VII SIMPOSIO NACIONAL
de ONCOLOGÍA de PRECISIÓN
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Anticuerpos biespecíficos
Papel en cáncer de mama

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Conflictos de interés

Trabajo en Osakidetza /Servicio Vasco de Salud

He colaborado como ponente/asesor: Pfizer, Novartis, Lilly, Pierre Fabre, Roche , Gilead, Astra Zeneca, Daiichi-Sankyo, GSK, MSD.

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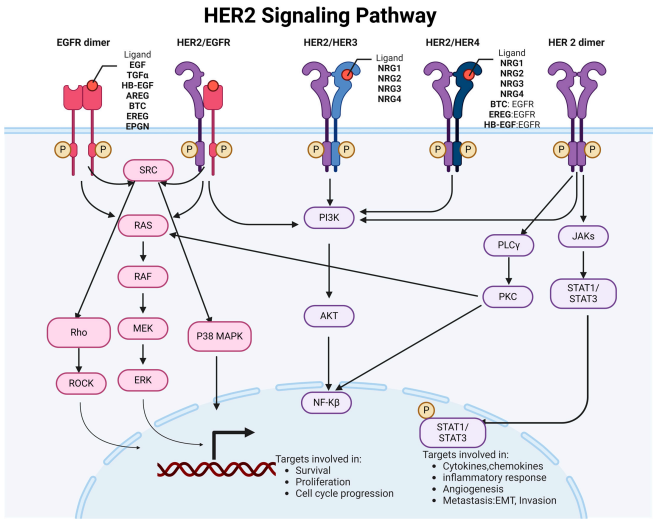
BsAb estudios preclínicos cáncer de mama

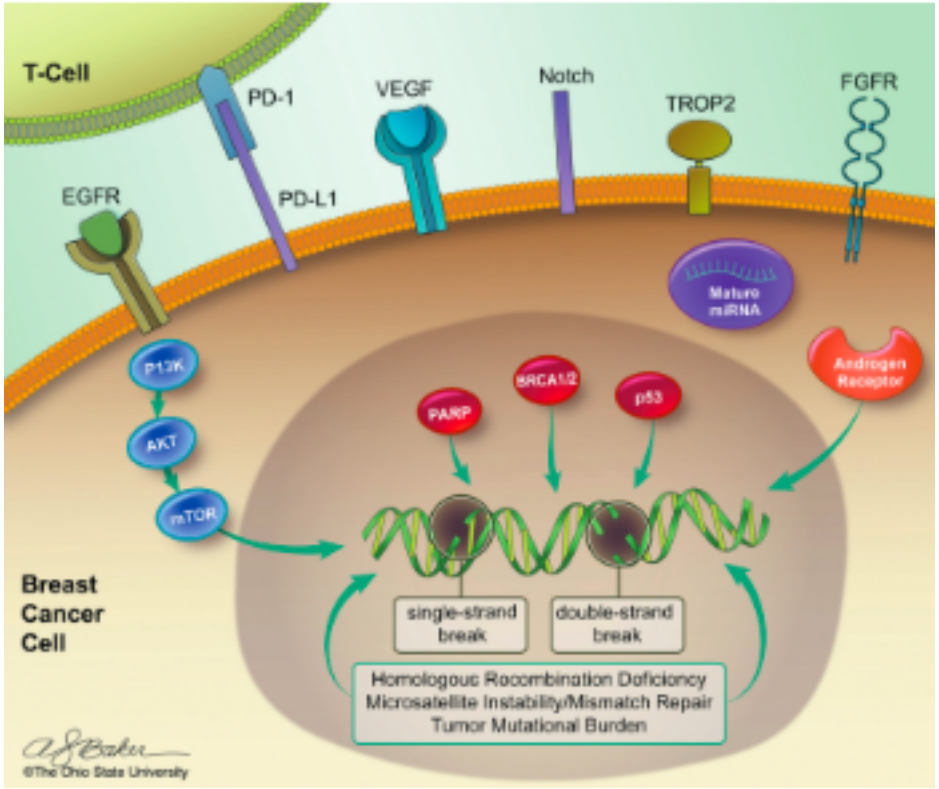
BsAbs	BsAbs Targets	Details of study	Outcomes
HB-32	DLL4 and VEGF Derived from Bevacizumab and H3L2 was use as the parental mAb The anti-DLL4 antibody (H3L2) was generated using the hybridoma technique and humanized transformation	*In vitro* MDA-MB-231 cells *In vivo* BALB/c nude mice	•Effectively inhibited the proliferation migration and tube formation of HUVEC which are involved in angiogenesis •HB-32 inhibited the proliferation of BCa cells and induces tumor cell apoptosis more effectively than treatment with an anti-VEGF antibody or an anti-DLL4 antibody alone
HER2xPRLR bispecific ADC	HER2 and PRLR A fully human mAb to human PRLR and "in-house trastuzumab"	*In vitro* HEK293 cells	•Significantly enhanced the degradation of HER2 and the cell-killing activity of a noncompeting HER2 ADC—in BCa cells that coexpressed HER2 and PRLR
PRLR-DbsAb	PRLR and CD3	*In vitro* MDA-MB-231 MCF-7 and SKBR-3 cells *In vivo* Female NOD/ SCID mice	•Activated T cells and stimulated the release of antitumor cytokines •Showed significant inhibition of tumor growth and increased survival compared to traditional mAb treatment
MDX-21	HER2 and FcγRI (CD64)	*In vitro* SK-BR-3 BT-20 T-47D	•Induce phagocytosis and cytolysis of BCa cells by human MDMs •Induced ADCP and ADCC •Combining MDX-H210 and G-CSF did not demonstrate significant therapeutic efficacy regarding clinical responses •Isolated neutrophils from patients undergoing G-CSF treatment displayed high cytotoxicity in the presence of MDX-210
MesobsFab	Mesothelin and FcγRIII (CD16)	*In vitro* BT-474 HCC1806 SK-BR-3 and MDA-MB-231 *In vivo* Humanized xenograft models	•Facilitated the recruitment and infiltration of NK cells into tumor spheroids •Induced ADCC •Elicited dose-dependent cell-mediated cytotoxicity against mesothelin-positive tumor cells •Induced cytokine secretion •Reduced cell invasiveness
HER2bsFab	HER2 and FcγRIII (CD16) Fab-like BsAb	*In vitro* SK-OV-3 SK-BR-3 BT-474 MCF-7	•Effectively inhibited the growth of HER2-high tumors by recruiting resident effector cells expressing mouse FcγRIII and IV •Showed superior inhibition of HER2-low tumor growth compared to trastuzumab
BsAb	HER2 and FcγRIII (CD16) A trivalent anti-erbB2/anti-CD16 BsAb	*In vitro* SKBR3 cells	•Activated NK cells to enhance anti-tumor immune responses

