

乳腺癌新型分子靶向药物治疗研究进展

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Research progress in targeted drug therapies for breast cancer

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摘要:

乳腺癌是女性最常见的恶性肿瘤之一,尽管一系列较为有效的化疗药物被应用于乳腺癌的治疗,但晚期乳腺癌的疗效仍不乐观。近年来,曲妥珠单抗、拉帕替尼等药物在乳腺癌治疗中获得成功,为乳腺癌的分子靶向治疗开创了一条新的道路。随后出现的帕妥珠单抗、依维莫司、曲妥珠单抗-DM1等均已进入III期临床试验,这些新药为进一步提高乳腺癌的疗效,延长乳腺癌患者的生存提供了新的选择。

关键词: 乳腺肿瘤;靶向治疗;受体,表皮生长因子;抗体,单克隆;曲妥珠单抗;拉帕替尼;帕妥珠单抗;依维莫司

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参考文献:

- [1]SIEGEL R,NAISHADHAM D,JEMAL A.Cancer statistics,2012[J].CA Cancer J Clin,2012,62(1):10-29.
- [2]BERTHOLD D.Third consensus on medical treatment of metastatic breast cancer[J].Ann Oncol,2010,21(3):655-656.
- [3]ROSEN LS,ASHURST HL,CHAP L.Targeting signal transduction pathways in metastatic breast cancer:a comprehensive review[J].Oncologist,2010,15(3):216-235.
- [4]SLAMON DJ,LEYLAND-JONES B,SHAK S,et al.Use of chemotherapy plus a monoclonal antibody against HER2 for metastatic breast cancer that overexpresses HER2[J].N Engl J Med,2001,344(11):783-792.
- [5]CLEMENS M,EIDTMANN H,NITZ U,et al.Trastuzumab single-drug therapy after failure of cytotoxic treatment for metastatic breast cancer[J].Onkologie,2010,33(8-9):425-430.
- [6]VALERO V,FORBES J,PEGGRAM MD,et al.Multicenter phase III randomized trial comparing docetaxel and trastuzumab with docetaxel,carboplatin,and trastuzumab as first-line chemotherapy for patients with HER2-gene-amplified metastatic breast cancer(BCIRG 007 study):two highly active therapeutic regimens[J].J Clin Oncol,2011,29(2):149-156.
- [7]ANDERSSON M,LIDBRINK E,BJERRE K,et al.Phase III randomized study comparing docetaxel

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plus trastuzumab plus vinorelbine plus trastuzumab as first-line therapy of metastatic or locally advanced human epidermal growth factor receptor 2-positive breast cancer:the HERNATA study[J].J Clin Oncol,2011,29(3):264-271.

[8]EXTRA JM,ANTOINE EC,VINCENT-SALOMON A,et al.Efficacy of trastuzumab in routine clinical practice and after progression for metastatic breast cancer patients:the observational Hermine study[J].Oncologist,2010,15(8):799-809.

[9]von MINCKWITZ G,DU BOIS A,SCHMIDT M,et al.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].J Clin Oncol,2009,27(12):1999-2006.

[10]de LAURENTIIS M,ARPINO G,MASSARELLI E,et al.A meta-analysis on the interaction between HER-2 expression and response to endocrine treatment in advanced breast cancer[J].Clin Cancer Res,2005,11(13):4741-4748.

[11]MONTEMURRO F,ROSSI V,COSSU RM,et al.Hormone-receptor expression and activity of trastuzumab with chemotherapy in HER2-positive advanced breast cancer patients[J].Cancer,2012,118(1):17-26.

[12]KAUFMAN B,MACKAY JR,CLEMENS MR,et al.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].J Clin Oncol,2009,27(33):5529-5537.

[13]VALACHIS A,MAURI D,POLYZOS NP,et al.Trastuzumab combined to neoadjuvant chemotherapy in patients with HER2-positive breast cancer:a systematic review and meta-analysis[J].Breast,2011,20(6):485-490.

[14]BRIA E,CUPPONE F,FORNIER M,et al.Cardiototoxicity and incidence of brain metastases after adjuvant trastuzumab for early breast cancer:the dark side of the moon?A meta-analysis of the randomized trials[J].Breast Cancer Res Treat,2008,109(2):231-239.

