, et al. Emerging therapeutic options for breast cancer chemotherapy during pregnancy. Annals of oncology: official journal of the European Society for Medical Oncology / ESMO. 2008;19(4):607-13.

544. Bader AA, Schlembach D, Tamussino KF, Pristauz G, Petru E. Anhydramnios associated with administration of trastuzumab and paclitaxel for metastatic breast cancer during pregnancy. Lancet Oncol. 2007;8(1):79-81.

545. Witzel ID, Muller V, Harps E, Janicke F, Dewit M. Trastuzumab in pregnancy associated with poor fetal outcome. Annals of oncology : official journal of the European Society for Medical Oncology / ESMO. 2008;19(1):191-2.

546. Shlensky V, Hallmeyer S, Juarez L, Parilla BV. Management of Breast Cancer during Pregnancy: Are We Compliant with Current Guidelines? AJP Rep. 2017;7(1):e39-e43.

547. Cordeiro CN, Gemignani ML. Breast Cancer in Pregnancy: Avoiding Fetal Harm When Maternal Treatment Is Necessary. The breast journal. 2017;23(2):200-5.

548. Schnetz M, Stravodimou A, Cisarovsky C, Dunand A, Prior JO, Nicod Lalonde M, et al. [Breast cancer during pregnancy]. Rev Med Suisse. 2021;17(739):957-61.

549. Sakorafas GH, Blanchard K, Sarr MG, Farley DR. Paget's disease of the breast. Cancer Treat Rev. 2001;27(1):9-18.

550. Kollmorgen DR, Varanasi JS, Edge SB, Carson WE, 3rd. Paget's disease of the breast: a 33-year experience. Journal of the American College of Surgeons. 1998;187(2):171-7.

551. Morrogh M, Morris EA, Liberman L, Van Zee K, Cody HS, 3rd, King TA. MRI identifies otherwise occult disease in select patients with Paget disease of the nipple. Journal of the American College of Surgeons. 2008;206(2):316-21.

552. Laronga C, Hasson D, Hoover S, Cox J, Cantor A, Cox C, et al. Paget's disease in the era of sentinel lymph node biopsy. American journal of surgery. 2006;192(4):481-3.

553. Sukumvanich P, Bentrem DJ, Cody HS, 3rd, Brogi E, Fey JV, Borgen PI, et al. The role of sentinel lymph node biopsy in Paget's disease of the breast. Ann Surg Oncol. 2007;14(3):1020-3.

554. Olson JA, Jr., Morris EA, Van Zee KJ, Linehan DC, Borgen PI. Magnetic resonance imaging facilitates breast conservation for occult breast cancer. Ann Surg Oncol. 2000;7(6):411-5.

555. Varadarajan R, Edge SB, Yu J, Watroba N, Janarthanan BR. Prognosis of occult breast carcinoma presenting as isolated axillary nodal metastasis. Oncology. 2006;71(5-6):456-9.

556. Ries LAG, Harkins D, Krapcho M, Mariotto A, Miller BA, Feuer EJ, et al. SEER Cancer Statistics Review, 1975-2003, National Cancer Institute. Bethesda, MD, http://seer.cancer.gov/csr/1975_2003/, based on November 2005 SEER data submission, posted to the SEER web site, 2006.

557. Mohile SG, Bylow K, Dale W, Dignam J, Martin K, Petrylak DP, et al. A pilot study of the vulnerable elders survey-13 compared with the comprehensive geriatric assessment for identifying disability in older patients with prostate cancer who receive androgen ablation. Cancer. 2007;109(4):802-10.

558. Luciani A, Ascione G, Bertuzzi C, Marussi D, Codeca C, Di Maria G, et al. Detecting disabilities in older patients with cancer: comparison between comprehensive geriatric assessment and vulnerable elders survey-13. J Clin Oncol. 2010;28(12):2046-50.

559. Rockwood K, Mitnitski A. Frailty defined by deficit accumulation and geriatric medicine defined by frailty. Clinics in geriatric medicine. 2011;27(1):17-26.