BsAbs	BsAbs Targets	Details of study	Outcomes
TP_L	HER2 epitops BsAb Sources: trastuzumab and pertuzumab	*In vitro* BT-474 SK-BR-3 HCC-1954 MDA-MB-231 MDA-MB-468 and MCF-7 *In vivo* female BALB/c mice	•Superior blocking action against HER2 heterodimerization compared to the combination of trastuzumab and pertuzumab •Effectively inhibits HER2 signaling in trastuzumab-resistant BCa cell lines •Outperforms trastuzumab plus pertuzumab in inhibiting the growth of trastuzumab-resistant BCa cell lines •Eradicates established trastuzumab-resistant tumors in mice
p95HER2-TCB	P95HER2 and CD3ε	*In vitro* MCF7 MCF10A Jurkat cells *In vivo* Humanized xenograft models	•Potent anti-tumor effects on primary BCas and brain lesions that express p95HER2 •Unlike TCBs targeting HER2 the p95HER2-TCB had no impact on nontransformed cells that do not overexpress HER2
Four types of BsAbs	HER2 and CD3 IgG-based bsAbs	*In vitro* SKBR3 Her2 3 +; MDA MB453 Her2 2 +; MDA MB231 Her2 1 +; MDA MB468 Her2 0 *In vivo* xenograft NGS mice model	•Different valencies of the BsAbs did not significantly impact their effectiveness in fighting tumors •Fc domain enhanced the BsAbs' ability to induce cytotoxic activity against the cancer cells •The Fc domain also triggered T-cell activation in a manner unrelated to the presence of the target antigen •The BsAbs efficiently redirected T cells to effectively eliminate all cancer cells expressing HER2 including those with low levels of HER2 expression
BiMAbs	HER2/EGFR/CEA/EpCAM and αCD3/αCD28 IgG1-Fc based format	*In vitro* MCF-7 HT-1080/FAP	•Effectively activated T cells and induced cytotoxicity only in the presence of tumor cells •Combination treatment with αTAA–αCD3 BiMAb and co-stimulatory αTAA–αCD28 or αTAA–TNFL fusion proteins significantly enhanced T cell activation proliferation activation marker expression cytokine secretion and tumor cytotoxicity
HER2-BsAb	HER2 and CD3	*In vitro* HCC1954 *In vivo* BALB-$Rag2^{-/-}$IL-2R-γc-KO (DKO) mice	•Promoted of T-cell infiltration and suppression of tumor growth mainly when used in conjunction with human PBMC or ATC
BAb	CEA and HER2 Murine IgG1 subclass	*In vitro* SKOv3-CEA-1B9 *In vivo* Double-positive tumour-bearing nude mice	•Enhanced tumor localization compared to single-specificity antibodies
DF3xH22	MUC-1 and HER2	*In vitro* R75-1 MCF-7 BT-20 T-47D SKBR-3	•Mediated the phagocytosis of MUC-1-expressing target cells •Inducing ADCP
BsAb; mPEG × HER2	mPEG and HER2 Anti-HER2 scFv and anti-DNS scFv	*In vitro* MCF7/HER2 ($HER2^{high}$) and MCF7/neo1 ($HER2^{low}$) *In vivo* BALB/c nude mice	•One-step formulation of PLD using mPEG × HER2 enhanced tumor specificity increased drug internalization and improve the anticancer activity of PLD against HER2-overexpressing and doxorubicin-resistant BCa
TC-BsAb	EGFR and HER2	*In vitro* BT-474 and SK-BR-3 *In vivo* female BALB/c nude mice	•Demonstrated significantly greater potency in inhibiting the growth of BCa cell lines compared to trastuzumab cetuximab and the combination of trastuzumab plus cetuximab
Anti-EGFR/ VEGFR2 BsAb	EGFR and VEGFR2 Cetuximab IgG linked to the scFv of ramucirumab via a glycine linker	*In vitro* MDA-MB-231 BT-20 MDA-MB-468 BT549 and HS578 T *In vivo* female athymic nude mice	•Inhibited EGFR and VEGFR2 in TNBC cells disrupting the autocrine mechanism •Inhibited ligand-induced activation of VEGFR2 and blocked the paracrine pathway mediated by VEGF secreted from TNBC cells in endothelial cells

Lan HR, Front Immunol. 2023 Dec 4;14:1266450.

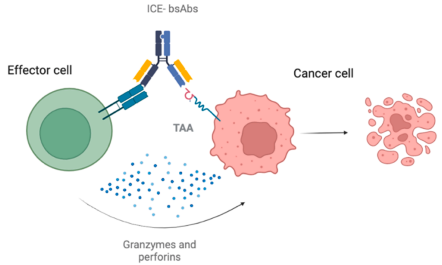
BsAb en cáncer de mama: principales líneas





Cheng, X. *Genes* 2024, *15*, 903.

