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Práctica Cáncer de Mama

MANUAL PRÁCTICO PARA LA CONSULTA DE PACIENTES CON CÁNCER DE MAMA

NOVARTIS

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Avales

PARA INFORMACIÓN ADICIONAL, CONSULTAR EL RESTO DE LOS CAPÍTULOS

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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 5. CÁNCER DE MAMA LOCALMENTE AVANZADO

A. PARTICULARIDADES

¿Qué es el cáncer de mama localmente avanzado?

¿Cuáles son los factores pronósticos?

VER RESUMEN
5. Cáncer de mama localmente avanzado
a) Particularidades

¿Qué es el cáncer de mama localmente avanzado?

DEFINICIÓN

El término "cáncer de mama localmente avanzado" (CMLA) hace referencia a tumores grandes, de más de 5 cm, asociados a afectación cutánea o a pared torácica (T4), con o sin adenopatías axilares fijas o empastadas.

La afectación metastásica de la cadena ganglionar mamaria interna o de los ganglios infra/supraclaviculares ipsilaterales (N2 o N3), así como el carcinoma inflamatorio, son considerados como CMLA. En algunos casos el término se amplía para pacientes con estadio clínico IIB: tumores >5 cm (T3) y N0.

Todas las pacientes tienen en común la presencia de gran masa tumoral o importante afectación ganglionar con ausencia de metástasis a distancia. Su comportamiento clínico y biológico es heterogéneo: algunas pacientes presentan una rápida evolución, mientras que otras refieren historia de crecimiento tumoral de larga evolución (334).

En conclusión, la mayoría de expertos consideran CMLA en aquellas pacientes con:

- **Tumores inoperables** IIIB-IIIC por afectación de pared torácica, piel, cambios inflamatorios, masa *bulky* axilar fija y/o afectación supraclavicular o mamaria interna.
    - En estos casos iniciaremos el tratamiento sistémico.

      Representa el 4-8,5 % de todos los casos, siendo su incidencia mayor en países en vías de desarrollo. Ante una paciente con una masa tumoral mamaria de las características señaladas anteriormente, se seguirá el mismo procedimiento diagnóstico establecido en el capítulo anterior.
- **Tumores "grandes operables" estadio clínico** IIB-IIIA.
    - En estos casos las pacientes tras la cirugía recibirán el tratamiento adyuvante recomendado
    - Se pueden manejar con las mismas estrategias que los tumores inoperables.

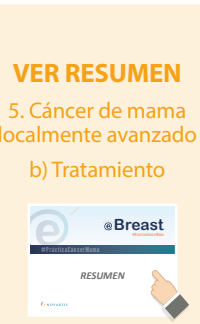
¿Cuáles son los factores pronósticos?

FACTORES PRONÓSTICOS

- Son los mismos que para el cáncer de mama con enfermedad localizada, siendo la afectación ganglionar y el tamaño tumoral los de mayor impacto en la supervivencia.
- Más del 80 % de las pacientes tratadas solo con cirugía, según series antiguas, a los 10 años han fallecido (335).
- En el Álamo III, la SLE y la SG a cinco años para las pacientes con estadio III eran del 58,6 % (56-61,1 %) y del 74,8 % (IC 95 % 72,5-77,0), respectivamente (336).

B. TRATAMIENTO

VER RESUMEN
5. Cáncer de mama localmente avanzado
b) Tratamiento



ELECCIÓN DEL TRATAMIENTO

Históricamente eran pacientes tratadas con mastectomía, pero fueron Haagensen y Cols (337) quienes definieron los **conceptos de cáncer de mama operable e inoperable**:

- Ulceración de la piel, edema y eritema
- Fijación del tumor a la pared torácica
- Afectación axilar *bulky* fija y/o afectación supraclavicular o mamaria interna

Estos factores se correlacionaron con el fracaso del tratamiento y se convirtieron en marcadores de irresecabilidad.