560. Cadena MO, Lopez JH, Insuasty JS, Santacruz JG, Becerra H. Importancia de la valoración geriátrica integral en el manejo de pacientes con cáncer. MÉDUIS. 2012;25(2):121-8.

561. Vogel CL, Wojtukiewicz MZ, Carroll RR, Tjulandin SA, Barajas-Figueroa LJ, Wiens BL, et al. First and subsequent cycle use of pegfilgrastim prevents febrile neutropenia in patients with breast cancer: a multicenter, double-blind, placebo-controlled phase III study. J Clin Oncol. 2005;23(6):1178-84.

562. Citron ML, Berry DA, Cirrincione C, Hudis C, Winer EP, Gradishar WJ, et al. Randomized trial of dose-dense versus conventionally scheduled and sequential versus concurrent combination chemotherapy as postoperative adjuvant treatment of node-positive primary breast cancer: first report of Intergroup Trial C9741/Cancer and Leukemia Group B Trial 9741. J Clin Oncol. 2003;21(8):1431-9.

563. Chirivella I, Bermejo B, Insa A, Perez-Fidalgo A, Magro A, Rosello S, et al. Optimal delivery of anthracycline-based chemotherapy in the adjuvant setting improves outcome of breast cancer patients. Breast cancer research and treatment. 2009;114(3):479-84.

564. Lyman GH, Kuderer NM. The economics of the colony-stimulating factors in the prevention and treatment of febrile neutropenia. Critical reviews in oncology/hematology. 2004;50(2):129-46.

565. Cosler LE, Eldar-Lissai A, Culakova E, Kuderer NM, Dale D, Crawford J, et al. Therapeutic use of granulocyte colony-stimulating factors for established febrile neutropenia: effect on costs from a hospital perspective. PharmacoEconomics. 2007;25(4):343-51.

566. Bohlius J, Herbst C, Reiser M, Schwarzer G, Engert A. Granulopoiesis-stimulating factors to prevent adverse effects in the treatment of malignant lymphoma. Cochrane Database Syst Rev. 2008(4):CD003189.

567. Sung L, Nathan PC, Alibhai SM, Tomlinson GA, Beyene J. Meta-analysis: effect of prophylactic hematopoietic colony-stimulating factors on mortality and outcomes of infection. Ann Intern Med. 2007;147(6):400-11.

568. Kuderer NM, Dale DC, Crawford J, Lyman GH. Impact of primary prophylaxis with granulocyte colony-stimulating factor on febrile neutropenia and mortality in adult cancer patients receiving chemotherapy: a systematic review. J Clin Oncol. 2007;25(21):3158-67.

569. Munoz Langa J, Gascon P, de Castro J, Seom. SEOM clinical guidelines for myeloid growth factors. Clin Transl Oncol. 2012;14(7):491-8.

570. Siena S, Piccart MJ, Holmes FA, Glaspy J, Hackett J, Renwick JJ. A combined analysis of two pivotal randomized trials of a single dose of pegfilgrastim per chemotherapy cycle and daily Filgrastim in patients with stage II-IV breast cancer. Oncology reports. 2003;10(3):715-24.

571. Pinto L, Liu Z, Doan Q, Bernal M, Dubois R, Lyman G. Comparison of pegfilgrastim with filgrastim on febrile neutropenia, grade IV neutropenia and bone pain: a meta-analysis of randomized controlled trials. Current medical research and opinion. 2007;23(9):2283-95.

572. Carrico DJ, Peters KM, Diokno AC. Guided imagery for women with interstitial cystitis: results of a prospective, randomized controlled pilot study. Journal of alternative and complementary medicine. 2008;14(1):53-60.

573. Aapro M, Beguin Y, Bokemeyer C, Dicato M, Gascón P, Glaspy J, et al. Management of anaemia and iron deficiency in patients with cancer: ESMO Clinical Practice Guidelines. Annals of oncology : official journal of the European Society for Medical Oncology / ESMO. 2018;29(Suppl 4):iv96-iv110.