The immune cell engagers (ICEs) era in breast cancer



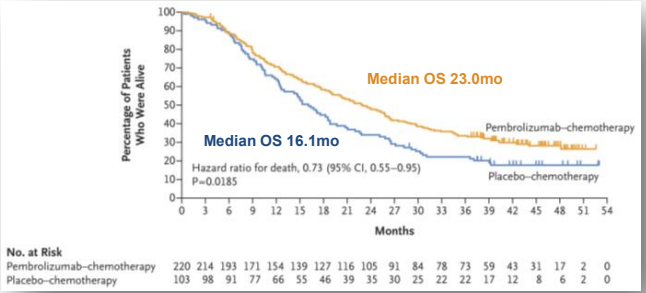
Trial Identifier	Drug	Phase	Engagement	Cancer type	Main AEs	Outcomes	Trial status
NCT00351858	Ertumaxomab	I	HER2xCD3	HER2+ BC	G3 Lymphocytopenia (76 %) G3 Elevation of liver enzymes (47 %) 1 severe hypotension and ARDS 1 SIRS and AKI	1/15 CR 2/15 PR 2/15 SD	Terminated
NCT01569412	Ertumaxomab	I/II	HER2xCD3	HER2+ advanced solid tumors	G3 Fatigue (43 %) G3 Fever (14 %) G3 Pain (21 %) 1 Allergic reaction 1 SIRS	1/11 PR 2/11 SD	Terminated
NCT03330561	PRS−343	I	HER2x4–1BB	HER2+ solid tumors	IRR (25 %) Nausea (7 %) Arthralgia (5 %)	12 % ORR 52 % DCR	Completed
NCT03922204	MCLA−145	I	PD-L1x4–1BB	Advanced solid tumors	G3 febrile neutropenia ALT/AST elevation Fatigue Myositis	NA	Recruiting
NCT04128423	AMV564 +/-Pembrolizumab	I	CD33xCD3	Advanced solid tumors	Pyrexia, injection site reactions, fatigue, anemia, hypotension, pruritis, chills, and nausea G2 CRS	1/20 CR	Active, not Recruiting
NCT02324257	RO6958688	I	CD3xCEA	CEA+ advanced solid tumours	G3 IRR (16.3 %) G3 diarrhea (5 %)	2/36 PR	Completed
NCT02650713	RO6958688 + Atezolizumab	I	CD3xCEA	CEA+ Advanced solid tumours	IRR, Diarrhea, G3 dyspnea, G3 hypoxia G4 colitis G5 respiaratory failure	2/10 PR	Completed
NCT04501744	M701	I	CD3xEpCAM	EpCAM+ tumor cells in ascites	Hypoproteinemia anemi hypokalemia hyponatremia	ORR 62.5 %; DCR 100 %;	Recruiting
NCT04143711	DF1001	I/II	HER2xCD3xCD16	HER2+ advanced solid tumors	infusion related reactions (26 %) asthenia (15 %) fatigue (12 %),	5 PR 22 SD CBR 39.7 %	Recruiting

Caltavituro A.Crit Rev Oncol Hematol. 2025

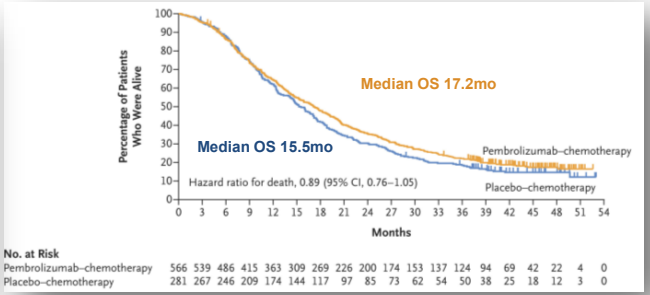
CMMTN Inmuno-quimioterapia

- **KEYNOTE (KN)-355:** Demonstration of the efficacy of PD-1 blockade with pembrolizumab in combination with chemotherapy as a first-line for patients with mTNBC with high expression of PD-L1 (CPS ≥ 10).

Overall Survival (OS) in CPS ≥ 10 Subgroup



OS in the ITT population – All CPS



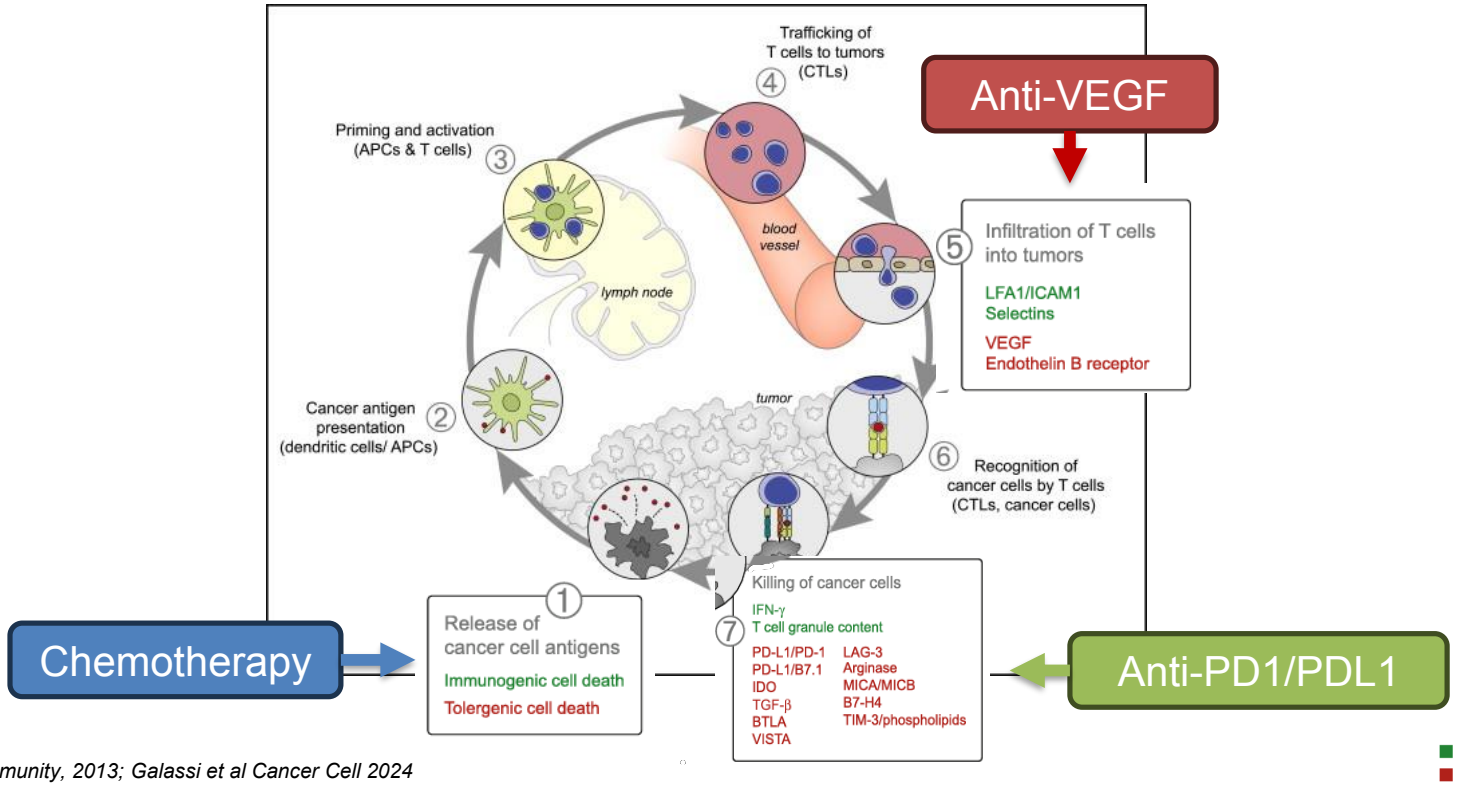
ITT – All CPS		
	Pembro + Chemo	**Placebo + Chemo**
	N = 566	**N = 281**
ORR	41.0% (36.9 - 45.2)	35.9% (30.3 - 41.9)
PFS, median	7.5 mo (6.3 - 7.7)	5.6 mo (5.4 - 7.3)
OS, median	17.2 mo (15.3-19.0)	15.5 mo (13.9 -17.2)

