Clinical trials of angiogenesis inhibitors for advanced breast cancer (metastatic) in first line therapy

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1 combination with CT (without taxanes)

Trial	Treatments	Patients	Trials design and methods
bevacizumab + capecitabine vs capecitabine			
RIBBON-I (Robert) on top capecitabine , 2009 n=NA follow-up:	Capecitabine + bevacizumab 15 mg/kg iv every 3 weeks versus capecitabine (Cape; 2,000 mg/m(2) for 14 days),	irst-line treatment of human epidermal growth factor receptor 2-negative, locally recurrent or metastatic breast cancer	double-blind

References

RIBBON-I (Robert) on top capecitabine, 2009:

Robert NJ, Dieras V, Glaspy J, Brufsky A, Bondarenko I, LipatovO, Perez E, Yardley E, Zhou X, Phan S RIBBON-1: randomized, double-blind, placebo-controlled, phase III trial of chemotherapy with or without bevacizumab for first-line treatment of HER2-negative locally recurrent or metastatic breast cancer J Clin Oncol 2009;27:15s (abstr 1005)

Robert NJ, Diras V, Glaspy J, Brufsky AM, Bondarenko I, Lipatov ON, Perez EA, Yardley DA, Chan SY, Zhou X, Phan SC, O'Shaughnessy J RIBBON-1: randomized, double-blind, placebo-controlled, phase III trial of chemotherapy with or without bevacizumab for first-line treatment of human epidermal growth factor receptor 2-negative, locally recurrent or metastatic breast cancer. J Clin Oncol 2011;29:1252-60 [21383283]

2 combination with ET

Trial	Treatments	Patients	Trials design and methods
bevacizumab + endocrine therapy vs endocrine therapy			
LEA n=NA follow-up:	bevacizumab + letrozole/fulvestrant versus letrozole or fulvestrant	first-line therapy in postmenopausal patients with human epidermal growth factor receptor 2 (HER2) -negative and hormone receptor-positive advanced breast cancer	

References

LEA, :

Martn M, Loibl S, von Minckwitz G, Morales S, Martinez N, Guerrero A, Anton A, Aktas B, Schoenegg W, Muoz M, Garcia-Saenz J, Gil M, Ramos M, Margeli M, Carrasco E, Liedtke C, Wachsmann G, Mehta K, De la Haba-Rodriguez JR Phase III trial evaluating the addition of bevacizumab to endocrine therapy as first-line treatment for advanced breast cancer: the letrozole/fulvestrant and avastin (LEA) study. J Clin Oncol 2015;33:1045-52 [25691671]

3 combination with taxanes

Trial	Treatments	Patients	Trials design and methods
bevacizumab + docetaxel vs docetaxel			
AVADO (Miles) 7.5mg , 2010 n=248/241 follow-up:	bevacizumab 7.5mg/kg every 3 weeks plus docetaxel versus placebo plus docetaxel	first-line treatment of HER2-negative metastatic breast cancer	double-blind
AVADO (Miles) 15mg , 2009 n=NA follow-up:	-	first-line treatment of HER2-negative metastatic breast cancer	
bevacizumab + paclitaxel vs paclitaxel			
Martin bevacizumab , 2011 n=NA follow-up:	bevacizumab 10 mg/kg intravenously on days 1 and 15 of each 28-day cycle versus control	patients with HER2-negative locally recurrent or metastatic breast cancer	open design
motesanib + paclitaxel vs paclitaxel			
Martin (motesanib) , 2011 [NCT00356681] n=91/94 follow-up:	motesanib 125 mg orally once per da versus placebo	patients with untreated HER2-negative metastatic breast cancer	double-blind
bevacizumab + taxanes vs taxanes			
E2100 (Miller) , 2007 [NCT00028990] n=368/354 follow-up:	paclitaxel + bevacizumab 10 mg/kg iv every 2 weeks versus paclitaxel 90 mg per square meter of body-surface area on days 1, 8, and 15 every 4 weeks	patients with metastatic breast cancer not previously treated	Parallel groups open
RIBBON-I (Robert) on top Tax or anthra , 2009 n=NA follow-up:	Taxanes or anthracyclines + bevacizumab 15 mg/kg iv every 3 weeks versus taxane (Tax) -based (nab-paclitaxel 260 mg/m(2), docetaxel 75 or 100 mg/m(2)), or anthracycline (Anthra) -based (doxorubicin or epirubicin combinations [doxorubicin/cyclophosphamide, epirubicin/cyclophosphamide, fluorouracil/epirubicin/cyclophosphamide, o	irst-line treatment of human epidermal growth factor receptor 2-negative, locally recurrent or metastatic breast cancer	

References

AVADO (Miles) 7.5mg, 2010:

Miles DW, Chan A, Dirix LY, Corts J, Pivot X, Tomczak P, Delozier T, Sohn JH, Provencher L, Puglisi F, Harbeck N, Steger GG, Schneeweiss A, Wardley AM, Chlistalla A, Romieu G Phase III study of bevacizumab plus docetaxel compared with placebo plus docetaxel for the first-line treatment of human epidermal growth factor receptor 2-negative metastatic breast cancer. J Clin Oncol 2010;28:3239-47 [20498403] 10.1200/JCO.2008.21.6457

AVADO (Miles) 15mg , 2009:

Pivot X, Verma S, Thomssen C, Passos-Coelho JL, Latini L,Ciruelos E, Silva M, von Moos R, Chang H, Miles DW Clinical benefit of bevacizumab plus first-line docetaxel in elderly patients with locally recurrent or Metastatic breast cancer. J Clin Oncol 2009;27:15s (abstr 1094)

Miles DW, Chan A, Dirix LY, Corts J, Pivot X, Tomczak P, Delozier T, Sohn JH, Provencher L, Puglisi F, Harbeck N, Steger GG, Schneeweiss A, Wardley AM, Chlistalla A, Romieu G Phase III study of bevacizumab plus docetaxel compared with placebo plus docetaxel for the first-line treatment of human epidermal growth factor receptor 2-negative metastatic breast cancer. J Clin Oncol 2010;28:3239-47 [20498403]

Martin bevacizumab, 2011:

Martin M, Roche H, Pinter T, Crown J, Kennedy MJ, Provencher L, Priou F, Eiermann W, Adrover E, Lang I, Ramos M, Latreille J, Jagiello-Gruszfeld A, Pienkowski T, Alba E, Snyder R, Almel S, Rolski J, Munoz M, Moroose R, Hurvitz S, Baos A, Adewoye H, Hei Y Motesanib, or open-label bevacizumab, in combination with paclitaxel, as first-line treatment for HER2-negative locally recurrent or metastatic breast cancer: a phase 2, randomised, double-blind, placebo-controlled study. Lancet Oncol 2011;12:369-76 [21429799] 10.1016/S1470-2045(11)70037-7

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E2100 (Miller), 2007:

Miller K, Wang M, Gralow J, Dickler M, Cobleigh M, Perez EA, Shenkier T, Cella D, Davidson NE Paclitaxel plus bevacizumab versus paclitaxel alone for metastatic breast cancer. N Engl J Med 2007;357:2666-76 [18160686] 10.1056/NEJMoa072113

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4 About TrialResults-center.org

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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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