Debido a las repercusiones en la estadificación, se recomienda incluir estudios de imagen del tórax, abdomen y óseo con anterioridad al tratamiento sistémico.

El tratamiento es multidisciplinar: tratamiento sistémico, cirugía y radioterapia:

- La secuencia óptima no se ha establecido, pero parece que empezar por el tratamiento sistémico es ventajoso, al aumentar la resecabilidad y permitir una cirugía conservadora. **Hoy en día, el tratamiento sistémico previo a la cirugía se ha convertido en el estándar para todas las pacientes con CMLA.**
- Tratamiento sistémico: se seguirán las mismas recomendaciones dadas en el capítulo anterior.
- En el CMLA existen pocos estudios que evalúen el papel de la hormonoterapia previa a la cirugía, por lo que solo la recomendaremos a aquellas pacientes con tumores hormonosensibles no candidatas a quimioterapia, así como la actitud quirúrgica en caso de respuesta.

TRAS EL TRATAMIENTO SISTÉMICO

- En aquellos casos en los que no se consigue que el tamaño tumoral sea menor de 5 cm, se propone mastectomía con disección axilar (nivel I/II +/- reconstrucción inmediata)
- Si conseguimos una buena respuesta clínica y por imagen, considerar cirugía conservadora con disección axilar (nivel I/II).
- En caso de progresión durante la quimioterapia, se aconseja radioterapia para conseguir un control local y posteriormente tratamiento sistémico.

TRAS LA CIRUGÍA

- Radioterapia: debido al riesgo de recurrencia local, las pacientes recibirán tratamiento sobre la pared torácica y las áreas ganglionares.
- Se completará el tratamiento hormonal +/- terapia biológica siguiendo las mismas indicaciones que en el cáncer de mama precoz.

C. CARCINOMA INFLAMATORIO

¿Cuáles son los criterios diagnósticos?

¿Cuáles son los factores de riesgo para tener un CMI?

¿Cuál es el estudio de imagen que debemos hacer?

El tratamiento neoadyuvante es el estándar, pero ¿hay alguna diferencia?

¿Se puede hacer biopsia del ganglio centinela tras tratamiento neoadyuvante en el CMI? ¿Y reconstrucción inmediata?

VER RESUMEN

5. Cáncer de mama localmente avanzado

c) Carcinoma inflamatorio

Se considera un subgrupo del CMLA con características biológicas y comportamiento clínico diferente, por lo que algunos autores lo consideran una entidad aparte (338, 339). Representa entre el 1 y el 5 % de todos los tumores de mama, siendo el más agresivo de todos, con una supervivencia global media del 30-40 % a los cinco años (340).

En diciembre de 2008 se creó el Grupo internacional de expertos en cáncer de mama inflamatorio (CMI), con el fin de actualizar áreas de investigación, tratamiento y diagnóstico (341). Muchas de las ideas aquí reflejadas son del último consenso (342).

Se debe diferenciar del **"cáncer de mama secundario inflamatorio"**: son los cambios cutáneos que simulan un CMI pero que representan la recurrencia sobre la mama o pared torácica tratada previamente por un cáncer de mama no inflamatorio.

¿Cuáles son los criterios diagnósticos?

CRITERIOS DIAGNÓSTICOS

Es importante hacer un diagnóstico precoz, por el impacto que tiene en la supervivencia de la paciente el iniciar cuanto antes el tratamiento.

- **El diagnóstico es clínico con la confirmación histológica de un tumor invasivo en la mama.**
- **La afectación dérmica linfovascular es patognomónica, pero no necesaria para el diagnóstico (343).**
- **El diagnóstico diferencial se hará con una mastitis inflamatoria.**

Criterios mínimos para el diagnóstico:

En 2011 se publicó un documento de consenso con unos criterios mínimos diagnósticos así como recomendaciones de evaluación y tratamiento(342):

