

Clinical trials of HER2 inhibitors for advanced breast cancer (metastatic) in HER2 positive patients

TrialResults-center www.trialresultscenter.org

1 margetuximab

Trial	Treatments	Patients	Trials design and methods
margetuximab vs trastuzumab + chemotherapy			
SOPHIA <i>ongoing</i> [NCT02492711] n=NA follow-up:	Margetuximab Plus Chemotherapy versus Trastuzumab Plus Chemotherapy	patients with advanced HER2+ breast cancer who have received prior treatment with trastuzumab, pertuzumab, and ado-trastuzumab emtansine in the neoadjuvant, adjuvant, or metastatic setting, and who have received at least one, and no more than two, lines of therapy in the metastatic setting	

References

SOPHIA, :

2 pertuzumab

Trial	Treatments	Patients	Trials design and methods
pertuzumab + trastuzumab + aromatase inhibitor vs trastuzumab + aromatase inhibitor			
MO27775 <i>ongoing</i> [NCT01491737] n=NA follow-up:	-	patients with HER2-positive and hormone receptor-positive advanced breast cancer	open label
pertuzumab + trastuzumab + capecitabine vs trastuzumab + capecitabine			
PHEREXA <i>ongoing</i> [NCT01026142] n=NA follow-up:	-	patients with HER2-positive metastatic breast can	
pertuzumab + trastuzumab + chemotherapy vs trastuzumab + chemotherapy			
APHINITY (BIG 04-11) <i>ongoing</i> [NCT01358877] n=NA follow-up:	-	HER2-positive nonmetastatic breast cancer	

continued...

Trial	Treatments	Patients	Trials design and methods
pertuzumab + trastuzumab + docetaxel vs trastuzumab + docetaxel			
neoSphere (Group B) , 2012 [NCT00545688] n=107/107 follow-up:	pertuzumab and trastuzumab plus docetaxel versus trastuzumab plus docetaxel	women with locally advanced, inflammatory, or early HER2-positive breast cancer	
CLEOPATRA , 2012 [NCT00567190] n=406/402 follow-up:	pertuzumab plus trastuzumab plus docetaxel versus placebo plus trastuzumab plus docetaxel	patients with HER2-positive metastatic breast cancer	Parallel groups double-blind

References

MO27775, 0:

PHEREXA, 0:

APHINITY (BIG 04-11), :

neoSphere (Group B), 2012:

Gianni L, Pienkowski T, Im YH, Roman L, Tseng LM, Liu MC, Lluch A, Staroslawska E, de la Haba-Rodriguez J, Im SA, Pedrini JL, Poirier B, Morandi P, Semiglazov V, Srimuninnimit V, Bianchi G, Szado T, Ratnayake J, Ross G, Valagussa P 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;13:25-32 [22153890] [10.1016/S1470-2045\(11\)70336-9](https://doi.org/10.1016/S1470-2045(11)70336-9)

Bianchini G, Kiermaier A, Bianchi GV, Im YH, Pienkowski T, Liu MC, Tseng LM, Dowsett M, Zabaglo L, Kirk S, Szado T, Eng-Wong J, Amler LC, Valagussa P, Biomarker analysis of the NeoSphere study: pertuzumab, trastuzumab, and docetaxel versus trastuzumab plus docetaxel, pertuzumab plus trastuzumab, or pertuzumab plus docetaxel for the neoadjuvant treatment of HER2-positive breast cancer. *Breast Cancer Res* 2017;19:16 [28183321]

CLEOPATRA, 2012:

Baselga J, Corts J, Kim SB, Im SA, Hegg R, Im YH, Roman L, Pedrini JL, Pienkowski T, Knott A, Clark E, Benyunes MC, Ross G, Swain SM Pertuzumab plus trastuzumab plus docetaxel for metastatic breast cancer. *N Engl J Med* 2012 Jan 12;366:109-19 [22149875] [10.1056/NEJMoa1113216](https://doi.org/10.1056/NEJMoa1113216)

Baselga J, Swain SM CLEOPATRA: a phase III evaluation of pertuzumab and trastuzumab for HER2-positive metastatic breast cancer. *Clin Breast Cancer* 2010 Dec 1;10:489-91 [21147694] [10.3816/CBC.2010.n.065](https://doi.org/10.3816/CBC.2010.n.065)

Swain SM, Baselga J, Kim SB, Ro J, Semiglazov V, Campone M, Ciruelos E, Ferrero JM, Schneeweiss A, Heeson S, Clark E, Ross G, Benyunes MC, Corts J Pertuzumab, trastuzumab, and docetaxel in HER2-positive metastatic breast cancer. *N Engl J Med* 2015;372:724-34 [25693012]

3 trastuzumab

Trial	Treatments	Patients	Trials design and methods
trastuzumab + anastrozole vs anastrozole alone			
TAnDEM (Kaufman) , 2009 n=NA follow-up:	anastrozole (1 mg/d orally) with trastuzumab (4 mg/kg intravenous infusion on day 1, then 2 mg/kg every week) until progression versus anastrozole	postmenopausal women with human epidermal growth factor receptor 2-positive, hormone receptor-positive metastatic breast cancer	
trastuzumab + capecitabine vs capecitabine alone			

continued...