[15]CAMERON D,CASEY M,OLIVA C,et al.Lapatinib plus capecitabine in women with HER-2-positive advanced breast cancer:final survival analysis of a phase III randomized trial[J].Oncologist,2010,15(9):924-934.

[16]di LEO A,GOMEZ HL,AZIZ Z,et al.Phase III, double-blind, randomized study comparing lapatinib plus paclitaxel with placebo plus paclitaxel as first-line treatment for metastatic breast cancer[J].J Clin Oncol,2008,26(34):5544-5552.

[17]JOHNSTON S,PIPPEN JJ,PIVOT X,et al.Lapatinib combined with letrozole versus letrozole and placebo as first-line therapy for postmenopausal hormone receptor-positive metastatic breast cancer[J].J Clin Oncol,2009,27(33):5538-5546.

[18]LIN NU,MAYER IA,NAJITA NS,et al.TBCRC003:Phase II trial of trastuzumab(T) and lapatinib(L) in patients(pts) with HER2+ metastatic breast cancer(MBC)[C/OL].(2011-05-20)[2012-09-24].http://meeting.ascopubs.org/cgi/content/abstract/29/15_suppl/527?sid=a54d64b1-0e18-4615-9ece-1523d6dbe0fc.html.

[19]BLACKWELL KL,BURSTEIN HJ,STORNIOLO AM,et al.Randomized study of Lapatinib alone or in combination with trastuzumab in women with ErbB2-positive, trastuzumab-refractory metastatic breast cancer[J].J Clin Oncol,2010,28(7):1124-1130.

[20]BASELGA J,BRADBURY I,EIDTMANN H,et al.Lapatinib with trastuzumab for HER2-positive early breast cancer(NeoALTTO):a randomised, open-label, multicentre, phase 3 trial[J].Lancet,2012,379(9816):633-640.

[21]BASELGA J,GELMON KA,VERMA S,et al.Phase II trial of pertuzumab and trastuzumab in patients with human epidermal growth factor receptor 2-positive metastatic breast cancer that progressed