- Rápida aparición en la mama de eritema, edema y/o piel de naranja, y/o aumento de la temperatura mamaria, con o sin masa palpable subyacente.
- Puede existir aplastamiento, formación de costras o retracción del pezón.
- Mastitis refractaria al tratamiento antibiótico durante una semana como mínimo.
- Historia clínica de <6 meses de evolución.
- Eritema mamario que ocupa al menos 1/3 de la mama.
- A la exploración clínica: puede existir una masa palpable subyacente con o sin ganglios linfáticos palpables locorregionales con o sin anomalías del pezón.
- Confirmación histológica de carcinoma invasivo.
- Se recomienda obtener una adecuada biopsia cutánea (un mínimo de dos muestras de 2 - 8 mm) que documente la afectación linfovascular dérmica por émbolos tumorales.

El TNM lo define como T4d con la clínica descrita anteriormente (induración difusa de la piel con eritema, margen erisipeloide) y generalmente sin masa subyacente.

Como el tratamiento neoadyuvante es el estándar en estos pacientes, se recomienda que el TNM inicial sea clínico.

Diferencias con el carcinoma de mama invasivo no inflamatorio

A nivel histológico, el CMI:

- Suele presentar ausencia o mínimo componente de CDIS.
- Crecimiento menos compacto que en el CM no inflamatorio.
- A menudo presenta infiltración intraparenquimatosa con émbolos tumorales linfovasculares.
- Los cambios cutáneos se deben a la invasión linfática dérmica, émbolos tumorales, responsable de su alto potencial metastásico.

A nivel inmunohistoquímico:

- El 83 % presenta RH-; es además un factor pronóstico establecido en el CMI (340).
- EL CMI presenta un mayor porcentaje de positividad para HER2 (40 %), comparado con el CMLA y con el cáncer de mama no T4 (344).

Tanto la positividad de RH como de HER2 son factores predictores de respuesta en el CMI.

¿Cuáles son los factores de riesgo para tener un CMI?

FACTORES DE RIESGO

Los datos de los que disponemos son limitados, pero a diferencia del cáncer de mama no inflamatorio, hay un mayor porcentaje de pacientes con CMI en aquellas con (345):

- Menarquia temprana y edad del primer embarazo joven
- Pacientes premenopáusicas
- Sin embargo, el único factor de riesgo consistente relacionado es la obesidad(346)

¿Cuál es el estudio de imagen que debemos hacer?

ESTUDIO DE IMAGEN (347)

- **Mamografía y ecografía** con estadiaje ganglionar: se suele objetivar el engrosamiento cutáneo y, en el 95 % de los casos, la lesión mamaria a biopsiar.
- **RM mamaria**: tiene una mayor sensibilidad para detectar lesiones en la mama y facilitar la biopsia.
- **TAC toracoabdominal y gammagrafía ósea**: el 30 % de las pacientes con CMI presentan metástasis *de novo*.
- El papel del PET/TAC en este grupo de pacientes aún no está establecido.

El tratamiento neoadyuvante es el estándar pero ¿hay alguna diferencia?

TRATAMIENTO

- El tratamiento es MULTIDISCIPLINAR.
- En pacientes con CMI no metastásico el tratamiento incluye quimioterapia neoadyuvante, cirugía y disección ganglionar; posteriormente, radioterapia y tratamiento hormonal en caso de RH positivos, y anti-HER2 si hay sobreexpresión de HER2.
- No hay estudios específicos aleatorizados con quimioterapia para este subgrupo de pacientes, solo datos de estudios pequeños prospectivos o extrapolados de neoadyuvancia y, por ende, no hay un esquema quimioterápico específico.

En general se seguirán los mismos esquemas que para el tratamiento neoadyuvante.

- Se recomienda el uso de antraciclinas y taxanos.
- En pacientes con tumores HER2+ se recomienda el uso de trastuzumab y pertuzumab.

- Durante un mínimo de 4-6 meses, las pacientes deben recibir quimioterapia previa a la cirugía.
- En caso de progresión durante la quimioterapia:
  - No se recomiendan altas dosis de quimioterapia ni de bevacizumab.
  - No hay datos del uso de quimioterapia en la enfermedad residual en esta población.