574. Leyland-Jones B, Semiglazov V, Pawlicki M, Pienkowski T, Tjulandin S, Manikhas G, et al. Maintaining normal hemoglobin levels with epoetin alfa in mainly nonanemic patients with metastatic breast cancer receiving first-line chemotherapy: a survival study. J Clin Oncol. 2005;23(25):5960-72.

575. Aapro M, Leonard RC, Barnadas A, Marangolo M, Untch M, Malamos N, et al. Effect of once-weekly epoetin beta on survival in patients with metastatic breast cancer receiving anthracycline- and/or taxane-based chemotherapy: results of the Breast Cancer-Anemia and the Value of Erythropoietin (BRAVE) study. J Clin Oncol. 2008;26(4):592-8.

576. Bohlius J, Schmidlin K, Brillant C, Schwarzer G, Trelle S, Seidenfeld J, et al. Recombinant human erythropoiesis-stimulating agents and mortality in patients with cancer: a meta-analysis of randomised trials. Lancet. 2009;373(9674):1532-42.

577. Aapro M, Moebus V, Nitz U, O'Shaughnessy J, Pronzato P, Untch M, et al. Safety and efficacy outcomes with erythropoiesis-stimulating agents in patients with breast cancer: a meta-analysis. Annals of oncology : official journal of the European Society for Medical Oncology / ESMO. 2015;26(4):688-95.

578. Leyland-Jones B, Bondarenko I, Nemsadze G, Smirnov V, Litvin I, Kokhreidze I, et al. A Randomized, Open-Label, Multicenter, Phase III Study of Epoetin Alfa Versus Best Standard of Care in Anemic Patients With Metastatic Breast Cancer Receiving Standard Chemotherapy. J Clin Oncol. 2016;34(11):1197-207.

579. Lipton A, Fizazi K, Stopeck AT, Henry DH, Brown JE, Yardley DA, et al. Superiority of denosumab to zoledronic acid for prevention of skeletal-related events: a combined analysis of 3 pivotal, randomised, phase 3 trials. Eur J Cancer. 2012;48(16):3082-92.

580. Saad F, Brown JE, Van Poznak C, Ibrahim T, Stemmer SM, Stopeck AT, et al. Incidence, risk factors, and outcomes of osteonecrosis of the jaw: integrated analysis from three blinded active-controlled phase III trials in cancer patients with bone metastases. Annals of oncology : official journal of the European Society for Medical Oncology / ESMO. 2012;23(5):1341-7.

581. Coleman RE. Metastatic bone disease: clinical features, pathophysiology and treatment strategies. Cancer Treat Rev. 2001;27(3):165-76.

582. Yong M, Jensen AO, Jacobsen JB, Norgaard M, Fryzek JP, Sorensen HT. Survival in breast cancer patients with bone metastases and skeletal-related events: a population-based cohort study in Denmark (1999-2007). Breast cancer research and treatment. 2011;129(2):495-503.

583. Theriault RL, Lipton A, Hortobagyi GN, Leff R, Gluck S, Stewart JF, et al. Pamidronate reduces skeletal morbidity in women with advanced breast cancer and lytic bone lesions: a randomized, placebo-controlled trial. Protocol 18 Aredia Breast Cancer Study Group. J Clin Oncol. 1999;17(3):846-54.

584. Rosen LS, Gordon D, Kaminski M, Howell A, Belch A, Mackey J, et al. Zoledronic acid versus pamidronate in the treatment of skeletal metastases in patients with breast cancer or osteolytic lesions of multiple myeloma: a phase III, double-blind, comparative trial. Cancer journal (Sudbury, Mass). 2001;7(5):377-87.

585. Stopeck AT, Lipton A, Body JJ, Steger GG, Tonkin K, de Boer RH, et al. Denosumab compared with zoledronic acid for the treatment of bone metastases in patients with advanced breast cancer: a randomized, double-blind study. J Clin Oncol. 2010;28(35):5132-9.

586. Barrett-Lee P, Casbard A, Abraham J, Hood K, Coleman R, Simmonds P, et al. Oral ibandronic acid versus intravenous zoledronic acid in treatment of bone metastases from breast cancer: a randomised, open label, non-inferiority phase 3 trial. Lancet Oncol. 2014;15(1):114-22.