Trial	Treatments	Patients	Trials design and methods
von Minckwitz , 2009 n=NA follow-up:	trastuzumab + capecitabine versus capecitabine alone	Patients with HER-2-positive breast cancer that progresses during treatment with trastuzumab	
trastuzumab + docetaxel vs docetaxel alone			
Marty , 2005 [M77001] n=NA follow-up:	-	patients with human epidermal growth factor receptor 2-positive metastatic breast cancer administered as first-line treatment	
trastuzumab + lapatinib vs lapatinib alone			
Blackwell , 2010 n=NA follow-up:	lapatinib + trastuzumab versus lapatinib alone	women with ErbB2-positive, trastuzumab-refractory metastatic breast cancer	
trastuzumab + letrozole vs letrozole alone			
Huober , 2012 n=NA follow-up:	letrozole plus trastuzumab versus letrozole alone	patients with HER2-positive, hormone-receptor-positive metastatic breast cancer	
trastuzumab + paclitaxel vs paclitaxel alone			
Gasparini , 2006 n=NA follow-up:	trastuzumab + weekly paclitaxel versus weekly paclitaxel	patients with advanced breast cancer overexpressing HER-2.	
trastuzumab + standard chemotherapy vs standard chemotherapy alone			
Slamon , 2001 n=NA follow-up:	standard chemotherapy plus trastuzumab versus standard chemotherapy alone	women with metastatic breast cancer that overexpressed HER2	

References

TAnDEM (Kaufman), 2009:

Kaufman, B 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;27:5529-37 [[19786670](#)] [10.1200/JCO.2008.20.6847](#)

von Minckwitz, 2009:

NA, NA Trastuzumab Improves the Efficacy of Chemotherapy in Breast Cancer Treatment beyond Progression. *Breast Care (Basel)* 2008;3:364-365 [[20824032](#)] [NA](#)

von Minckwitz, G Trastuzumab beyond progression: overall survival analysis of the GBG 26/BIG 3-05 phase III study in HER2-positive breast cancer. *Eur. J. Cancer* 2011;47:2273-81 [[21741829](#)] [10.1016/j.ejca.2011.06.021](#)

von Minckwitz, G 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;27:1999-2006 [[19289619](#)] [10.1200/JCO.2008.19.6618](#)

von Minckwitz G, Zielinski C, Maarteense E, Vogel P, Schmidt M, Eidtmann H, et al. Capecitabine vs capecitabine+trastuzumab in patients with HER2-positive metastatic breast cancer progressing during trastuzumab treatment: The TBP phase III study (GBG 26/BIG 3-05) [Abstract 1025]. *American Society of Clinical Oncology.* 2008.

Marty, 2005:

Marty, M Randomized phase II trial of the efficacy and safety of trastuzumab combined with docetaxel in patients with human epidermal growth factor receptor 2-positive metastatic breast cancer administered as first-line treatment: the M77001 study group. *J. Clin. Oncol.* 2005;23:4265-74 [[15911866](#)] [10.1200/JCO.2005.04.173](#)

Extra JM, Cognetti F, Chan S, Maraninchi D, Snyder R, Lluch A, Tubiana-Hulin M, et al. Randomised phase II trial (M77001) of trastuzumab (Herceptin) plus docetaxel versus docetaxel alone, as first-line therapy in patients with HER2- positive metastatic breast cancer. *European Journal of Cancer* 2003;1:Abstract 672.

Blackwell, 2010:

Blackwell, KL 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;30:2585-92 [22689807] [10.1200/JCO.2011.35.6725](#)

Blackwell, KL Randomized study of Lapatinib alone or in combination with trastuzumab in women with ErbB2-positive, trastuzumab-refractory metastatic breast cancer. *J. Clin. Oncol.* 2010;28:1124-30 [20124187] [10.1200/JCO.2008.21.4437](#)

Wu, Y Impact of lapatinib plus trastuzumab versus single-agent lapatinib on quality of life of patients with trastuzumab-refractory HER2+ metastatic breast cancer. *Ann. Oncol.* 2011;22:2582-90 [21406472] [10.1093/annonc/mdr014](#)

O'Shaughnessy J, Blackwell KL, Burstein H, Storniolo AM, Sledge G, Baselga J, et al. A randomized study of lapatinib alone or in combination with trastuzumab in heavily pretreated HER2+ metastatic breast cancer progressing on trastuzumab therapy [Abstract 1015]. American Society of Clinical Oncology. 2008.

Huober, 2012:

Huober, J 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;21:27-33 [21862331] [10.1016/j.breast.2011.07.006](#)

Gasparini, 2006:

Gasparini, G Randomized Phase II Trial of weekly paclitaxel alone versus trastuzumab plus weekly paclitaxel as first-line therapy of patients with Her-2 positive advanced breast cancer. *Breast Cancer Res. Treat.* 2007;101:355-65 [16850247] [10.1007/s10549-006-9306-9](#)

Gasparini G, Gion M, Crivellari D, Morabito A, Rocco S, Spada A, et al. Interim analysis of a randomized phase IIb study of weekly paclitaxel (PCT) with or without trastuzumab (T) as first-line therapy of patients (pts) with HER-2/neu positive metastatic breast cancer (MBC): Clinical and biological results [Abstract 138]. American Society of Clinical Oncology. 2003.