Tabla 65. Esquemas usados en CMI en el estudio de Ueno et al. (348).

Estudio	Tipo de estudio	N	Esquema de tratamiento	pRC (%)	Respuesta (%)	SG (%)
Ueno et al (348)	Análisis combinado de 4 EECC prospectivos	178	Basado en A	NA	71	40 (5 años)

A: antraciclina; EECC: ensayos clínicos; NA: no aportado; SG: supervivencia global; pRC: respuesta patológica completa.

Tabla 66. Esquemas usados en CMI en el estudio de Harris et al. (349).

Estudio	Tipo de estudio	N	Esquema de tratamiento	pRC (%)	Respuesta (%)	SG (%)
Harris et al (349)	Retrospectivo	54	CMF, FAC o ambos	30	NA	56 (5 años)

CMF: ciclofosfamida, metrotexate y 5-FU; FAC: ciclofosfamida, adriamicina y 5-FU; NA: No aportado; SG: supervivencia global; pRC: respuesta patológica completa.

Tabla 67. Esquemas usados en CMI en el estudio de Baldini et al. (350).

Estudio	Tipo de estudio	N	Esquema de tratamiento	pRC (%)	Respuesta (%)	SG (%)
Baldini et al (350)	Análisis combinado de 2 EECC prospectivos	68	CEF o FAC	5,9	73,6	44 (5 años)

CEF: ciclofosfamida, epirrubicina, 5-FU; EECC: ensayos clínicos; FAC: ciclofosfamida, adriamicina y 5-FU; SG: supervivencia global; pRC: respuesta patológica completa.

Tabla 68. Esquemas usados en CMI en el estudio de Low et al. (351).

Estudio	Tipo de estudio	N	Esquema de tratamiento	pRC (%)	Respuesta (%)	SG (%)
Low et al (351)	Prospectivo	46	CAFM	NA	57	26,7 (10 años)

CAFM: ciclofosfamida, adriamicina, 5-FU, metrotexato; NA: no aportado; SG: supervivencia global; pRC: respuesta patológica completa.

Tabla 69. Esquemas usados en CMI en el estudio de Cristofanilli et al. (352).

Estudio	Tipo de estudio	N	Esquema de tratamiento	pRC (%)	Respuesta (%)	SG (%)
Cristofanilli et al (352)	Retrospectivo	240	FAC vs. FAC+P	10 vs. 25	74 vs. 82	41 vs. 52

FAC: ciclofosfamida, adriamicina y 5-FU; SG: supervivencia global; P: paclitaxel; pRC: respuesta patológica completa.

Tabla 70. Esquemas usados en CMI en el estudio de Hurley et al. (353).

Estudio	Tipo de estudio	N	Esquema de tratamiento	pRC (%)	Respuesta (%)	SG (%)
Hurley et al (353)	Prospectivo	48	D + CDDP +TR	17	NA	86 (4 años)

CDDP: cisplatino; D: docetaxel; NA: no aportado; SG: supervivencia global; pRC: respuesta patológica completa; TR: trastuzumab.

Tabla 71. Esquemas usados en CMI en el estudio de Gianni et al. (329). Estudio NOAH

Estudio	Tipo de estudio	N	Esquema de tratamiento	pRC (%)	Respuesta (%)	SLE (%)
Gianni et al (329). Estudio NOAH	Prospectivo	235 (63 con CMI)	AP + TR → P + TR → CMF + TR vs Misma QT sin TR	38 (con TR) vs. 19 (sin TR)	NA	71 (con TR) vs. 56 (sin TR) (3 años)

AP: adriamicina y paclitaxel; CMF: ciclofosfamida, metrotexate y 5-FU; CMI: cáncer de mama inflamatorio; NA: no aportado; SLE: supervivencia libre de enfermedad; pRC: respuesta patológica completa; TR: trastuzumab.

Tabla 72. Esquemas usados en CMI en el estudio de Boussen et al. (354).