In Pre-KN522 era
60-70% of patients are not candidates for anti-PD1 in 1st line setting

Cortes et al NEJM 2022; Rugo et al SABCS 2021; Cortes et al Lancet 2020; Sigurjonsdottir et al Breast Cancer Res 2023

ITT : Intention to treat
Mo: months
ORR: Objective Response Rate
PFS progression free survival

CMMTN Incrementar Inmunogenicidad



Chen, Daniel S. et al. Immunity, 2013; Galassi et al Cancer Cell 2024

VII SIMPOSIO NACIONAL de ONCOLOGÍA de PRECISIÓN

CMMTN 1ª línea taxanos+ antiVEGF-Anti PD1/PDL1

BARCELONA 2024 ESMO congress

A Phase Ib/II Study to Assess the Safety and Efficacy of PM8002/BNT327 in Combination with Nab-Paclitaxel for First Line Treatment of Locally Advanced or Metastatic Triple-Negative Breast Cancer

Jiong Wu[1,2], Jian Zhang[2,3], Zhongsheng Tong[4], Qingyuan Zhang[5], Yongsheng Wang[6], Qiao Cheng[7], Xin Chen[8], Zhihua Li[9], Yongmei Yin[10], Yiqun Du[2], Yanchun Meng[2]

[1]Department of Breast Surgery, Fudan University Shanghai Cancer Center, Shanghai, China. [2]Department of Oncology, Fudan University Shanghai Cancer Center, Shanghai, China. [3]Phase I Clinical Trial Center, Fudan University Shanghai Cancer Center, Shanghai, China. [4]Department of Breast Oncology, Tianjin Medical University Cancer Hospital, Tianjin, China. [5]Department of Breast Oncology, Harbin Medical University Cancer Hospital, Heilongjiang, China. [6]Breast Disease Center, Shandong Cancer Hospital, Shandong, China. [7]Department of Breast Surgery, The First Affiliated Hospital Of Chongqing Medical University, Chongqing, China. [8]Department of Oncology, The Second People's Hospital of Yibin, Sichuan, China. [9]Department of Breast Surgery, Nanchang People's Hospital, Jiangxi, China. [10]Department of Oncology, Jiangsu Province Hospital, Jiangsu, China.

Presenter: Dr Yanchun Meng

Phase I Clinical Trial Center, Fudan University Shanghai Cancer Center, Shanghai, China.

BARCELONA 2024 ESMO congress

Evaluation of the Safety and Efficacy of Ivonescimab in Combination with Chemotherapy as First-line (1L) Treatment for Triple-negative Breast Cancer (TNBC)

Quchang Ouyang[1], Xiaojia Wang[2], Can Tian[1], Xiying Shao[2], Jian Huang[2], Zhanhong Chen[2], Yongsheng Wang[3], Tao Sun[4], Tienan Yi[5], Xufang Yu[6], Zhongmin Wang[6], Baiyong Li[6], Yu Xia[6]

[1]Breast Medicine Department, Hunan Provincial Tumor Hospital, Changsha, China; [2]Breast Medicine Department, Zhejiang Cancer Hospital, Hangzhou, China; [3]Breast surgery Section One, Affiliated Cancer Hospital of Shandong First Medical University, Jinan, China; [4]Breast Medicine Department, Liaoning Cancer Hospital and Institute, Shenyang, China; [5]Oncology Department, Xiangyang Central Hospital, Xiangyang, China;[6]Akeso Biopharma, Inc., Zhongshan, China

Presenter : Dr. Xiaojia Wang

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DECEMBER 10–13, 2024

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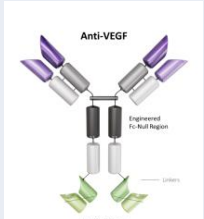
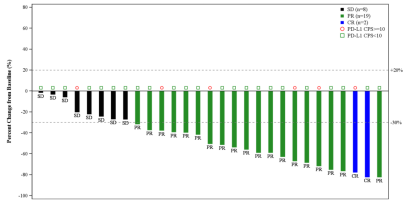
CMMTN 1ª línea taxanos+ antiVEGF-Anti PD1/PDL1

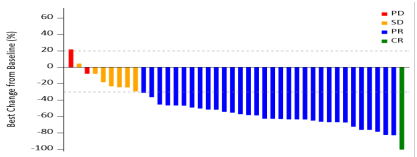
	Ivonescimab	PM8002/BNT327
Type	anti–PD1 and VEGF-A bispecific antibody	anti–PDL1 and VEGF-A bispecific antibody
Structure		
Study Design	Phase II	Phase Ib/II
Population	No previous systemic therapy DFI ≥12 months	No previous systemic therapy
Intervention	Ivonescimab + Paclitaxel or nab-Paclitaxel	PM8002/BNT327 + nab-Paclitaxel
N	36	42
PD-L1 CPS ≥10	6 (16.7%)	9 (21.4%)
Liver/Brain metastases	7 (19.4%) / 1 (2.8%)	16 (38.1%) / 2 (4.8%)
Neo/adjuvant Taxane	28 (66.7%)	20 (55.6%)
Neo/adjuvant anti-PDL1	No ?	No