587. Coleman R, Hadji P, Body JJ, Santini D, Chow E, Terpos E, et al. Bone health in cancer: ESMO Clinical Practice Guidelines. Annals of oncology : official journal of the European Society for Medical Oncology / ESMO. 2020;31(12):1650-63.

588. Amadori D, Aglietta M, Alessi B, Gianni L, Ibrahim T, Farina G, et al. Efficacy and safety of 12-weekly versus 4-weekly zoledronic acid for prolonged treatment of patients with bone metastases from breast cancer (ZOOM): a phase 3, open-label, randomised, non-inferiority trial. Lancet Oncol. 2013;14(7):663-70.

589. Hortobagyi G, Lipton A, Chew HK, Gradishar WJ, Sauter NP, Mohanlal RW, et al. Efficacy and safety of continued zoledronic acid every 4 weeks versus every 12 weeks in women with bone metastases from breast cancer: Results of the OPTIMIZE-2 trial. 2014 ASCO Annual Meeting. J Clin Oncol 32:5s, 2014 (suppl; abstr LBA9500^).

590. Himelstein AL, Qin R, Novotny PJ, Seisler DK, Khatcheressian JL, Roberts JD, et al. CALGB 70604 (Alliance): A randomized phase III study of standard dosing vs. longer interval dosing of zoledronic acid in metastatic cancer. 2015 ASCO Annual Meeting. J Clin Oncol 33, 2015 (suppl; abstr 9501).

591. Coleman R, Cameron D, Dodwell D, Bell R, Wilson C, Rathbone E, et al. Adjuvant zoledronic acid in patients with early breast cancer: final efficacy analysis of the AZURE (BIG 01/04) randomised open-label phase 3 trial. Lancet Oncol. 2014;15(9):997-1006.

592. Early Breast Cancer Trialists' Collaborative G, Coleman R, Powles T, Paterson A, Gnant M, Anderson S, et al. Adjuvant bisphosphonate treatment in early breast cancer: meta-analyses of individual patient data from randomised trials. Lancet. 2015;386(10001):1353-61.

593. Gnant M, Mlineritsch B, Stoeger H, Luschin-Ebengreuth G, Heck D, Menzel C, et al. Adjuvant endocrine therapy plus zoledronic acid in premenopausal women with early-stage breast cancer: 62-month follow-up from the ABCSG-12 randomised trial. Lancet Oncol. 2011;12(7):631-41.

594. Gnant M, Pfeiler G, Dubsky PC, Hubalek M, Greil R, Jakesz R, et al. Adjuvant denosumab in breast cancer (ABCSG-18): a multicentre, randomised, double-blind, placebo-controlled trial. Lancet. 2015;386(9992):433-43.

595. Coleman R, Finkelstein DM, Barrios C, Martin M, Iwata H, Hegg R, et al. Adjuvant denosumab in early breast cancer (D-CARE): an international, multicentre, randomised, controlled, phase 3 trial. Lancet Oncol. 2020;21(1):60-72.

596. Higuchi Y, Sumiyoshi T, Seo T, Miyanishi T, Kawasaki Y, Suzuki M. Mismatch negativity and cognitive performance for the prediction of psychosis in subjects with at-risk mental state. PloS one. 2013;8(1):e54080.

597. Coleman RE, Rathbone E, Brown JE. Management of cancer treatment-induced bone loss. Nature reviews Rheumatology. 2013;9(6):365-74.

598. Hadji P, Aapro MS, Body JJ, Bundred NJ, Brufsky A, Coleman RE, et al. Management of aromatase inhibitor-associated bone loss in postmenopausal women with breast cancer: practical guidance for prevention and treatment. Annals of oncology : official journal of the European Society for Medical Oncology / ESMO. 2011;22(12):2546-55.

599. Curigliano G, Lenihan D, Fradley M, Ganatra S, Barac A, Blaes A, et al. Management of cardiac disease in cancer patients throughout oncological treatment: ESMO consensus recommendations. Annals of oncology : official journal of the European Society for Medical Oncology / ESMO. 2020;31(2):171-90.

