Clinical trials of multi target TKI for advanced breast cancer (metastatic) in all type of patients

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1 combination

Trial	Treatments	Patients	Trials design and methods
lapatinib + standard therapy vs standard therapy alone			
DETECT III *ongoing* [NCT01619111] n=NA follow-up:	standard chemo- or endocrine therapy + lapatinib versus standard therapy (standard chemo- or endocrine therapy)	patients, with initially HER2-negative metastatic breast cancer and HER2-positive circulating tumor cells	open label Germany
lapatinib + trastuzumab vs trastuzumab alone			
112515 *ongoing* [NCT00968968] n=NA follow-up:	Oral Lapatinib 1000 mg once daily plus Trastuzumab versus Trastuzumab	women with HER2-positive metastatic breast cancer	open label

References

DETECT III, 0:

Fehm T, Mller V, Aktas B, Janni W, Schneeweiss A, Stickeler E, Lattrich C, Lhberg CR, Solomayer E, Rack B, Riethdorf S, Klein C, Schindlbeck C, Brocker K, Kasimir-Bauer S, Wallwiener D, Pantel K HER2 status of circulating tumor cells in patients with metastatic breast cancer: a prospective, multicenter trial. Breast Cancer Res Treat 2010;124:403-12 [20859679]

112515, 0:

2 combination with CT

Trial	Treatments	Patients	Trials design and methods
lapatinib + capecitabine vs capecitabine alone			
Geyer , 2006 [NCT00078572] n=399 follow-up:	lapatinib at a dose of 1250 mg per day continuously plus capecitabine at a dose of 2000 mg per square meter of body-surface area on days 1 through 14 of a 21-day cycle versus monotherapy (capecitabine alone at a dose of 2500 mg per square meter on days 1 through 14 of a 21-day cycle)	Women with HER2-positive, locally advanced or metastatic breast cancer that had progressed after treatment with regimens that included an anthracycline, a taxane, and trastuzumab	Parallel groups open-label

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Trial	Treatments	Patients	Trials design and methods
100151 *ongoing* [NCT00078572] n=NA follow-up:	Lapatinib 1250 mg once daily plus capecitbine daily dose divided and given twice daily orally, for 14 days, every 21 days. The capecitabine starting dose for the combination arm was 2000 mg/m2 versus Capecitabine daily dose divided and given twice daily orally, for 14 days, every 21 days. The capecitabine starting dose for the monotherapy arm was 2500 mg/m2	women with locally advanced or metastatic breast cancer that has not responded to previous therapy	open label
sorafenib + capecitabine vs capecitabine alone			
Baselga , 2012 n=NA follow-up:	- or second-line capecitabine 1,000 mg/m(2) orally twice a day for days 1 to 14 of every 21-day cycle with sorafenib 400 mg orally twice a day versus capecitabine alone	HER2-negative locally advanced or metastatic breast cancer	Parallel groups double-blind
RESILIENCE , 2013 *ongoing* n=NA follow-up:	-	advanced HER2-negative breast cancer	
sorafenib + gemcitabine or capecitabine vs gemcitabine or capecitabine alone			
Schwartzberg , 2013 [NCT00493636] n=NA follow-up:	sorafenib (400 mg, twice daily) versus placebo	patients with HER-2-negative advanced breast cancer that progressed during or after bevacizumab	Parallel groups double-blind
neratinib + capecitabine vs lapatinib + capecitabine			
NALA *ongoing* [NCT01808573] n=NA follow-up:	neratinib plus capecitabine versus lapatinib plus capecitabine	HER2+ MBC patients who have received two or more prior HER2 directed regimens in the metastatic setting	open label
lapatinib + capecitabine vs trastuzumab + capecitabine			
111438 *ongoing* [NCT00820222] n=NA follow-up:	Lapatinib 1250 mg once daily and capecitabine 2000mg/m2/day, days 1-14, every 21 days versus trastuzumab loading dose of 8mg/kg followed by 6mg/kg q3weekly infusions, and capecitabine 2500mg/m2/day, days 1-14, every 21 days	ErbB2 (HER2) positive metastatic breast cancer patients exposed to prior taxanes or anthracyclines	open label
BIBW 2992 + vinorelbine vs trastuzumab + vinorelbine			

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Trial	Treatments	Patients	Trials design and methods
1200.75 *ongoing* [NCT01125566] n=NA follow-up:	BIBW 2992 with vinorelbine BIBW 2992 tablets once daily combined with weekly intravenous infusion of vinorelbine versus trastuzumab with vinorelbine weekly intravenous infusion of trastuzumab and vinorelbine	patients with HER2-overexpressing, metastatic breast cancer, who failed one prior trastuzumab treatment	open label

References

Geyer, 2006:

Geyer CE, Forster J, Lindquist D, Chan S, Romieu CG, Pienkowski T, Jagiello-Gruszfeld A, Crown J, Chan A, Kaufman B, Skarlos D, Campone M, Davidson N, Berger M, Oliva C, Rubin SD, Stein S, Cameron D Lapatinib plus capecitabine for HER2-positive advanced breast cancer. N Engl J Med 2006;355:2733-43 [17192538] 10.1056/NEJMoa064320