Estudio	Tipo de estudio	N	Esquema de tratamiento	pRC (%)	Respuesta (%)	SG (%)
Boussen et al (354)	Prospectivo	49	L + P	18,2	78,1	NA

L: lapatinib; NA: no aportado; SG: supervivencia global; P: paclitaxel; pRC: respuesta patológica completa. Se reportan sólo los resultados en pacientes HER2 positivos.

Tabla 73. Esquemas usados en CMI en el estudio de Van Pelt et al. (355).

Estudio	Tipo de estudio	N	Esquema de tratamiento	pRC (%)	Respuesta (%)	SG (%)
Van Pelt et al (355)	Prospectivo	22 (9 con CMI)	TR + D	NA	40,9 %	NA

CMI: cáncer de mama inflamatorio; D: docetaxel; NA: no aportado; SG: supervivencia global; pRC: respuesta patológica completa; TR: trastuzumab.

Tabla 74. Esquemas usados en CMI en el estudio de Veyret et al. (356).

Estudio	Tipo de estudio	N	Esquema de tratamiento	pRC (%)	Respuesta (%)	SG (%)
Veyret et al (356)	Prospectivo	120	CEF -HD	14.7	91,1	41,2 (10 años)

CEF: ciclofosfamida, epirrubicina, 5-FU; HD: altas dosis; NA: no aportado; SG: supervivencia global; pRC: respuesta patológica completa.

Tabla 75. Esquemas usados en CMI en el estudio de Cheng et al. (357).

Estudio	Tipo de estudio	N	Esquema de tratamiento	pRC (%)	Respuesta (%)	SG (%)
Cheng et al (357)	Prospectivo	177 (10 % con CMI)	CBT →TMA	NA	NA	36 (5 años)

CBT: ciclofosfamida, carmustina, tiotepa; CMI: cáncer de mama inflamatorio; NA: no aportado; SG: supervivencia global; pRC: respuesta patológica completa; TMA: trasplante de células madre autólogo.

Tabla 76. Esquemas usados en CMI en el estudio de Viens et al. (358).

Estudio	Tipo de estudio	N	Esquema de tratamiento	pRC (%)	Respuesta (%)	SG (%)
Viens et al (358)	Prospectivo	90	CA	32	90	70 (3 años)

CA: ciclofosfamida, adriamicina; NA: no aportado; SG: supervivencia global; pRC: respuesta patológica completa.

MONITORIZACIÓN DE LA RESPUESTA

Se recomienda que sea una combinación de:

- Exploración física (cada 3-4 semanas) (359).
- Pruebas de imagen al final del tratamiento (mamografía + ecografía) y, aunque los datos son escasos, también con RMN.

Los estudios muestran que con la exploración física y las pruebas de imagen se infraestima la enfermedad residual en el 60 % de las pacientes (360).

