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Intravenous and oral ibandronate reduce the risk of skeletal related events in patients with metastatic bone disease

J.-J. Body[1], D. Tripathy[2], M. Pecherstorfer[3], B. Bergstrom[4]. [1] *Institut Jules Bordet, Brussels, Belgium;* [2] *University of Texas Southwestern Medical Center, Dallas, USA;* [3] *Wilhelminenspital, Vienna, Austria;* [4] *F. Hoffmann-LaRoche Inc, Nutley, USA*

Background: Ibandronate is a highly potent, third-generation bisphosphonate that targets the underlying pathophysiology of metastatic bone disease (MBD) by inhibiting osteoclast-mediated bone resorption. Three multicenter, randomized, double-blind, placebo-controlled phase III trials have investigated the impact of intravenous (i.v.) and oral ibandronate on the occurrence of skeletal related events (SREs) in women diagnosed with MBD from breast cancer.

Methods: In the i.v. study, patients were randomized to treatment with ibandronate 6mg (n=154) or placebo (n=158) infused over 12 hours every 4 weeks. In two trials of oral ibandronate, patients were randomized to receive placebo (n=277) or ibandronate 50mg (n=287) once daily. A multivariate Poisson regression analysis was conducted on the data from the i.v. study and from the oral studies, to assess the number of SREs arising in each treatment group during the 96-week treatment period.

Results: The multivariate Poisson regression analysis of the i.v. study demonstrated that patients treated with i.v. ibandronate 6mg experienced a statistically significant 40% reduction in the risk of SREs compared with placebo (p=0.0033). Analysis of the pooled oral dataset revealed that a daily dose of oral ibandronate 50mg provided a similar reduction in the risk of SREs (38%), which was also statistically significant ($p<0.0001$ versus placebo).

Conclusions: Ibandronate 6mg i.v. and oral ibandronate 50mg have equivalent clinical effects on bone events in patients with MBD from breast cancer. The risk reductions reported for both the i.v. and oral formulations of ibandronate appear to be comparable to zoledronic acid [1] and greater than for pamidronate and clodronate in MBD [2], warranting further investigation in direct comparative studies. Oral ibandronate offers an effective and convenient alternative to other i.v. bisphosphonates, with the potential for at-home treatment. This would eliminate the need for unnecessary, time consuming hospital visits, especially in patients who are not receiving chemotherapy.

References

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A multicenter phase II study of capecitabine plus paclitaxel in metastatic breast cancer: Survival update

W. Gradishar[1], L. Meza[2], T. Hill[3], D. Samid[4], Y.-M. Chen[5], B. Amin[6]. [1] *Northwestern University, Chicago, USA;* [2] *South West Oncology Associates, Lafayette, USA;* [3] *Roche Labs Inc., Nutley, USA;* [4] *Mid Dakota Clinic, Bismark, USA*

Background: Capecitabine (Xeloda), a novel oral fluropyrimidine, is converted to 5-FU through three enzymatic steps. The final activation step involves thymidine phosphorylase (TP), an enzyme present at higher levels in malignant tissues compared to normal cells. TP can be further upregulated by various agents, including taxanes. The combination of capecitabine and paclitaxel has synergistic antitumor activity in pre-clinical models. Consistent with this finding, results of a large phase III trial of capecitabine combined with docetaxel showed superior response rate, time to tumor progression, and overall survival compared to docetaxel monotherapy.

Methods: This multicenter phase II study evaluated the efficacy and safety of the combination of capecitabine (825 mg/m^2 twice daily d1-14, q3 weeks) and paclitaxel (175mg/m^2 d1, q3w) as a first or second line treatment of metastatic breast cancer.

Results: Forty-eight patients were enrolled, of whom 47 were evaluable for this analysis. Patient characteristics at baseline were median age 52 years (range 35-76 years) and median Karnofsky Performance Status 90 (range 70-100). Patients received a median of 7 treatment cycles (mean=9.0, range 1-42). There were, 7 (14.9%) complete responses, and 17 (36.2%) partial responses observed, for an overall objective response rate of 51.1%. Median time to tumor response was 3.9 months, to disease progression was 10.6 months and median overall survival time was 29.9 months. The most common related grade 3/4 adverse reactions were neutropenia (n=7, 15%), alopecia (n=6, 13%) and hand-foot syndrome (grade 4 not applicable) (n=5, 11%).