Cameron D, Casey M, Press M, Lindquist D, Pienkowski T, Romieu CG, Chan S, Jagiello-Gruszfeld A, Kaufman B, Crown J, Chan A, Campone M, Viens P, Davidson N, Gorbounova V, Raats JI, Skarlos D, Newstat B, Roychowdhury D, Paoletti P, Oliva C, Rubin S, Stein A phase III randomized comparison of lapatinib plus capecitabine versus capecitabine alone in women with advanced breast cancer that has progressed on trastuzumab: updated efficacy and biomarker analyses. Breast Cancer Res Treat 2008;112:533-43 [18188694] 10.1007/s10549-007-9885-0

100151, 0:

Geyer CE, Forster J, Lindquist D, Chan S, Romieu CG, Pienkowski T, Jagiello-Gruszfeld A, Crown J, Chan A, Kaufman B, Skarlos D, Campone M, Davidson N, Berger M, Oliva C, Rubin SD, Stein S, Cameron D Lapatinib plus capecitabine for HER2-positive advanced breast cancer. N Engl J Med 2006;355:2733-43 [17192538]

Baselga, 2012:

Baselga J, Segalla JG, Roch H, Del Giglio A, Pinczowski H, Ciruelos EM, Filho SC, Gmez P, Van Eyll B, Bermejo B, Llombart A, Garicochea B, Durn M, Hoff PM, Espi M, de Moraes AA, Ribeiro RA, Mathias C, Gil Gil M, Ojeda B, Morales J, Kwon Ro S, Li S, C Sorafenib in combination with capecitabine: an oral regimen for patients with HER2-negative locally advanced or metastatic breast cancer. J Clin Oncol 2012;30:1484-91. [22412143] 10.1200/JCO.2011.36.7771

RESILIENCE, 2013:

Baselga J, Costa F, Gomez H, Hudis CA, Rapoport B, Roche H, Schwartzberg LS, Petrenciuc O, Shan M, Gradishar WJ, A phase 3 tRial comparing capecitabinE in combination with SorafenIb or pLacebo for treatment of locally advanced or metastatIc HER2-Negative breast CancEr (the RESILIENCE study): study protocol for a randomized controlled trial. Trials 2013;14:228. [23876062] 10.1186/1745-6215-14-228

Schwartzberg, 2013:

Schwartzberg LS, Tauer KW, Hermann RC, Makari-Judson G, Isaacs C, Beck JT, Kaklamani V, Stepanski EJ, Rugo HS, Wang W, Bell-McGuinn K, Kirshner JJ, Eisenberg P, Emanuelson R, Keaton M, Levine E, Medgyesy DC, Qamar R, Starr A, Ro SK, Lokker NA, Hudis CA, Sorafenib or placebo with either gemcitabine or capecitabine in patients with HER-2-negative advanced breast cancer that progressed during or after bevacizumab. Clin Cancer Res 2013;19:2745-54. [23444220] 10.1158/1078-0432.CCR-12-3177

NALA, 0:

111438, 0:

1200.75, 0:

3 combination with endocrine therapy

Trial	Treatments	Patients	Trials design and methods
lapatinib + fulvestrant vs fulvestrant alone			

continued...

Trial	Treatments	Patients	Trials design and methods
NCI-2009-00475 *ongoing* [NCT00390455] n=NA follow-up:	1500 mg lapatinib ditosylate PO QD on days 1-28 and fulvestrant IM on days 1 (500 mg) and 15 (250 mg) of course 1 and on day 1 (250 mg)of each subsequent course versus placebo PO QD on days 1-28 and fulvestrant IM on days 1 (500 mg) and 15 (250 mg) of course 1 and on day 1 (250 mg) of each subsequent course.	postmenopausal women with stage III or stage IV breast cancer that is hormone receptor-positive	double-blind
CDR0000596572 *ongoing* [NCT00688194] n=NA follow-up:	lapatinib +fulvestrant (+/- aromatase inhibitor (AI) therapy (e.g., exemestane, anastrozole, or letrozole) according to standard treatment rgulations) versus placebo	postmenopausal women with metastatic breast cancer that progressed after previous aromatase inhibitor therapy	double-blind
lapatinib + letrozole vs letrozole alone			
Johnston (EGF30008) , 2009 [NCT00073528] n=1286 follow-up:	daily letrozole (2.5 mg orally) plus lapatinib (1,500 mg orally) versus letrozole	hormone receptor-positive metastatic breast cancer	Parallel groups double-blind

References

NCI-2009-00475, 0:

CDR0000596572, 0:

Johnston (EGF30008) , 2009:

Delea TE, Amdahl J, Chit A, Amonkar MM Cost-effectiveness of lapatinib plus letrozole in her2-positive, hormone receptor-positive metastatic breast cancer in Canada. Curr Oncol 2013 Oct;20:e371-87 [24155635]

