

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

TrialResults-center [www.trialresultscenter.org](http://www.trialresultscenter.org)

## 1 combination

Trial	Treatments	Patients	Trials design and methods
<b>lapatinib + standard therapy vs standard therapy alone</b>			
<b>DETECT III</b> <i>ongoing</i> [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
<b>lapatinib + trastuzumab vs trastuzumab alone</b>			
<b>112515</b> <i>ongoing</i> [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
<b>lapatinib + capecitabine vs capecitabine alone</b>			
<b>Geyer , 2006</b> [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

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
100151 <i>ongoing</i> [NCT00078572] n=NA follow-up:	Lapatinib 1250 mg once daily plus capecitabine 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/m <sup>2</sup> 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/m <sup>2</sup>	women with locally advanced or metastatic breast cancer that has not responded to previous therapy	open label
<b>sorafenib + capecitabine vs capecitabine alone</b>			
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 <i>ongoing</i> n=NA follow-up:	-	advanced HER2-negative breast cancer	
<b>sorafenib + gemcitabine or capecitabine vs gemcitabine or capecitabine alone</b>			
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
<b>neratinib + capecitabine vs lapatinib + capecitabine</b>			
NALA <i>ongoing</i> [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
<b>lapatinib + capecitabine vs trastuzumab + capecitabine</b>			
111438 <i>ongoing</i> [NCT00820222] n=NA follow-up:	Lapatinib 1250 mg once daily and capecitabine 2000mg/m <sup>2</sup> /day, days 1-14, every 21 days versus trastuzumab loading dose of 8mg/kg followed by 6mg/kg q3weekly infusions, and capecitabine 2500mg/m <sup>2</sup> /day, days 1-14, every 21 days	ErbB2 (HER2) positive metastatic breast cancer patients exposed to prior taxanes or anthracyclines	open label
<b>BIBW 2992 + vinorelbine vs trastuzumab + vinorelbine</b>			

continued...

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...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>NCI-2009-00475</b> <i>ongoing</i> [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
<b>CDR0000596572</b> <i>ongoing</i> [NCT00688194] n=NA follow-up:	lapatinib +fulvestrant (+/- aromatase inhibitor (AI) therapy (e.g., exemestane, anastrozole, or letrozole) according to standard treatment regulations) versus placebo	postmenopausal women with metastatic breast cancer that progressed after previous aromatase inhibitor therapy	double-blind
<b>lapatinib + letrozole vs letrozole alone</b>			
<b>Johnston (EGF30008) , 2009</b> [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, Pippin 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

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>lapatinib + paclitaxel vs paclitaxel alone</b>			
<b>Di Leo , 2008</b> [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

continued...

Trial	Treatments	Patients	Trials design and methods
<b>EGF104535</b> <i>ongoing</i> [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
<b>sorafenib + paclitaxel vs paclitaxel alone</b>			
<b>Gradishar , 2013</b> n=NA follow-up:	paclitaxel (90mg/m <sup>2</sup> ), weekly, intravenously, 3 weeks on/1 week off) plus sorafenib (400mg, orally, twice daily) versus paclitaxel (90mg/m <sup>2</sup> ), 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, Guerrero 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
<b>lapatinib + paclitaxel + trastuzumab vs paclitaxel + trastuzumab</b>			

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>ICORG 11-10</b> <i>ongoing</i> [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 toxicity 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
<b>lapatinib + trastuzumab + aromatase inhibitor vs trastuzumab +aromatase inhibitor</b>			
<b>NCT01160211</b> <i>ongoing</i> [NCT01160211] n=NA follow-up:	Lapatinib plus trastuzumab plus aromatase inhibitor versus trastuzumab 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.

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.