600. Zagar TM, Cardinale DM, Marks LB. Breast cancer therapy-associated cardiovascular disease. Nat Rev Clin Oncol. 2016;13(3):172-84.

601. Lopez-Fernandez T, Martin Garcia A, Santaballa Beltran A, Montero Luis A, Garcia Sanz R, Mazon Ramos P, et al. Cardio-Onco-Hematology in Clinical Practice. Position Paper and Recommendations. Rev Esp Cardiol (Engl Ed). 2017;70(6):474-86.

602. Kalam K, Marwick TH. Role of cardioprotective therapy for prevention of cardiotoxicity with chemotherapy: a systematic review and meta-analysis. Eur J Cancer. 2013;49(13):2900-9.

603. Seicean S, Seicean A, Alan N, Plana JC, Budd GT, Marwick TH. Cardioprotective effect of beta-adrenoceptor blockade in patients with breast cancer undergoing chemotherapy: follow-up study of heart failure. Circulation Heart failure. 2013;6(3):420-6.

604. Cardinale D, Colombo A, Sandri MT, Lamantia G, Colombo N, Civelli M, et al. Prevention of high-dose chemotherapy-induced cardiotoxicity in high-risk patients by angiotensin-converting enzyme inhibition. Circulation. 2006;114(23):2474-81.

605. Gulati G, Heck SL, Ree AH, Hoffmann P, Schulz-Menger J, Fagerland MW, et al. Prevention of cardiac dysfunction during adjuvant breast cancer therapy (PRADA): a 2 x 2 factorial, randomized, placebo-controlled, double-blind clinical trial of candesartan and metoprolol. Eur Heart J. 2016;37(21):1671-80.

606. Noori A, Lindenfeld J, Wolfel E, Ferguson D, Bristow MR, Lowes BD. Beta-blockade in adriamycin-induced cardiomyopathy. Journal of cardiac failure. 2000;6(2):115-9.

607. Cardinale D, Colombo A, Lamantia G, Colombo N, Civelli M, De Giacomi G, et al. Anthracycline-induced cardiomyopathy: clinical relevance and response to pharmacologic therapy. J Am Coll Cardiol. 2010;55(3):213-20.

608. Curigliano G, Cardinale D, Suter T, Plataniotis G, de Azambuja E, Sandri MT, et al. Cardiovascular toxicity induced by chemotherapy, targeted agents and radiotherapy: ESMO Clinical Practice Guidelines. Annals of oncology : official journal of the European Society for Medical Oncology / ESMO. 2012;23 Suppl 7:vii155-66.

609. Viani GA, Afonso SL, Stefano EJ, De Fendi LI, Soares FV. Adjuvant trastuzumab in the treatment of her-2-positive early breast cancer: a meta-analysis of published randomized trials. BMC cancer. 2007;7:153.

610. Moja L, Tagliabue L, Balduzzi S, Parmelli E, Pistotti V, Guarneri V, et al. Trastuzumab containing regimens for early breast cancer. Cochrane Database Syst Rev. 2012;4:CD006243.

611. de Azambuja E, Procter MJ, van Veldhuisen DJ, Agbor-Tarh D, Metzger-Filho O, Steinseifer J, et al. Trastuzumab-associated cardiac events at 8 years of median follow-up in the Herceptin Adjuvant trial (BIG 1-01). J Clin Oncol. 2014;32(20):2159-65.

612. Martin M, Sanchez-Rovira P, Munoz M, Baena-Canada JM, Mel JR, Margeli M, et al. Pegylated liposomal doxorubicin in combination with cyclophosphamide and trastuzumab in HER2-positive metastatic breast cancer patients: efficacy and cardiac safety from the GEICAM/2004-05 study. Annals of oncology : official journal of the European Society for Medical Oncology / ESMO. 2011;22(12):2591-6.