Wu J, Wang Q
ESMO 24 /SABCS24

CMMTN 1ª línea taxanos+ antiVEGF-Anti PD1/PDL1

	Ivonescimab N=36	PM8002/BNT327 N=42
ORR	**80.0% (63.1-91.1)**	**73.8% (58.0, 86.1)**
Progressive Disease	0	2 (4.8%)
PFS Median, mo	9.36 mo (6.24 - NE)	13.5 mo (9.4 - 19.3)
OS	-	12-mo OS rate: 80.8% (65.3 - 89.9)





	PDL1 CPS <1 N=17	PDL1 CPS <10 N=29	PDL1 CPS ≥10 N=6
ORR	88.2% (63.6-98.5)	79.3% (60.3-92.0)	83.3% (35.9-99.6)
PFS	9.30mo (5.26-NE)	9.30mo (5.55-NE)	NR (5.36-NE)

	PDL1 CPS<1 N=13	PDL1 1≤CPS<10 N=16	PDL1 CPS≥10 N=9
ORR	76.9% (46.2, 95.0)	56.3% (29.9, 80.3)	100% (66.4, 100)
PFS	18.1mo (5.7, NR)	14.0mo (7.2, NR)	10.8mo (5.5, 13.5)

Significant antitumor activity and low primary resistance
ORR and PFS seem independent of PDL1 expression

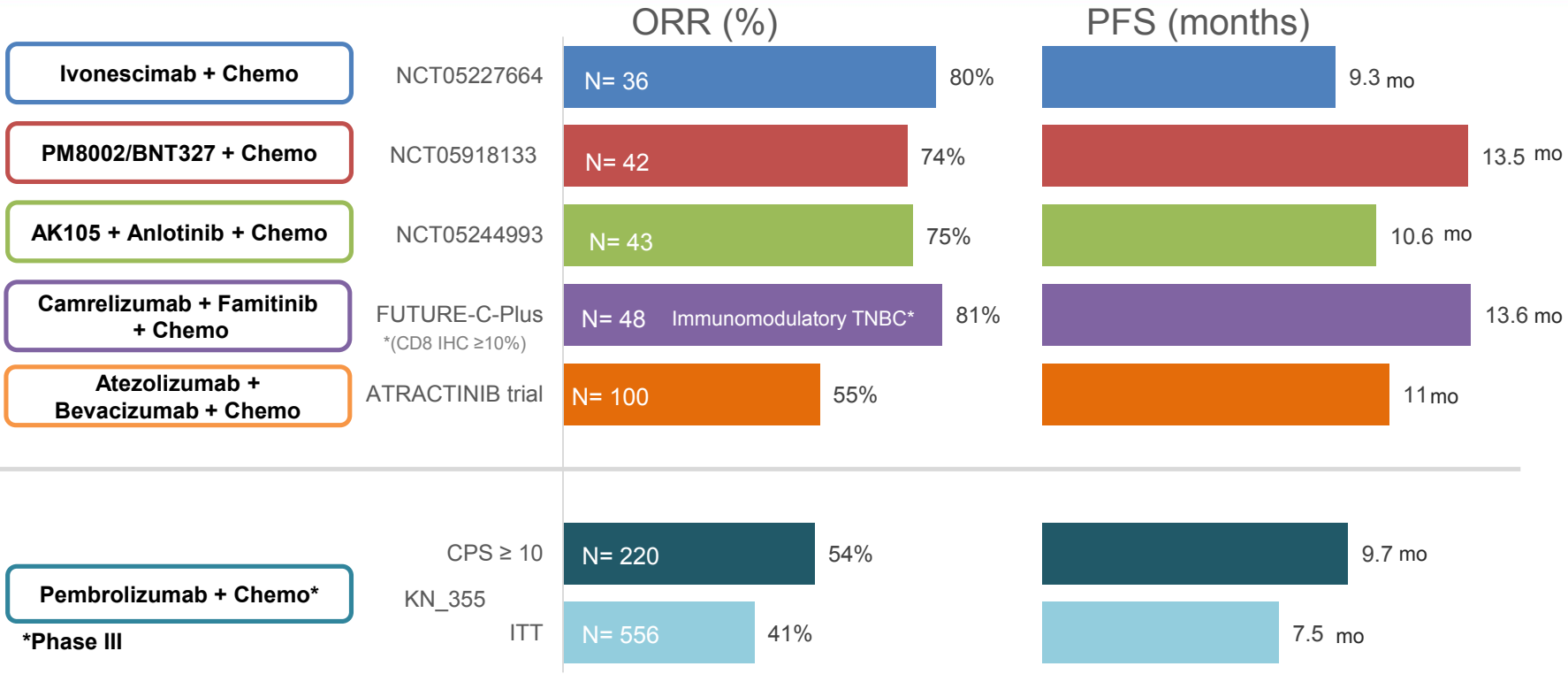
Wu J, Wang Q
ESMO 24
SABCS24

CMMTN 1ª línea taxanos+ antiVEGF-Anti PD1/PDL1

	Ivonescimab (Any/G3-4) N=36		PM8002/BNT327 (Any/G3-4) N=42	
TRAEs	100%	50%	100%	59.5%
TRAEs leading to discontinuation	0		9.5%	
Hematological • Neutrophil decreased • Anemia	 56% 47%	 19% 3%	 85% 76%	 20% 5%
Hepatotoxicity	50%	5.6%	28%	<5%
Anti-VEGF toxicities • Hypertension • Proteinuria	 -	 -	 23.8% 64%	 5% 5%
IrAEs	-	-	31.0%	9.5%
Death	0		0	

