5068 POSTER

Cardiac safety of non-pegylated liposomal doxorubicin in combination with docetaxel as 1st line treatment in locally advanced or metastatic HER2 negative breast cancer (MYOTAX study)

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Background: Doxorubicin is an effective agent in metastatic breast cancer (BC), however it is cardiotoxic. Incidence of heart failure is 2−4% and increases considerably with cumulative doses over 450–550 mg/m^2. In Myocet® doxorubicin is encapsulated in liposomes. It is delivered predominantly to areas with increased capillary permeability such as tumors and reduces cardiac exposure. We conducted an open non-comparative study to assess cardiac safety of Myocet® in combination with docetaxel.
Materials and Methods: 60 females with locally advanced or metastatic HER2 negative BC. 6 cycles of Myocet® 60 mg/m^2 and docetaxel 75 mg/m^2 q3w as 1st line therapy. Left ventricular ejection fraction (LVEF, echo or MUGA) and disease status were assessed after cycle 2, 4 and 6. Primary endpoint: signs and symptoms of heart failure (HF, NYHA III-IV) or LVEF <50% and decrease ⩾5% (with symptoms) or ⩾10% (without symptoms).
Results: To date, data on 39/60 patients (pats) are available. 3 pats had locally advanced and 36 metastatic BC. Mean age 58.5 years (y) (31−81), mean disease duration 6.7 y (1 month-18 y), 16 pats received anthracyclines (anthra) in the past. 23 pats received 6 cycles of study medication, mean no. of cycles 4.8 (1−6). 1 pat (anthra pretreated) had symptoms of dypnea, atrial fibrillation and LVEF decrease from 78 to 51% (2nd cycle). In 1 pat (not anthra pretreated) LVEF decreased to <50% (62 to 43%, 2nd cycle).

	Mean LVEF		
	all pats	pats with 6 cycles Myocet®/docetaxel	anthracyclin pretreated pats
baseline	65.0 (n = 39)	65.8 (n = 23)	64.6 (n = 16)
cycle 2	61.3 (n = 35)	61.9 (n = 23)	59.9 (n = 14)
cycle 4	60.5 (n = 26)	60.9 (n = 23)	59.3 (n = 11)
cycle 6	59.7 (n = 23)	59.7 (n = 23)	58.0 (n = 11)

32 grade ⩾3 toxicities occurred in 20 pats in 187 cycles in total; most frequent: neutropenia (±fever) 15 pats, mucositis 11 pats (2 with GI perforation, possibly related to treatment). Premature discontinuations: progressive disease 10, cardiotoxicity 2, other toxicity 4 pats. Partial remission was confirmed in 16 pats and stable disease in 10.
Conclusion: 1/39 pats developed symptomatic HF during the study. Mean LVEF decreased from 65 to 60% over time. The decrease in the anthra pretreated group was not different from the not pretreated pats. PR was observed in 44% of evaluable pats. These preliminary data suggest that liposomal doxorubicin might provide more cardiac safety, especially at higher cumulative doses, compared to conventional anthracyclins. The combination of Myocet® and docetaxel is efficacious and sufficiently well tolerated and is currently investigated in combination with trastuzumab in HER2 positive pats.

5069 POSTER

Ibandronate in clinical practice: renal safety and tolerability in patients with metastatic breast cancer

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Background: Bisphosphonates are the standard of care for patients with bone metastases. A major goal in treating metastatic bone disease with bisphosphonates is the recovery of quality of life. Many patients already have reduced quality of life due to the effects of their disease and their anticancer treatments. Therefore, drug tolerability and route of administration are important when choosing a bisphosphonate treatment. Ibandronate (Bondronat®) is a non-cyclic, third-generation aminobisphosphonate that is available in intravenous and oral formulation. Phase III registration trials support that the renal safety of ibandronate is comparable to placebo. Here we report an interim analysis of renal safety and tolerability data from a post-marketing surveillance of ibandronate.
Patients and Methods: In this 24-week analysis, 1897 patients (aged 63.3±11.9 years) received standard intravenous ibandronate 6 mg every 4 weeks or daily oral ibandronate 50 mg for 24 weeks. For analysis, patients were divided into three subgroups according to previous treatment – bisphosphonate naïve (1219) – prior ibandronate treatment (n = 213) – prior treatment with other bisphosphonates (n = 465). Renal safety was monitored using serum creatinine levels. Tolerability was estimated by physicians and patients using a standard scale (range: poor, moderate, good, and excellent).
Results: Mean (±SD) baseline creatinine values remained stable throughout ibandronate treatment but 26% of the zoledronate pretreated patients showed a decreased renal function at baseline (>1.2 mg/dl). This proportion was considerably higher than in bisphosphonate naïve patients (8%), pamidronate pretreated patients (16%), clodronate pretreated patients (17%) and ibandronate pretreated patients (11%). Nearly all physicians (99%) rated ibandronate as good or very good, Patient-assessed tolerability was also high (97% rated ibandronate as good/very good).
Conclusions: The data shows that the renal safety profile of ibandronate shown in clinical trials transfers to actual clinical practice. Both formulations of ibandronate were rated as well tolerated by physicians and patients.
These findings confirm the safety and tolerability of ibandronate und practical condition.

5070 POSTER

Real-life usage of capecitabine (X) for advanced breast cancer (ABC) in Germany: efficacy and safety results from a large (n = 870) non-interventional study

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Background: Although capecitabine (X) is an established chemotherapy for ABC, anecdotal evidence, retrospective studies and market research suggest wide variation in the starting dose and duration of treatment of X.
Materials and Methods: Patients with ABC pretreated with or ineligible for anthracycline therapy received X as monotherapy or combination therapy at the physician's discretion. Data on dose, treatment duration, treatment delays/interruptions, concomitant anti-cancer therapy and efficacy were collected until disease progression.
Results: Between 2002 and 2007, 870 patients were recruited from 135 centres. Most patients (62%) were aged 50−69 years and 46% had received prior taxane therapy. The majority (64%) received X monotherapy (median starting dose 1070 mg/m^2 bid). In those receiving X combination therapy, the median starting dose was 987 mg/m^2 bid. X was typically combined with vinorelbine or docetaxel. Generally, patients receiving X alone were slightly older and more likely to have hormone receptor-positive disease than those receiving combination therapy. X was given 1st line in 35% of patients and 2nd line in 33%. Patients received a median of 7 cycles; 26% received ⩾12 cycles. In the monotherapy group, the X dose decreased constantly throughout cycles 6−12; in the combination group, the dose remained stable. The median dose across all cycles was almost identical in the two cohorts (962 and 964 mg/m^2 bid, respectively). The most common non-haematological adverse event was hand-foot syndrome (all grades: 54%; grade 3: 7%), leading to premature treatment discontinuation in 6%. Myelosuppression and alopecia were less common with X monotherapy than X combination therapy. Overall response rate (RR) was 41% (95% CI: 38−45). Median progression-free survival (PFS) was 7.5 months (95% CI: 7.1−8.3). RR was higher with combination therapy (49%) than monotherapy (37%), but PFS was similar in the two cohorts. Good performance status at baseline was a significant predictor of efficacy.
Conclusions: X, either alone or in combination, is a feasible and effective treatment for ABC. The starting dose and median delivered dose were considerably lower than the registered dose. Our findings in real-life clinical practice compare favourably with results from interventional studies, perhaps reflecting the longer treatment duration possible at a more tolerable dose.
Study ML16743 was supported by Roche Pharma AG, Germany.