Slamon, 2001:

Burstein, HJ Isolated central nervous system metastases in patients with HER2-overexpressing advanced breast cancer treated with first-line trastuzumab-based therapy. *Ann. Oncol.* 2005;16:1772-7 [16150805] [10.1093/annonc/mdi371](#)

Muktabhant, B Diet or exercise, or both, for preventing excessive weight gain in pregnancy. *Cochrane Database Syst Rev* 2015;6:CD007145 [26068707] [10.1002/14651858.CD007145.pub3](#)

Osoba, D Effects on quality of life of combined trastuzumab and chemotherapy in women with metastatic breast cancer. *J. Clin. Oncol.* 2002;20:3106-13 [12118024] NA

Slamon, DJ Use of chemotherapy plus a monoclonal antibody against HER2 for metastatic breast cancer that overexpresses HER2. *N. Engl. J. Med.* 2001;344:783-92 [11248153] [10.1056/NEJM200103153441101](#)

Tripathy, D Effect of cardiac dysfunction on treatment outcomes in women receiving trastuzumab for HER2-overexpressing metastatic breast cancer. *Clin. Breast Cancer* 2004;5:293-8 [15507176] NA

Tripathy, D Safety of treatment of metastatic breast cancer with trastuzumab beyond disease progression. *J. Clin. Oncol.* 2004;22:1063-70 [15020607] [10.1200/JCO.2004.06.557](#)

Baselga J, Kerrigan M, Burchmore M, Ash M. Healthrelated quality of life (HRQL) in women with HER2- overexpressing metastatic breast cancer (MBC) in a phase III study of Herceptin (R) plus chemotherapy versus chemotherapy alone. *European Journal of Cancer* 1999;35: Abstract 1276.

Eiermann W, on behalf of the International Herceptin Study Group. Trastuzumab combined with chemotherapy for the treatment of HER2-positive metastatic breast cancer: pivotal trial data. *Annals of Oncology* 2001;12(1):5762.

Osoba D, Slamon DJ, Burchmore M, Murphy M. Effects of treatment with Her2mab (trastuzumab/Herceptin) plus chemotherapy (H+C) versus chemotherapy alone (C) on health-related quality of life (HRQL) in women with HER- 2/neu-overexpressing metastatic breast cancer [Abstract 109]. American Society of Clinical Oncology. 2001.

4 trastuzumab emtansine

Trial	Treatments	Patients	Trials design and methods
trastuzumab emtansine vs lapatinib plus capecitabine			

continued...

Trial	Treatments	Patients	Trials design and methods
EMILIA , 2012 [NCT00829166] n=496/495 follow-up:	Trastuzumab emtansine versus lapatinib plus capecitabine	patients with HER2-positive advanced breast cancer, who had previously been treated with trastuzumab and a taxane	Parallel groups
trastuzumab emtansine vs usual care			
TH3RESA , 2014 [NCT01419197] n=404/198 follow-up:	trastuzumab emtansine versus physician's choice	patients with progressive HER2-positive advanced breast cancer who had received two or more HER2-directed regimens in the advanced setting	Parallel groups open-label

References

EMILIA, 2012:

Verma S, Miles D, Gianni L, Krop IE, Welslau M, Baselga J, Pegram M, Oh DY, Diras V, Guardino E, Fang L, Lu MW, Olsen S, Blackwell K Trastuzumab emtansine for HER2-positive advanced breast cancer. *N Engl J Med* 2012;367:1783-91 [[23020162](#)]

TH3RESA, 2014:

Krop IE, Kim SB, Gonzalez-Martn A, LoRusso PM, Ferrero JM, Smitt M, Yu R, Leung AC, Wildiers H 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 Jun;15:689-99 [[24793816](#)] [10.1016/S1470-2045\(14\)70178-0](#)

Entry terms: ado-trastuzumab emtansine, trastuzumab-DM1, trastuzumab-DM1 conjugate, T-DM1 cpd, trastuzumab emtansine, huN901-DM1, Kadcyła

CT

5 About TrialResults-center.org

TrialResults-center is an innovative knowledge database that collects the results of RCTs and provides dynamic interactive systematic reviews and meta-analysis in the field of all major heart and vessels diseases.

The TrialResults-center database provides a unique view of the treatment efficacy based on all data provided directly from clinical trial results, offering a valuable alternative to personal bibliographic search, published meta-analysis, etc. Furthermore, it would allow comparing easily the various concurrent therapeutic for the same clinical condition.

Rigorous meta-analysis method is used to populate TrialResults-center: widespread search of published and non published trials, study selection using pre-specified criteria, data extraction using standard form.

TrialResults-center is continually updated on a weekly basis. We continually search all new results (whatever their publication channel) and these news results are immediately added to the database with a maximum of 1 week.

TrialResults-center is non-profit and self-funded.