Wu J, Wang Q
ESMO 24
SABCS24

CMMTN 1ª línea antiVEGF-Anti PD1/PDL1: Contexto



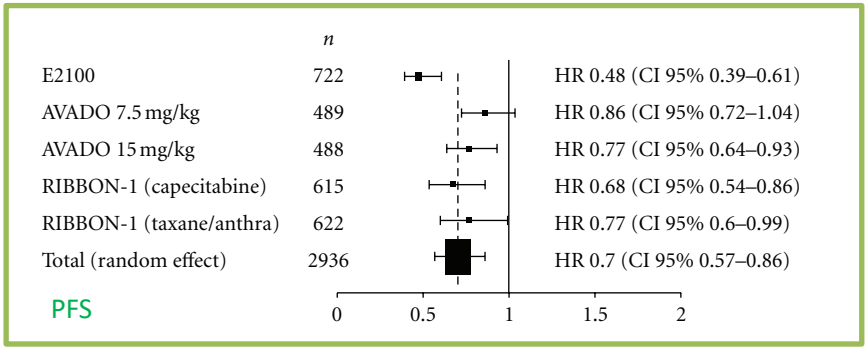
Ouyang et al, Wu et al, Zhang et al SABCS24; Gion M SABCS 2023; Chen et al Clinical Cancer Research 2022; Cortes et al NEJM 2022

⚠ **indirect and informal comparison**

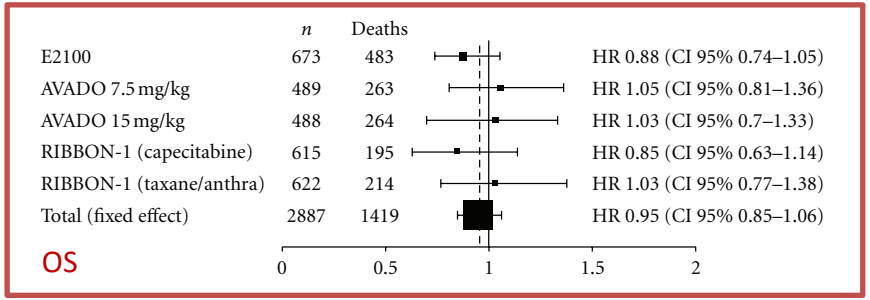
CMMTN 1ª línea antiVEGF-Anti PD1/PDL1

Conclusiones

Datos prometedores
Estudios precoces No randomizados



- Necesario confirmar actividad “ triplete”→ ¿SG?
- ¿Quién necesita “Triplete”?
- Biespecíficos > doble boqueo ?
- ¿Combo ideal? ¿QT? ¿ADC?
- ¿Biomarcadores?
- Otros subtipos tumorales



Rossari JCO 2012

Recruiting

PM8002 or Placebo Plus Nab-Paclitaxel as First-line Treatment in Inoperable Locally Advanced/ Metastatic Triple-negative Breast Cancer

ClinicalTrials.gov ID NCT06419621

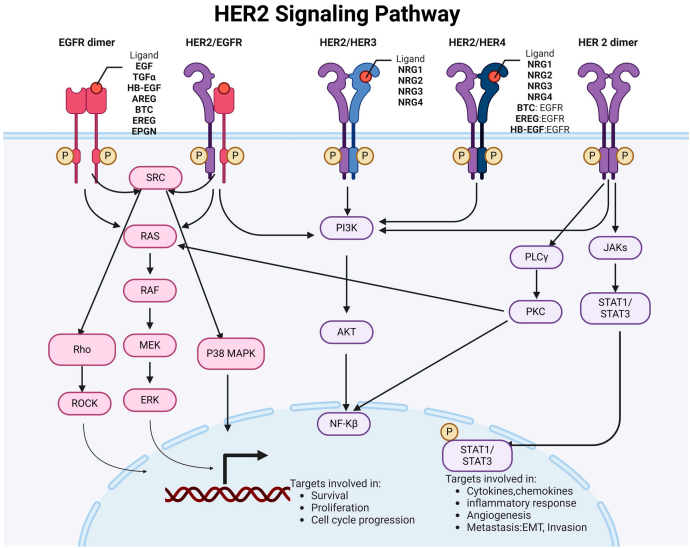
Sponsor Biotheus Inc.

Information provided by Biotheus Inc. (Responsible Party)

Last Update Posted 2024-12-03

Ca. Mama →BsAb via Her2

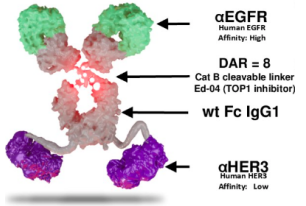
BsAbs	BsAbs Targets	Details of study	Outcomes	Ref/NCT
Combination of G-CSF and MDX-210	HER2 and FcγRI	*In vitro* *In vivo* Phase I clinical trial	•Effectively induced lysis of HER2 overexpressing BCa cell lines •The therapy was generally well tolerated although some patients experienced fever and short periods of chills which correlated with elevated plasma levels of IL-6 and TNF-α •A decrease in total WBC count and ANC •Isolated neutrophils from patients undergoing G-CSF treatment displayed high cytotoxicity in the presence of MDX-210	(127)
Combination of G-CSF and MDX-210	HER2 and FcγRI	Phase I clinical trial	•Common side effects included fevers in 19 patients diarrhea in 7 patients and allergic reactions in 3 patients which did not necessitate discontinuation of therapy •The beta-elimination half-life of MDX-H210 ranged from 4 to 8 hours at doses up to 20 mg/m2 •Release of cytokines IL-6 G-CSF and TNF-α •Increasing human anti-BsAb after the third infusion •No objective clinical responses	(128)
KN026	HER2 (domain II and IV) From heavy chains of pertuzumab and trastuzumab27 with a common light chain	KN026-CHN-001 Phase I first-in-human multicenter open-label single agent dose-escalation and dose-expansion study	•Increased ORR and median PFS in patients with co-amplification of HER2/CDK12	(129) NCT03619681
HER2 BATs	HER2 and CD3 Two cross-linked mAbs	Phase II clinical trial	•Increased Th1 cytokines Th2 cytokines and chemokines were observed after HER2 BATs infusions •Enhanced adaptive and innate antitumor responses Immune consolidation with HER2 BATs after chemotherapy increased the proportion of patients who remain stable at four months and improves the median OS for both HER2-HR$^+$ and TNBC patient groups	(130) NCT01022138
HER2Bi armed anti-CD3–activated T cells in combination with low-dose IL-2 and GM-CSF	HER2 and CD3 BsAb sources: Trastuzumab heteroconjugated to OKT3	Phase I clinical trial	•Increasing OS •Increasing IFN-γ and Th1 cytokines in the patient's blood indicating enhanced immune responses. These infusions induced •Inducing antigen-specific T cell and antibody responses against HER2 CEA and EGFR	(131) NCT00027807



Lan HR, Front Immunol. 2023 Dec 4;14:1266450.