Conclusion: This data indicates that the combination of capecitabine and paclitaxel is an effective and safe treatment in patients with metastatic breast cancer.

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Efficacy and toxicity of docetaxel or cisplatin chemotherapy in combination with trastuzumab in the treatment of patients with chemotherapy pre-treated HER-2/neu overexpressed metastatic breast cancer

B. Bauer-Kosinska, I. Lemanska, I. Glogowska, R. Sienkiewicz, T. Pienkowski. *The Maria Sklodowska-Curie Memorial Cancer Centre, Breast Cancer Department, Warsaw, Poland*

Objective: to asses the efficacy of cisplatin or docetaxel in combination with trastuzumab in metastatic HER-2/neu overexpressed breast cancer patients, treated previously with other chemotherapy regimens.

Material and methods: forty one patients with metastatic HER-2/neu overexpressed breast cancer were treated with weekly trastuzumab (4mg/kg at initial dose and 2 mg/kg as maintenance dose) and - I - docetaxel 100 mg/m^2 (N = 18) or II - cisplatin 75 mg/m^2 (N = 23) every three weeks. Median age was I: 56 years (range: 36 79); II: 47 years (range: 35-47); median number of metastatic sites I: 2,5 (range 1 4); II 2,0 (range 1 5). Median number of previous chemotherapy regimens I 2,0; II 2,0. All of the patients were evaluable for tumour response. The response was assesed according to RECIST criteria.

Results: the objective response (OR) obtained in docetaxel + trastuzumab group - 55%, stable disease (SD) - 23%, progressive disease (PD) - 22% median TTP: 26 weeks. In cisplatin + trastuzumab group: OR 48%, SD 35%, PD 17%, median TTP 22 weeks.

In case no life-threatening toxicity was observed.

Conclusion: both docetaxel and cisplatin are effecive in combination with trastuzumab in metastatic, haevily pretreated HER-2/neu overexpressed breast cancer patients.

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Hepatic intra-arterial chemotherapy in i.v. chemoresistant breast cancer pts with liver metastases.

M. Airoldi[1], C. Zanon[2], F. Pedani[1], R. Clara[2], S. Marchionatti[1], M. Bortolini[2]. [1] *S.Giovanni Antica Sede Hospital, Medical Oncology Department, Torino, Italy;* [2] *S.Giovanni Antica Sede Hospital, Surgical Oncology Department, Torino, Italy*

Liver metastases (LM) have been associated with poor overall survival in metastatic BC; patients with liver progressive disease after conventional chemotherapy have a very poor prognosis. Twelve patients (median age = 58 yrs; median ECOG PS = 1) affected by polymetastatic liver disease (more than 5 metastases) with progressive disease after taxanes, anthracyclines and vinorelbine were submitted to Intra-Arterial Chemotherapy (HIAC). All patients had received two or more lines of chemotherapy for metastatic Breast Cancer (BC) with the previous reported drugs; in all patients liver was the only site of metastasis as shown by total body CT and PET scan. We performed HIAC by a percutaneous positioning of arterial port-a-cath (Zanon-Grosso procedure) introduced by the left subclavian artery. Fluorouracil 1000 mg/m^2/d on day 1-3 as continous infusion, Cisplatin 10 mg/m^2 and Mytomicin-C 2 mg/m^2 both twice daily on days 1-3, were used. Courses were repeated after 5-6 weeks. A median of 5 courses were administered. Neither toxic deaths nor severe catheter-related complications, nor severe clinical infection were observed. Two cases of iatrogenic gastro-duodenal ulcer were documented. Catheter displacement occurred in 1 patient without relevant therapy changes. We observed 3 CR (25%) lasting 24, 18+ and 12+ months; 5 PR (42%) with a median duration of 6+ months, 2 NC (16%) and 2 PD (16%). One patient in CR developed lung metastases after 24 months without CT and PET evidence of LM. In conclusion HIAC can obtain significant overall response rates in poor prognosis BC patients with LM.