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High efficacy of the combination of oral vinorelbine (NVBo), capecitabine (X) and trastuzumab (H) in HER2-positive metastatic breast cancer (MBC): updated results of an international phase II trial with a median follow-up of 39 months

A. Chan[1], V. Ganju[2], D. Becquart[3], P.F. Conte[4], L. Petruzelka[5], M. Gil-Gil[6], M. Morand[7], N. Vaissiere[7], G. Villanova[7], N. Tubiana-Mathieu[8]. *[1]Mount Hospital, Medical Oncology, Perth, Australia; [2]Frankston Hospital, Medical Oncology, Frankston, Australia; [3]AZ Middelheim, Medical Oncology, Antwerp, Belgium; [4]Policlinico de Modena, Medical Oncology, Modena, Italy; [5]General Teaching Hospital, Medical Oncology, Prague, Czech Republic; [6]Hospital Duran y Reynals, Medical Oncology, L'Hospitalet de Llobregat, Spain; [7]Institut de Recherche Pierre Fabre, Clinical Research, Boulogne-Billancourt, France; [8]CHU Dupuytren, Medical Oncology, Limoges, France*

Background: Chemotherapy (CT) plus H is the standard treatment for HER2-positive MBC. H plus vinorelbine combination therapy is an active and safe regimen in the first-line setting. The all-oral CT combination of NVBo and X has shown activity and good tolerability in MBC. We report the latest results from a multinational phase II study assessing the efficacy and safety of NVBo, X and H in HER2-positive MBC after a median follow-up of 39 months.
Materials and Methods: In this multicenter trial, main eligibility criteria included: HER2-positive disease (3+ IHC or FISH+), documented measurable metastatic disease previously untreated by CT, relapse $\geqslant$6 months after the end of neoadjuvant or adjuvant CT, Karnofsky PS $\geqslant$70. NVBo was given as a 60 mg/m^2 (cycle 1) or 80 mg/m^2 (from cycle 2) dose D1 & D8 every 3 weeks, X at 1000 (750 if $\geqslant$65 y) mg/m^2/bid D1-D14 every 3 weeks, H at 4 mg/kg on D1 as a loading dose then 2 mg/kg i.v. weekly starting on D8. Treatment was continued until progression.
Results: Main patient (pt) characteristics in the full population (n = 50): median age: 53.5 years (18% $\geqslant$65); prior (neo)adjuvant CT 27 pts (54%); visceral involvement 41 pts (82%), >2 metastatic sites 17 pts (34%); median number of cycles: 10 (range:1−71); 72% of pts received more than 6 cycles, 58% more than 8 cycles and 32% more than 16 cycles; median number of NVBo administrations: 20 (range:1–141); median number of trastuzumab administrations: 30 (range:1–218); median relative dose intensity: NVBo 76%, X 78%, H 96%; NVBo dose escalation to 80 mg/m^2: 84%. G3/4 NCI CTC v2 adverse events: neutropenia 71%, hand-foot syndrome 20%, diarrhoea 16%, vomiting 12%, asthenia 8%, febrile neutropenia 8%, infection 6%, LVEF decline 4%, stomatitis 4%, nausea 4%, alopecia (grade 2) 14%. Efficacy (n = 44 evaluable patients): objective response rate (RECIST) 77% (95% CI [62−89]), CR 21%, PR 57%, SD 18%, PD 5%, disease control (CR+PR+SD $\geqslant$6 months) 93% (95% CI [81−99]); median duration of response was 13.3 months (95% CI [9.8−15.7]) and median progression-free survival was 12.8 months (95% CI [10.8−16.9]). With a median follow-up of 39 months, overall survival results are not mature yet. 5 patients are still receiving full study treatment.
Conclusion: Combination chemotherapy with NVBo and X plus H is an active first-line regimen for HER2-positive MBC. Treatment could be continued until disease progression without a pre-planned maximum number of cycles in many patients.

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Influence of zoledronic acid on bone mineral density in premenopausal women with hormone receptor positive or negative breast cancer and neoadjuvant or adjuvant chemotherapy or endocrine treatment

M. Ziller[1], P. Hadji[1], K. Kauka[1], T. Bauer[1], U.S. Albert[1], M. Muth[2], M. Kalder[1]. *[1]Philipps University, Department of Endocrinology Reproductive Medicine and Osteoporosis, Marburg, Germany; [2]Novartis Pharma, BU Oncology, Nuernberg, Germany*

