Clinical trials of mTOR inhibitor for advanced breast cancer (metastatic) in all type of patients

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1 add-on to anti HER-2 agent

Trial	Treatments	Patients	Trials design and methods
everolimus + trastuzumab + paclitaxel vs trastuzumab + paclitaxel			
BOLERO-1 *ongoing* [NCT00876395] n=NA follow-up:	Everolimus 10 mg daily in combination with paclitaxel 80mg/m2 weekly on days 1, 8, 15 and trastuzumab 2mg/kg weekly on days 1, 8, 15, 22 versus Placebo of everolimus daily in combination with paclitaxel 80mg/m2 weekly on days 1, 8, 15 and trastuzumab 2mg/kg weekly on days 1, 8, 15, 22	patients with HER2+ advanced breast cancer who have not received trastuzumab in the metastatic setting	Parallel groups
everolimus + trastuzumab + vinorelbine vs trastuzumab + vinorelbine alone			
BOLERO-3 , 2014 [NCT01007942] n=284/285 follow-up:	daily everolimus (5 mg/day) plus weekly trastuzumab (2 mg/kg) and vinorelbine (25 mg/m(2)) in 3-week cycles versus placebo plus trastuzumab plus vinorelbine,	women with HER2-positive, trastuzumab-resistant, advanced breast carcinoma who had previously received taxane therapy	Parallel groups double-blind

References

BOLERO-1, :

Hurvitz SA, Andre F, Jiang Z, Shao Z, Mano MS, Neciosup SP, Tseng LM, Zhang Q, Shen K, Liu D, Dreosti LM, Burris HA, Toi M, Buyse ME, Cabaribere D, Li Combination of everolimus with trastuzumab plus paclitaxel as first-line treatment for patients with HER2-positive advanced breast cancer (BOLERO-1): a phase 3, randomised, double-blind, multicentre trial. Lancet Oncol 2015;16:816-29 [26092818]

BOLERO-3, 2014:

Andr F, O'Regan R, Ozguroglu M, Toi M, Xu B, Jerusalem G, Masuda N, Wilks S, Arena F, Isaacs C, Yap YS, Papai Z, Lang I, Armstrong A, Lerzo G, White M, Shen K, Litton J, Chen D, Zhang Y, Ali S, Taran T, Gianni L Everolimus for women with trastuzumab-resistant, HER2-positive, advanced breast cancer (BOLERO-3): a randomised, double-blind, placebo-controlled phase 3 trial. Lancet Oncol 2014;15:580-91 [24742739]

2 combination with endocrine therapy

Trial	Treatments	Patients	Trials design and methods
everolimus + exemestane vs capecitabine			

continued...

Trial	Treatments	Patients	Trials design and methods
BOLERO-6 (combination) *ongoing* [NCT01783444] n=NA follow-up:	Everolimus will oral 10 mg (2 5 mg) daily + Exemestane tablets of 25 mg will be taken orally once per day versus Capecitabine, oral 1250 mg/m2 twice daily for 2 weeks followed by one week rest (3-week cycle)	Postmenopausal patients with estrogen-receptor positive, HER2 negative, advanced breast cancer after recurrence or progression on letrozole or anastrozole	
everolimus + exemestane vs exemestane alone			
BOLERO-2 , 2011 [NCT00863655] n=485/239 follow-up:	everolimus and exemestane versus exemestane and placebo	patients with hormone-receptor-positive advanced breast cancer who had recurrence or progression while receiving previous therapy with a nonsteroidal aromatase inhibitor in the adjuvant setting or to treat advanced disease (or both).	Parallel groups double-blind
everolimus + letrozole vs letrozole alone			
BOLERO-4 *ongoing* [NCT01698918] n=NA follow-up:	-	Postmenopausal Women With ER+, HER2- Metastatic or Locally Advanced Breast Cancer	open-label
temsirolimus + letrozole vs letrozole alone			
HORIZON , 2013 [NCT00083993] n=556/556 follow-up:	oral letrozole 2.5 mg daily/temsirolimus 30 mg daily (5 days every 2 weeks) versus letrozole/placebo	first-line endocrine therapy in postmenopausal women with locally advanced or metastatic breast cancer	Parallel groups double-blind
everolimus + tamoxifen vs tamoxifen alone			
TAMRAD , 2012 [NCT01298713] n=54/57 follow-up:	tamoxifen 20 mg/d plus everolimus 10 mg/d versus tamoxifen 20 mg/d alone	postmenopausal women with hormone receptor-positive, human epidermal growth factor receptor 2-negative, AI-resistant mBC	open-label

References

BOLERO-6 (combination), :

BOLERO-2, 2011:

Baselga J, Campone M, Piccart M, Burris HA, Rugo HS, Sahmoud T, Noguchi S, Gnant M, Pritchard KI, Lebrun F, Beck JT, Ito Y, Yardley D, Deleu I, Perez A, Bachelot T, Vittori L, Xu Z, Mukhopadhyay P, Lebwohl D, Hortobagyi GN Everolimus in Postmenopausal Hormone-Receptor-Positive Advanced Breast Cancer. N Engl J Med 2011 Dec 7;: [22149876] 10.1056/NEJMoa1109653

Beaver JA, Park BH, The BOLERO-2 trial: the addition of everolimus to exemestane in the treatment of postmenopausal hormone receptor-positive advanced breast cancer. Future Oncol 2012;8:651-7. [22764762] 10.2217/fon.12.49

Piccart M, Hortobagyi GN, Campone M, Pritchard KI, Lebrun F, Ito Y, Noguchi S, Perez A, Rugo HS, Deleu I, Burris HA 3rd, Provencher L, Neven P, Gnant M, Shtivelband M, Wu C, Fan J, Feng W, Taran T, Baselga J Everolimus plus exemestane for hormone-receptor-positive, human epidermal growth factor receptor-2-negative advanced breast cancer: overall survival results from BOLERO-2. Ann Oncol 2014 Dec;25:2357-62 [25231953]

BOLERO-4, :

HORIZON, 2013:

Wolff AC, Lazar AA, Bondarenko I, Garin AM, Brincat S, Chow L, Sun Y, Neskovic-Konstantinovic Z, Guimaraes RC, Fumoleau P, Chan A, Hachemi S, Strahs A, Cincotta M, Berkenblit A, Krygowski M, Kang LL, Moore L, Hayes DF Randomized phase III placebo-controlled trial of letrozole plus oral temsirolimus as first-line endocrine therapy in postmenopausal women with locally advanced or metastatic breast cancer. J Clin Oncol 2013;31:195-202 [23233719]

TAMRAD , 2012:

Bachelot T, Bourgier C, Cropet C, Ray-Coquard I, Ferrero JM, Freyer G, Abadie-Lacourtoisie S, Eymard JC, Debled M, Spath D, Legouffe E, Allouache D, El Kouri C, Pujade-Lauraine E, Randomized phase II trial of everolimus in combination with tamoxifen in patients with hormone receptor-positive, human epidermal growth factor receptor 2-negative metastatic breast cancer with prior exposure to aromatase inhibitors: a GINECO study. J Clin Oncol 2012;30:2718-24. [22565002] 10.1200/JCO.2011.39.0708

3 maintenance mTOR inhibitor

Trial	Treatments	Patients	Trials design and methods
maintenance everolimus + AI vs AI alone			
MAIN-A *ongoing* [NCT02511639] n=NA follow-up:	Maintenance Aromatase Inhibitors (AIs) + Everolimus versus AIs	patients with HR+ metastatic breast cancer and Disease Control After First Line Chemotherapy	

References

MAIN-A, :

4 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.