- during trastuzumab therapy[J]. *J Clin Oncol*, 2010, 28(7): 1138-1144.
- [22] GIANNI L, PIENKOWSKI T, IM YH, et al. 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[J]. *Lancet Oncol*, 2012, 13(1): 25-32.
- [23] BASELGA J, CORTES J, KIM SB, et al. Pertuzumab plus trastuzumab plus docetaxel for metastatic breast cancer[J]. *N Engl J Med*, 2012, 366(2): 109-119.
- [24] BURRIS HR, RUGO HS, VUKLJA SJ, et al. Phase II study of the antibody drug conjugate trastuzumab-DM1 for the treatment of human epidermal growth factor receptor 2 (HER2)-positive breast cancer after prior HER2-directed therapy[J]. *J Clin Oncol*, 2011, 29(4): 398-405.
- [25] MARK DP, KIMBERLY LB, DAVID MILE, et al. Primary results from EMILIA, a phase III study of trastuzumab emtansine (T-DM1) versus capecitabine (X) and lapatinib (L) in HER2-positive locally advanced or metastatic breast cancer (MBC) previously treated with trastuzumab (T) and a taxane [C/OL]. (2012-09-20)[2012-09-24]. http://meeting.ascopubs.org/cgi/content/abstract/30/27_suppl/98?sid=30536e56-33c5-4987-ad1e-5224985e64d0.html.
- [26] LIN NU, WINER EP, WHEATLEY D, et al. A phase II study of afatinib (BIBW 2992), an irreversible ErbB family blocker, in patients with HER2-positive metastatic breast cancer progressing after trastuzumab[J]. *Breast Cancer Res Treat*, 2012, 133(3): 1057-1065.
- [27] GUNZER K, de MONT-SERRAT H, UTTENREUTHER-FISCHER MM, et al. Addition of BIBW 2992, an irreversible inhibitor of EGFR/HER1 and HER2, to letrozole in estrogen receptor (ER)-positive metastatic breast cancer (mBC) progressing on letrozole monotherapy [C/OL]. (2010-05-20)[2012-09-24]. http://meeting.ascopubs.org/cgi/content/abstract/28/15_suppl/1072?sid=002a6e24-928f-4e82-9c78-66368b26a0f2.html.
- [28] BURSTEIN HJ, SUN Y, DIRIX LY, et al. Neratinib, an irreversible ErbB receptor tyrosine kinase inhibitor, in patients with advanced ErbB2-positive breast cancer[J]. *J Clin Oncol*, 2010, 28(8): 1301-1307.
- [29] MILLER K, WANG M, GRALOW J, et al. Paclitaxel plus bevacizumab versus paclitaxel alone for metastatic breast cancer[J]. *N Engl J Med*, 2007, 357(26): 2666-2676.
- [30] MILES DW, CHAN A, DIRIX LY, et al. 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]. *J Clin Oncol*, 2010, 28(20): 3239-3247.
- [31] ROBERT NJ, DIERAS V, GLASPY J, et al. 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]. *J Clin Oncol*, 2011, 29(10): 1252-1260.
- [32] CORTES J, CALVO V, RAMIREZ-MERINO N, et al. Adverse events risk associated with bevacizumab addition to breast cancer chemotherapy: a meta-analysis[J]. *Ann Oncol*, 2012, 23(5): 1130-1137.
- [33] RANPURA V, HAPANI S, WU S. Treatment-related mortality with bevacizumab in cancer patients: a meta-analysis[J]. *JAMA*, 2011, 305(5): 487-494.
- [34] ISAACS C, HERBOLSHEIMER P, LIU MC, et al. Phase I / II study of sorafenib with anastrozole in patients with hormone receptor positive aromatase inhibitor resistant metastatic breast cancer[J]. *Breast Cancer Res Treat*, 2011, 125(1): 137-143.
- [35] BASELGA J, SEGALLA JG, ROCHE H, et al. Sorafenib in combination with capecitabine: an oral regimen for patients with HER2-negative locally advanced or metastatic breast cancer[J]. *J Clin Oncol*, 2012, 30(13): 1484-1491.
- [36] BARRIOS CH, LIU MC, LEE SC, et al. Phase III randomized trial of sunitinib versus capecitabine in patients with previously treated HER2-negative advanced breast cancer[J]. *Breast Cancer Res*

Treat,2010,121(1):121-131.

[37]BERGH J,BONDARENKO IM,LICHINITSER MR,et al.First-line treatment of advanced breast cancer with sunitinib in combination with docetaxel versus docetaxel alone:results of a prospective,randomized phase III study[J].J Clin Oncol,2012,30(9):921-929.

[38]BACHELOT T,BOURGIER C,CROPET C,et al.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].J Clin Oncol,2012,30(22):2718-2724.

[39]BASELGA J,CAMPONE M,PICCART M,et al.Everolimus in postmenopausal hormone-receptor-positive advanced breast cancer[J].N Engl J Med,2012,366(6):520-529.

[40]O SHAUGHNESSY J,OSBORNE C,PIPPEN JE,et al.Iniparib plus chemotherapy in metastatic triple-negative breast cancer[J].N Engl J Med,2011,364(3):205-214.

[41]TUTT A,ROBSON M,GARBER JE,et al.Oral poly(ADP-ribose)polymerase inhibitor olaparib in patients with BRCA1 or BRCA2 mutations and advanced breast cancer:a proof-of-concept trial [J].Lancet,2010,376(9737):235-244.

[42]FINN RS,BENGALA C,IBRAHIM N,et al.Dasatinib as a single agent in triple-negative breast cancer:results of an open-label phase 2 study[J].Clin Cancer Res,2011,17(21):6905-6913.

[43]MODI S,STOPECK A,LINDEN H,et al.HSP90 inhibition is ineffective in breast cancer:a phase II trial of tanespimycin(17-AAG)plus trastuzumab in patients with HER2-positive metastatic breast cancer progressing on trastuzumab[J].Clin Cancer Res,2011,17(15):5132-5139.

[44]RAMASWAMY B,FISKUS W,COHEN B,et al.Phase I - II study of vorinostat plus paclitaxel and bevacizumab in metastatic breast cancer:evidence for vorinostat-induced tubulin acetylation and Hsp90 inhibition in vivo[J].Breast Cancer Res Treat,2012,132(3):1063-1072.