BL-B01D1, a first-in-class EGFRxHER3 bispecific antibody-drug conjugate, in patients with Locally Advanced or Metastatic Breast Cancer and other Solid Tumor: Updated results from a Phase I study

Jiong Wu[1*], Jian Zhang[1*], Yiqun Du[1], Yanchun Meng[1], Sa Xiao[2], Hai Zhu[2], Yi Zhu[3]
[1]Fudan University Shanghai Cancer Center, [2]Baili-Bio (Chengdu) Pharmaceutical Co., Ltd., [3]Sichuan Biokin Pharmaceutical Co., Ltd., * Contributed equally



Safety

- The most common Grade ≥3 treatment-related adverse events (TRAEs) were anemia (41.4%), leukopenia (42.6%), neutropenia (52.5%), thrombocytopenia (26.5%).
- One drug-related death (febrile neutropenia) was observed.
- No interstitial lung disease (ILD) was observed.

Table 2. TRAE Summary (Freq ≥ 20%)

	Total (N = 162)	
Preferred Term (PT), n(%)	All Grade	Grade ≥G3
Anemia	149 (92.0)	67 (41.4)
Leukopenia	145 (89.5)	69 (42.6)
Neutropenia	141 (87.0)	85 (52.5)
Thrombocytopenia	111 (68.5)	43 (26.5)
Nausea	96 (59.3)	6 (3.7)
Stomatitis	79 (48.8)	9 (5.6)
Aspartate aminotransferase increased	78 (48.1)	0
Asthenia	75 (46.3)	17 (10.5)
Alanine aminotransferase increased	73 (45.1)	0
Vomiting	69 (42.6)	1 (0.6)
Hypertriglyceridaemia	62 (38.3)	2 (1.2)
Alopecia	55 (34.0)	0
Hypokalaemia	55 (34.0)	6 (3.7)
Decreased appetite	54 (33.3)	1 (0.6)
Hyperglycaemia	50 (30.9)	0
Constipation	44 (27.2)	1 (0.6)
Hyponatraemia	43 (26.5)	2 (1.2)
Hypoalbuminemia	42 (25.9)	0
Hypercholesterolemia	41 (25.3)	0
Urinary tract infection	38 (23.5)	1 (0.6)
Weight decreased	38 (23.5)	0
Blood alkaline phosphatase increased	36 (22.2)	0
Diarrhea	35 (21.6)	3 (1.9)
Blood lactate dehydrogenase increased	33 (20.4)	0

[1] Leukopenia combined white blood cell count decreased and leukopenia;
[2] Neutropenia combined neutrophil count decreased, neutropenia, and febrile neutropenia;
[3] Anemia combined anemia and hemoglobin count decreased;
[4] Thrombocytopenia combined platelet count decreased and thrombocytopenia;
[5] Stomatitis combined stomatitis, aphthous stomatitis, mouth ulceration, oral mucosa erosion, and oral mucosal blistering.

Table 3. Efficacy by Tumor subtype

	TNBC		HR+HER2- BC		HER2+ BC
	Total	Prior 1-2L chemotherapy	Total	Prior 1-2L chemotherapy	Total
	(N = 44)	(N = 26)	(N = 77)	(N = 46)	(N = 40)
Median prior line of therapy (Range)	2 (1-10)	2 (1-3)	3 (0-13)	3 (1-7)	4 (0-8)
Best Overall Response (BOR), n					
CR	1*	1*	1#	1#	0
PR	14	12	35	24	19
cPR	15	13	28	20	19
SD	21	7	25	13	13
PD	4	2	9	6	7
NE	4	4	7	2	1
ORR, % (95%CI)	34.1% (20.5, 49.9)	50.0% (29.9, 70.1)	46.8% (35.3, 58.5)	54.3% (39.0, 69.1)	47.5% (31.5, 63.9)
ORR confirmed, % (95%CI)	34.1% (20.5, 49.9)	50.0% (29.9, 70.1)	37.7% (26.9, 49.4)	45.7% (30.9, 61.0)	47.5% (31.5, 63.9)
DCR, % (95%CI)	81.8% (67.3, 91.8)	76.9% (56.4, 91.0)	79.2% (68.5, 87.6)	82.6% (68.6, 92.2)	80.0% (64.4, 91.0)
Median DOR (months) (95% CI)	11.5 (4.6, NR)	11.5 (4.6, NR)	7.4 (5.6, NR)	7.1 (5.4, 9.8)	7.4 (4.6, 9.8)
Median PFS (months) (95% CI)	5.8 (4.3, 12.7)	6.9 (4.0, 13.7)	7.0 (5.5, 8.5)	8.3 (5.7, 11.1)	7.0 (3.2, 9.0)
6-month PFS rate (%) (95% CI)	48.4 (31.5, 63.4)	58.2 (34.8, 75.8)	58.1 (45.2, 69.0)	66.8 (49.6, 79.4)	55.2 (37.5, 69.8)
Median OS (months) (95% CI)	NR (13.2, NR)	NR (13.2, NR)	NR (NR, NR)	NR (NR, NR)	NR (15.1, NR)
12-month OS rate (%) (95% CI)	68.9 (51.4, 81.2)	74.0 (50.6, 87.5)	67.7 (54.4, 77.9)	74.0 (56.2, 85.4)	78.9 (54.6, 91.1)

* CR was not confirmed as of cutoff date but was confirmed as of October 10th, 2024. # CR was confirmed as of cutoff date.
NE: assigned to patients enrolled without post baseline scan, except for one patient's post baseline evaluation was not evaluable.