613. Gavilá J, Oliveira M, Pascual T, Perez-Garcia J, Gonzàlez X, Canes J, et al. Safety, activity, and molecular heterogeneity following neoadjuvant non-pegylated liposomal doxorubicin, paclitaxel, trastuzumab, and pertuzumab in HER2-positive breast cancer (Opti-HER HEART): an open-label, single-group, multicenter, phase 2 trial. BMC medicine. 172019.

614. Martin M, Esteva FJ, Alba E, Khandheria B, Perez-Isla L, Garcia-Saenz JA, et al. Minimizing cardiotoxicity while optimizing treatment efficacy with trastuzumab: review and expert recommendations. The oncologist. 2009;14(1):1-11.

615. Krop IE, Lin NU, Blackwell K, Guardino E, Huober J, Lu M, et al. Trastuzumab emtansine (T-DM1) versus lapatinib plus capecitabine in patients with HER2-positive metastatic breast cancer and central nervous system metastases: a retrospective, exploratory analysis in EMILIA. Annals of oncology : official journal of the European Society for Medical Oncology / ESMO. 2015;26(1):113-9.

616. Lee JJ, Swain SM. Peripheral neuropathy induced by microtubule-stabilizing agents. J Clin Oncol. 2006;24(10):1633-42.

617. Sparano JA, Wang M, Martino S, Jones V, Perez EA, Saphner T, et al. Weekly paclitaxel in the adjuvant treatment of breast cancer. N Engl J Med. 2008;358(16):1663-71.

618. Seidman AD, Berry D, Cirrincione C, Harris L, Muss H, Marcom PK, et al. Randomized phase III trial of weekly compared with every-3-weeks paclitaxel for metastatic breast cancer, with trastuzumab for all HER-2 overexpressors and random assignment to trastuzumab or not in HER-2 nonoverexpressors: final results of Cancer and Leukemia Group B protocol 9840. J Clin Oncol. 2008;26(10):1642-9.

619. Mauri D, Kamposioras K, Tsali L, Bristianou M, Valachis A, Karathanasi I, et al. Overall survival benefit for weekly vs. three-weekly taxanes regimens in advanced breast cancer: A meta-analysis. Cancer Treat Rev. 2010;36(1):69-74.

620. Smith RE, Brown AM, Mamounas EP, Anderson SJ, Lembersky BC, Atkins JH, et al. Randomized trial of 3-hour versus 24-hour infusion of high-dose paclitaxel in patients with metastatic or locally advanced breast cancer: National Surgical Adjuvant Breast and Bowel Project Protocol B-26. J Clin Oncol. 1999;17(11):3403-11.

621. Reeves BN, Dakhil SR, Sloan JA, Wolf SL, Burger KN, Kamal A, et al. Further data supporting that paclitaxel-associated acute pain syndrome is associated with development of peripheral neuropathy: North Central Cancer Treatment Group trial N08C1. Cancer. 2012;118(20):5171-8.

622. Hershman DL, Lacchetti C, Dworkin RH, Lavoie Smith EM, Bleeker J, Cavaletti G, et al. Prevention and management of chemotherapy-induced peripheral neuropathy in survivors of adult cancers: American Society of Clinical Oncology clinical practice guideline. J Clin Oncol. 2014;32(18):1941-67.

623. Smith EM, Pang H, Cirrincione C, Fleishman S, Paskett ED, Ahles T, et al. Effect of duloxetine on pain, function, and quality of life among patients with chemotherapy-induced painful peripheral neuropathy: a randomized clinical trial. JAMA. 2013;309(13):1359-67.

624. Mansel RE, Fallowfield L, Kissin M, Goyal A, Newcombe RG, Dixon JM, et al. Randomized multicenter trial of sentinel node biopsy versus standard axillary treatment in operable breast cancer: the ALMANAC Trial. J Natl Cancer Inst. 2006;98(9):599-609.

625. McLaughlin SA, Wright MJ, Morris KT, Giron GL, Sampson MR, Brockway JP, et al. Prevalence of lymphedema in women with breast cancer 5 years after sentinel lymph node biopsy or axillary dissection: objective measurements. J Clin Oncol. 2008;26(32):5213-9.