Johnston S, Pippen J Jr, Pivot X, Lichinitser M, Sadeghi S, Dieras V, Gomez HL, Romieu G, Manikhas A, Kennedy MJ, Press MF, Maltzman J, Florance A, O'Rourke L, Oliva C, Stein S, Pegram M Lapatinib combined with letrozole versus letrozole and placebo as first-line therapy for postmenopausal hormone receptor-positive metastatic breast cancer. J Clin Oncol 2009;27:5538-46 [19786658]

4 combination with taxanes

Trial	Treatments	Patients	Trials design and methods
lapatinib + paclitaxel vs paclitaxel alone			
Di Leo , 2008 [NCT00075270] n=579 follow-up:	first-line therapy with paclitaxel 175 mg/m(2) every 3 weeks plus lapatinib 1,500 mg/d versus paclitaxel	first-line treatment for metastatic breast cancer	Parallel groups double-blind

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Trial	Treatments	Patients	Trials design and methods
EGF104535 *ongoing* [NCT00281658] n=NA follow-up:	Paclitaxel and Lapatinib versus Paclitaxel and Placebo	women and men who have metastatic breast cancer first line metastatic treatment	double-blind brazil
sorafenib + paclitaxel vs paclitaxel alone			
Gradishar , 2013 n=NA follow-up:	paclitaxel (90mg/m(2), weekly, intravenously, 3 weeks on/1 week off) plus sorafenib (400mg, orally, twice daily) versus paclitaxel (90mg/m(2), weekly, intravenously, 3 weeks on/1 week off)	first-line therapy in patients with HER2-negative advanced breast cancer	Parallel groups double-blind

References

Di Leo, 2008:

Sherrill B, Di Leo A, Amonkar MM, Wu Y, Zvirbule Z, Aziz Z, Bines J, Gomez HL Quality-of-life and quality-adjusted survival (Q-TWiST) in patients receiving lapatinib in combination with paclitaxel as first-line treatment for metastatic breast cancer. Curr Med Res Opin 2010 Apr;26:767-75 [20095796]

Finn RS, Press MF, Dering J, Arbushites M, Koehler M, Oliva C, Williams LS, Di Leo A Estrogen receptor, progesterone receptor, human epidermal growth factor receptor 2 (HER2), and epidermal growth factor receptor expression and benefit from lapatinib in a randomized trial of paclitaxel with lapatinib or placebo as first-line treatment in HER2-negative or unknown metastatic breast cancer. J Clin Oncol 2009;27:3908-15 [19620495]

Di Leo A, Gomez HL, Aziz Z, Zvirbule Z, Bines J, Arbushites MC, Guerrera SF, Koehler M, Oliva C, Stein SH, Williams LS, Dering J, Finn RS, Press MF Phase III, double-blind, randomized study comparing lapatinib plus paclitaxel with placebo plus paclitaxel as first-line treatment for metastatic breast cancer. J Clin Oncol 2008;26:5544-52 [18955454]

EGF104535, 0:

Gradishar, 2013:

Gradishar WJ, Kaklamani V, Sahoo TP, Lokanatha D, Raina V, Bondarde S, Jain M, Ro SK, Lokker NA, Schwartzberg L, A double-blind, randomised, placebo-controlled, phase 2b study evaluating sorafenib in combination with paclitaxel as a first-line therapy in patients with HER2-negative advanced breast cancer. Eur J Cancer 2013;49:312-22. [22954665] 10.1016/j.ejca.2012.08.005

5 triplet combination

Trial	Treatments	Patients	Trials design and methods
lapatinib + paclitaxel + trastuzumab vs paclitaxel + trastuzumab			

continued...

Trial	Treatments	Patients	Trials design and methods
ICORG 11-10 *ongoing* [NCT01526369] n=NA follow-up:	Paclitaxel, Trastuzumab and Lapatinib (Weekly paclitaxel (80 mg/m, for 3 weeks of a 4 week cycle) + trastuzumab (8 mg/kg loading dose on cycle 1 day 1 and 4 mg/kg every 2 weeks) + lapatinib (1,000 mg daily), until disease progression, unacceptable toxici versus Paclitaxel and Trastuzumab (Weekly paclitaxel (80mg/m, for 3 weeks of a 4 week cycle) + trastuzumab (8mg/kg loading dose on cycle 1 day 1 and 4mg/kg every 2 weeks) until disease progression, unacceptable toxicity or consent withdrawal	first line treatment of HER2 positive metastatic breast cancer	open label finland
lapatinib + trastuzumab + aromatase inhibitor vs trastuzmab +aromatase inhibitor			
NCT01160211 *ongoing* [NCT01160211] n=NA follow-up:	Lapatinib plus trastuzumab plus aromatase inhibitor versus trastuzmab plus aromatase inhibitor	hormone receptor positive, HER2+ metastatic breast cancer	open label

References

ICORG 11-10, 0:
NCT01160211, 0:

6 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.

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