Toxicidad hematológica (G3-G4)
Anemia 41.4%
Neutropenia 42.6%
Trombopenia 26.5%
No ILD

Zanidatamab in Combination With Evorpacept in HER2-Positive and HER2-Low Metastatic Breast Cancer: Results From a Phase 1b/2 Study

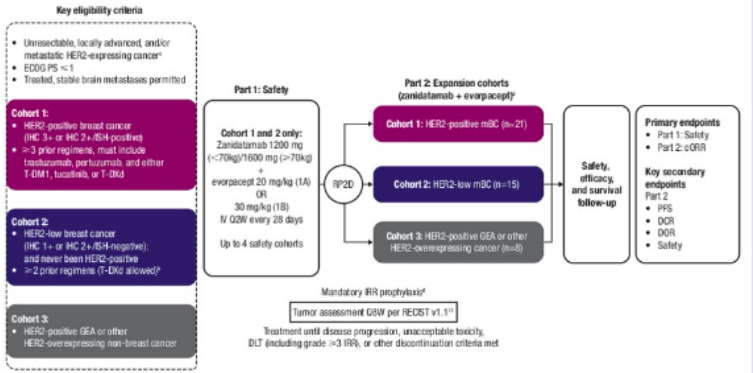


Table 2. Summary of Safety Outcomes (All Patients)

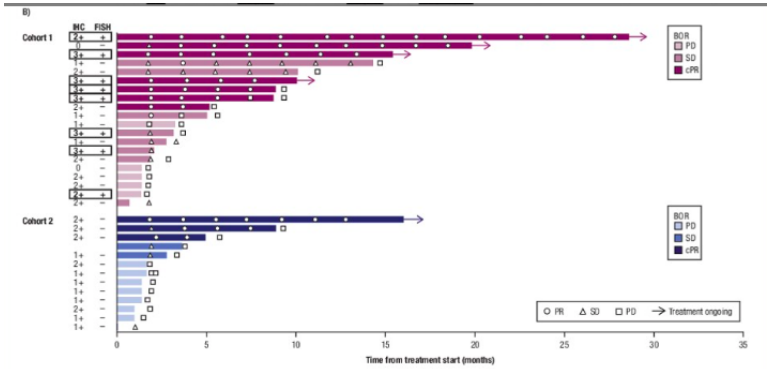
	All Patients (N=52)		
Any TRAE,[a] n (%)	45 (86.5)		
Grade 1-2	38 (73.1)		
Grade 3	7 (13.5)		
Grade 4-5	0 (0)		
Serious TRAEs, n (%)	3 (5.8)[b]		
TRAEs leading to treatment discontinuation, n (%)	2 (3.8)[c]		
TRAEs leading to dose reductions, n (%)	0 (0)		
Treatment-related AESI, n (%)			
Left ventricular dysfunction[d]	1 (1.9)		
IRR	12 (23.1)		
Non-infectious pulmonary toxicities	0 (0)		
Most common TRAEs,[a] n (%)	Grade 1	Grade 2	Grade 3
Diarrhea	20 (38.5)	9 (17.3)	3 (5.8)
Fatigue	9 (17.3)	7 (13.5)	1 (1.9)
Nausea	11 (21.2)	3 (5.8)	0 (0)
IRR	3 (5.8)	7 (13.5)	2 (3.8)

Table 3. Disease Response Endpoints

	Cohort 1				
	HER2-Positive by Central Assessment (n=9)	Not HER2-Positive by Central Assessment (n=12)	All (n=21)	Cohort 2 (n=15)	Cohort 3 (n=8)[a]
cORR, n (%) [95% CI]	5 (55.6) [21.2, 86.3]	2 (16.7) [2.1, 48.4]	7 (33.3) [14.6, 57.0]	3 (20.0) [4.3, 48.1]	1 (14.3) [0.4, 57.9]
CR, n (%)[b]	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
PR, n (%)	5 (55.6)	2 (16.7)	7 (33.3)	3 (20.0)	1 (14.3)[c]
SD, n (%)	2 (22.2)	6 (50.0)	8 (38.1)	3 (20.0)	2 (28.6)
PD, n (%)	1 (11.1)	4 (33.3)	5 (23.8)	7 (46.7)	4 (57.1)
NE, n (%)	1 (11.1)	0 (0)	1 (4.8)	2 (13.3)	0 (0)
DCR, n (%) [95% CI]	7 (77.8) [40.0, 97.2]	8 (66.7) [34.9, 90.1]	15 (71.4) [47.8, 88.7]	6 (40.0) [16.3, 67.7]	3 (42.9) [9.9, 81.6]
Median DOR, months (range)[d]	NE (5.6-25.9)	NE (3.6-15.0)	NE (3.6-25.9)	5.5 (3.6-11.0)	NE (14.8-14.8)
Median PFS, months (95% CI)	7.4 (0.6, NE)	3.5 (1.6, 14.6)	3.6 (1.8, 11.0)	1.9 (1.6, 3.9)	1.9 (1.1, 3.8)

[a]7 patients were response evaluable. [b]There was 1 HER2-positive mBC patient treated at the lower dose of evorpacept in Part 1 that achieved a CR (median DOR: 20.2 months). [c]Salivary gland cancer. [d]DOR was assessed in patients with a confirmed complete or partial response.

cORR, confirmed objective response rate; CI, confidence interval; CR, complete response; DCR, disease control rate; DOR, duration of response; HER2, human epidermal growth factor receptor 2; mBC, metastatic breast cancer; NE, not evaluable; PD, progressive disease; PFS, progression-free survival; PR, partial response; SD, stable disease.



NCT06435429 **Recruiting**

A Study Comparing the Efficacy and Safety of **Zanidatamab** to Trastuzumab, Each in Combination With Physician's Choice Chemotherapy, for the Treatment of Participants With Metastatic HER2-positive Breast Cancer

Conditions

Metastatic HER2-positive Breast Cancer

Anticuerpos biespecíficos
Papel en cáncer de mama

- Estudios iniciales prometedores
- Múltiples opciones futuras
- ¿Podremos vencer la heterogeneidad ?
- Múltiples combinaciones/sinergias en investigación
    - Inmunoterapia
    - Quimioterapia
    - Otros agentes: hormona, inhibidores vías de activación celular
    - ADC bi-triespecíficos

- Vencer resistencias y nuevas opciones terapéuticas

- Seguridad del tratamiento

- ¿Papel en cáncer de mama precoz?