626. 2ª Edidión de Manual SEOM de Cuidados Continuos. 2014 Sociedad Española De Oncología Médica. Disponible en: http://www.seom.org/en/publicaciones/publicaciones-seom/cuidados-continuos.

627. Droz J, Howard FM. Use of the Short-Form McGill Pain Questionnaire as a diagnostic tool in women with chronic pelvic pain. Journal of minimally invasive gynecology. 2011;18(2):211-7.

628. Janelsins MC, Kohli S, Mohile SG, Usuki K, Ahles TA, Morrow GR. An update on cancer- and chemotherapy-related cognitive dysfunction: current status. Seminars in oncology. 2011;38(3):431-8.

629. Jim HS, Phillips KM, Chait S, Faul LA, Popa MA, Lee YH, et al. Meta-analysis of cognitive functioning in breast cancer survivors previously treated with standard-dose chemotherapy. J Clin Oncol. 2012;30(29):3578-87.

630. Conde-Estévez D, Mateu-de Antonio J. [Update in the management of extravasations of cytocytostatic agent]. Farm Hosp. 2012;36(1):34-42.

631. Del Mastro L, Catzeddu T, Venturini M. Infertility and pregnancy after breast cancer: current knowledge and future perspectives. Cancer Treat Rev. 2006;32(6):417-22.

632. Poorvu PD, Frazier AL, Feraco AM, Manley PE, Ginsburg ES, Laufer MR, et al. Cancer Treatment-Related Infertility: A Critical Review of the Evidence. JNCI Cancer Spectr. 2019;3(1):pkz008.

633. Kim J, Turan V, Oktay K. Long-Term Safety of Letrozole and Gonadotropin Stimulation for Fertility Preservation in Women With Breast Cancer. The Journal of Clinical Endocrinology & Metabolism. 2016;101(4):1364-71.

634. Oktay K, Harvey BE, Partridge AH, Quinn GP, Reinecke J, Taylor HS, et al. Fertility Preservation in Patients With Cancer: ASCO Clinical Practice Guideline Update. Journal of Clinical Oncology. 2018;36(19):1994-2001.

635. Lambertini M, Peccatori FA, Demeestere I, Amant F, Wyns C, Stukenborg JB, et al. Fertility preservation and post-treatment pregnancies in post-pubertal cancer patients: ESMO Clinical Practice Guidelines(†). Annals of oncology : official journal of the European Society for Medical Oncology / ESMO. 2020;31(12):1664-78.

636. Muñoz M, Santaballa A, Seguí MA, Beato C, de la Cruz S, Espinosa J, et al. SEOM Clinical Guideline of fertility preservation and reproduction in cancer patients (2016). Clin Transl Oncol. 2016;18(12):1229-36.

637. Moore HC, Unger JM, Phillips KA, Boyle F, Hitre E, Porter D, et al. Goserelin for ovarian protection during breast-cancer adjuvant chemotherapy. N Engl J Med. 2015;372(10):923-32.

638. Pagani OP, A.; Azim, H.; Peccatori, F. A study evaluating the pregnancy outcomes and safety of interrupting endocrine therapy for young women with endocrine responsive breast cancer who desire pregnancy (POSITIVE). 2021 [Available from: https://www.ibcsg.org/en/patients-professionals/clinical-trials/closed-trials/2-ibcsg-48-14-positive.

639. Razeti MG, Spinaci S, Spagnolo F, Massarotti C, Lambertini M. How I perform fertility preservation in breast cancer patients. ESMO Open. 2021;6(3):100112.

640. Santaballa A, Márquez-Vega C, Rodríguez-Lescure Á, Rovirosa Á, Vázquez L, Zeberio-Etxetxipia I, et al. Multidisciplinary consensus on the criteria for fertility preservation in cancer patients. Clin Transl Oncol. 2021.

641. Sociedad Española de Oncología Médica (SEOM). Plan integral de atención a los largos supervivientes de cáncer. Madrid: Mares Ideas Publicitarias SL.; 2013.