Background: Depending on baseline bone mineral density (BMD), adjuvant chemotherapy or endocrine therapy of premenopausal breast cancer patients can lead to a substantially decrease in BMD and consequently increased risk of osteoporotic fractures. Hereby, a significant decrease of BMD > 10% after 2 years of therapy has been reported. Adjuvant therapy with zoledronic acid in early breast cancer was investigated in the ABCSG-12 and the Zo-Fast trial. Zoledronic acid 4 mg given every six months increased BMD in premenopausal and postmenopausal women receiving endocrine treatment. In addition, a significant increase in PFS could be observed in favor of zoledronic acid.
Material and Methods: The goal of the two monocentric, placebo-controlled, randomized studies Probone I and Probone II is to investigates the influence of adjuvant zoledronic acid therapy on BMD in premenopausal women with BC. Hormone receptor negative patients (Probone I) are treated with (neo)adjuvant chemotherapy, hormone receptor positive patients (Probone II) with endocrine treatment alone or in combination with (neo)adjuvant chemotherapy. Patients receive zoledronic acid or placebo i.v. every 3 months for 2 years. Primary objective is the change in BMD at the lumbar spine between baseline and month 24 (measured by DXA). Secondary objectives include disease free survival, BMD at total hip and os calcis, BMD measured by QUS at os calcis and phalanges, markers of bone turnover, pathologic fractures, safety and tolerability. BMD is measured at baseline, 12 and 24 months. QUS and markers of bone turnover are measured at baseline, 3, 6, 12 and 24 months.
Results: As of April 2009, 65 hormone receptor positive and 11 hormone receptor negative patients have been enrolled into the studies. 30 out of 74 patients have already finished treatment. The design of the study and demographic data of the enrolled patients will be presented.
Conclusion: Probone I/II are two ongoing studies to evaluate the effect of adjuvant zoledronic acid on BMD in premenopausal patients with breast cancer receiving chemotherapy and/or endocrine therapy. The results of these studies will be of great interest for clinical practice because of the lack of approved treatments for the prevention of cancer treatment induced bone loss (CTIBL) in patients with early breast cancer.

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Efficacy of combination treatment with epirubicin (EPI) plus docetaxel (DOC) in advanced breast cancer

Y. Hata[1], M. Takahashi[2], H. Takahashi[2], M. Hosoda[2], K. Taguchi[3], M. Tamura[4], N. Tomioka[1], S. Ohsawa[1], T. Nakagawa[1], S. Matsuoka[1]. *[1]Sapporo Social Insurance General Hospital, Surgery, Sapporo, Japan; [2]Hokkaido University Hospital, Surgery, Sapporo, Japan; [3]Hokkaido Cancer Center, Breast Surgery, Sapporo, Japan; [4]KKR Sapporo Medical Center, Surgery, Sapporo, Japan*

Background: The present study aimed at evaluating whether this new regimen could be effective in patients with primary advanced breast cancer.
Material and Methods: Thirty-two women (mean age 50.4 years, range 31−63) with primary advanced breast cancer were given epirubicin (EPI) 40−60 mg/m^2 and docetaxel (DOC) 50−60 mg/m^2 intravenously every three weeks. The efficacy was evaluated after 4 cycle treatments.
Results: There were 5 complete responses (CR) and 15 partial responses (PR), giving an overall response rate of 62.5%. There were 2 pathological CR (8.0%) which showed complete disappearance of cancer cells. The high dose group showed a better response than the low-dose group. The most common grade 3/4 adverse events were neutropenia (31.3%) and general fatigue (6.0%). The 5-year survival rate in stage IIIB (n = 9) and stage IV (n = 8) patients was 46.7%. When divided into subgroups according to response (RECIST), the median survival time (MST) was 64.4 months in the responder group (CR and PR) versus 23.3 months in the non-responder group (SD and PD) ($p < 0.05$).
Conclusions: The simutaneous combination treatment of EPI and DOC is effective for primary chemotherapy and can be performed safely for outpatients.

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Bevacizumab (Bev) combined with either capecitabine (X) or weekly paclitaxel (Pac) as first-line therapy for HER2-negative locally recurrent or metastatic breast cancer (LR/MBC): the CECOG phase III TURANDOT trial

I. Lang[1], M. Inbar[2], G. Steger[3], R. Greil[4], Z. Zvirbule[5], S. Beslija[6], Z. Kahán[7], V. Taskova[8], B. Kaufmann[9], C.C. Zielinski[3]. *[1]National Institute of Oncology, Department of Medical Oncology "B", Budapest, Hungary; [2]Tel Aviv Sourasky Medical Center, Division of Oncology, Tel Aviv, Israel; [3]Medical University of Vienna, Department of Medicine 1 and Cancer Centre Clinical Division of Oncology, Vienna, Austria; [4]Paracelsus Medical University Salzburg, 3rd Medical Department of Oncology Hematology Hemostaseology Rheumatology and Infectiology, Salzburg, Austria; [5]Riga Eastern University Hospital, Latvian Oncology Centre, Riga, Latvia; [6]Clinical Center University of Sarajevo, Institute of Oncology, Sarajevo, Bosnia-Herzegovina; [7]University of Szeged, Department of Oncotherapy, Szeged, Hungary; [8]Interdistrict Dispensary for Oncological Diseases "Dr. Marko Markov" – Varna Base No. 2, Department of Chemotherapy and Palliative Care, Varna, Bulgaria; [9]"Sheba" Medical Center, Oncology Department, Tel Hashomer, Israel*

Background: Bev combined with taxane-based therapy or X significantly improves progression-free survival (PFS) versus chemotherapy (CT) alone as first-line treatment for LR/MBC. However, the relative efficacy of Bev+X versus Bev+Pac is unknown.
Materials and Methods: Eligible patients (pts) have HER2-negative LR/MBC, ECOG PS 0−2 and have received no prior CT for LR/MBC.