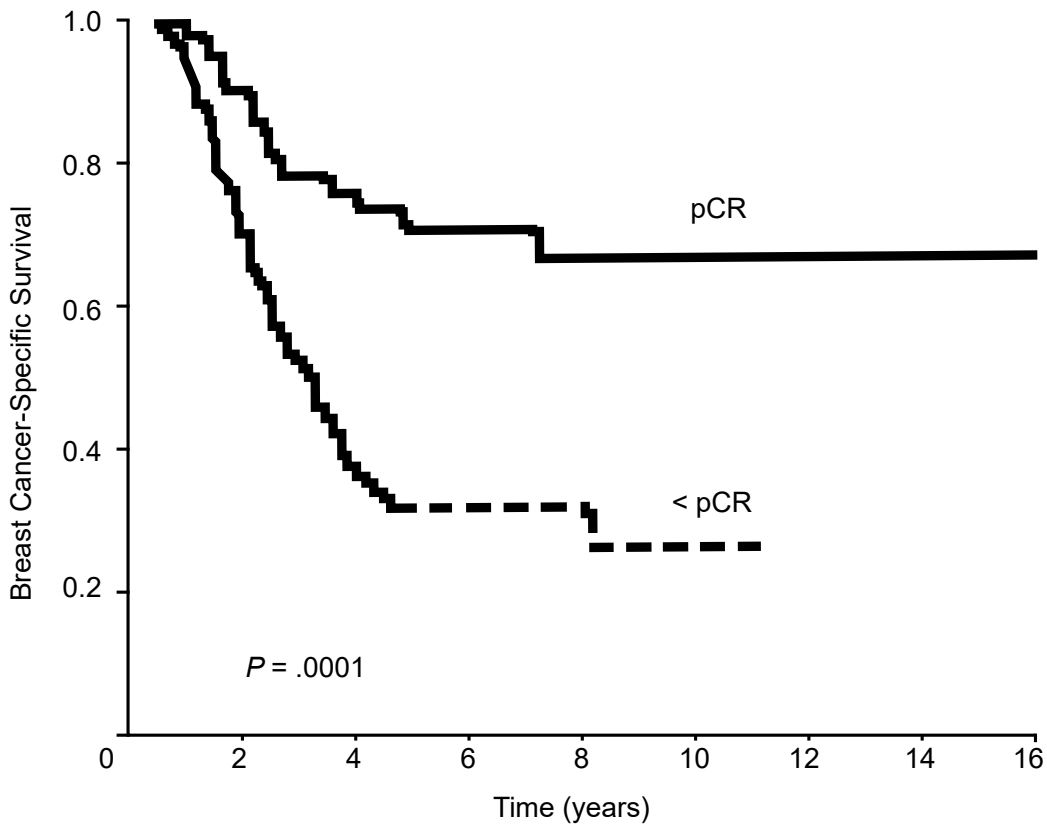
¿Se puede hacer biopsia del ganglio centinela tras tratamiento neoadyuvante en el CMI? ¿Y reconstrucción inmediata?

GANGLIO CENTINELA Y RECONSTRUCCIÓN INMEDIATA TRAS EL TRATAMIENTO NEOADYUVANTE

- **Está contraindicada la biopsia del ganglio centinela en pacientes con CMI (361); la tasa de falsos negativos es muy alta (362).**
- Tras el tratamiento neoadyuvante **se propondrá una MRM, estando contraindicada la mastectomía *skin sparing*.**

En el CMI, el grado de respuesta es un factor predictor del control local, supervivencia global y supervivencia libre de enfermedad (363) (Figura 14).

Figura 14. Supervivencia específica del cáncer de mama basada en la respuesta patológica completa (pRC) a la quimioterapia neoadyuvante seguida de mastectomía y radioterapia. ***Basada en Panades M. et al. (363).***



La **reconstrucción mamaria** es una opción tras la MRM, pero el *timing* es controvertido y por ello **se desaconseja que sea inmediata**, puesto que puede comprometer el campo de la radioterapia en la mama y los ganglios de la cadena mamaria interna (339).

- **Por tanto, todas las pacientes con CMI se tratarán con mastectomía y disección axilar.**

PAPEL DE LA RADIOTERAPIA EN EL CMI

Tras la mastectomía, todas las pacientes recibirán radioterapia sobre:

- Pared torácica
- Ganglios axilares, infraclavicular y supraclavicular

En el CMI la radioterapia mejora el control local sin haber mostrado una mejora en la supervivencia en estas pacientes. Generalmente se usan dosis >50 Gy.

El beneficio de una mayor dosis (66 Gy) es mayor en aquellas pacientes con más riesgo de recurrencia (364):

- <45 años
- Márgenes positivos o próximos
- ≥4 ganglios afectos tras la cirugía
- Pobre respuesta al tratamiento neoadyuvante

TRATAMIENTO HORMONAL NEOADYUVANTE

Para aquellas pacientes ancianas o con comorbilidades y tumores luminales de lento crecimiento y no candidatas a tratamiento citostático, se recomienda tratamiento hormonal neoadyuvante.

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