642. Rojas MP, Telaro E, Russo A, Moschetti I, Coe L, Fossati R, et al. Follow-up strategies for women treated for early breast cancer. Cochrane Database Syst Rev. 2005(1):CD001768.

643. Lash TL, Fox MP, Buist DS, Wei F, Field TS, Frost FJ, et al. Mammography surveillance and mortality in older breast cancer survivors. J Clin Oncol. 2007;25(21):3001-6.

644. Schootman M, Jeffe DB, Lian M, Aft R, Gillanders WE. Surveillance mammography and the risk of death among elderly breast cancer patients. Breast cancer research and treatment. 2008;111(3):489-96.

645. Lash TL, Fox MP, Silliman RA. Reduced mortality rate associated with annual mammograms after breast cancer therapy. The breast journal. 2006;12(1):2-6.

646. Yang SH, Yang KH, Li YP, Zhang YC, He XD, Song AL, et al. Breast conservation therapy for stage I or stage II breast cancer: a meta-analysis of randomized controlled trials. Annals of oncology : official journal of the European Society for Medical Oncology / ESMO. 2008;19(6):1039-44.

647. Grunfeld E, Noorani H, McGahan L, Paszat L, Coyle D, van Walraven C, et al. Surveillance mammography after treatment of primary breast cancer: a systematic review. Breast. 2002;11(3):228-35.

648. Khatcheressian JL, Hurley P, Bantug E, Esserman LJ, Grunfeld E, Halberg F, et al. Breast cancer follow-up and management after primary treatment: American Society of Clinical Oncology clinical practice guideline update. J Clin Oncol. 2013;31(7):961-5.

649. Pan H, Gray R, Davies D, Peto P, Bergh J, Pritchard K, et al. Predictors of recurrence during years 5-14 in 46,138 women with ER+ breast cancer allocated 5 years only of endocrine therapy (ET). 2016 ASCO Annual Meeting. J Clin Oncol 34, 2016 (suppl; abstr 505).

650. Chlebowski RT, Blackburn GL, Thomson CA, Nixon DW, Shapiro A, Hoy MK, et al. Dietary fat reduction and breast cancer outcome: interim efficacy results from the Women's Intervention Nutrition Study. J Natl Cancer Inst. 2006;98(24):1767-76.

651. Castello A, Pollan M, Buijsse B, Ruiz A, Casas AM, Baena-Canada JM, et al. Spanish Mediterranean diet and other dietary patterns and breast cancer risk: case-control EpiGEICAM study. Br J Cancer. 2014;111(7):1454-62.

652. Holmes MD, Chen WY, Hankinson SE, Willett WC. Physical activity's impact on the association of fat and fiber intake with survival after breast cancer. Am J Epidemiol. 2009;170(10):1250-6.

653. Bluethmann SM, Vernon SW, Gabriel KP, Murphy CC, Bartholomew LK. Taking the next step: a systematic review and meta-analysis of physical activity and behavior change interventions in recent post-treatment breast cancer survivors. Breast cancer research and treatment. 2015;149(2):331-42.

654. Schmid D, Leitzmann MF. Association between physical activity and mortality among breast cancer and colorectal cancer survivors: a systematic review and meta-analysis. Annals of oncology : official journal of the European Society for Medical Oncology / ESMO. 2014;25(7):1293-311.

655. Braithwaite D, Izano M, Moore DH, Kwan ML, Tammemagi MC, Hiatt RA, et al. Smoking and survival after breast cancer diagnosis: a prospective observational study and systematic review. Breast cancer research and treatment. 2012;136(2):521-33.

656. Izano M, Satariano WA, Hiatt RA, Braithwaite D. Smoking and mortality after breast cancer diagnosis: the health and functioning in women study. Cancer medicine. 2015;4(2):315-24.

657. Kwan ML, Kushi LH, Weltzien E, Tam EK, Castillo A, Sweeney C, et al. Alcohol consumption and breast cancer recurrence and survival among women with early-stage breast cancer: the life after cancer epidemiology study. J Clin Oncol. 2010;28(29):4410-6.