treated with trastuzumab and chemotherapy. Clinical trials are indicated to evaluate:1) if an active surveillance in HER2-overexpressing MBC pts (by TC or MRI) may be beneficial for early CNS metastases diagnosis and treatment; 2) or if there is indication to prophylactic cranial irradiation (PCI) in a population at high risk of developing brain metastases.

413 POSTER

A multicenter Phase II study of Epirubicin (E) with low-dose Herceptin (LD-H) as a first line treatment in HER-2 overexpressing metastatic breast cancer (MBC): Preliminary results

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Background: The combination of Doxorubicin and Herceptin (H) proved to be an effective regimen in advanced breast cancer, although it was associated with an increased risk of cardiotoxicity. The aim of this study was to evaluate the activity and cardiac safety of the combination of Epirubicin (E) with low-dose Herceptin (LD-H).
Material and methods: This was a two step study: In the first step, H was given at a loading dose of 2 mg/Kg on day 1, followed by 1 mg/Kg weekly; in the second step ($\geqslant$ 12 objective responses/21 pts), the dose of H was increased to 2 mg/kg weekly. E was administered at 90 mg/m^2 on day 1 every 3 weeks. After 6–8 courses of this combination, H was administered as a single agent for a maximum of 52 weeks. To assess cardiotoxicity, pts were evaluated for the Left Ventricular Ejection Fraction (LVEF) at baseline, every two cycles during E and LD-H, and every three months during LD-H alone. Either ultrasonography or angioscintigraphy were used. Cardiotoxicity was defined as the appearance of signs or symptoms of congestive heart failure in $\leqslant$10% of pts at an E dose of 720 mg/m^2 or in $\leqslant$20% of pts at an E dose > 720 <1000 mg/m^2.
Results: Twenty-one pts entered the first step: median age was 55 years (41–70 years), hormonal status was positive in 9 pts and negative in 10. Eight pts had received prior adjuvant anthracyclines, and 8 pts prior endocrine therapy. The majority of pts had > 2 organ sites of involvement with visceral lung metastases predominating. A median of 6 cycles (range 1–18) was administered with 134 cycles evaluable for toxicity. The regimen was well tolerated, with grade 3/4 neutropenia, alopecia, and thrombocytopenia occurring in 55%, 25% and 10% of the pts, respectively. Six episodes of cardiotoxicity were observed (an asymptomatic decrease in LVEF *15% in 4 pts and an asymptomatic decline of LVEF at $\leqslant$50% in 2 pts). At the time of analysis, 12 (57%) pts achieved a partial response, 6 (%) had stable disease, and 3 (%) had progressive disease. The median time to progression was 9.8 months (95%CI: 5. 5–14.1) and the median overall survival was not reached.
Conclusions: These preliminary results show that the combination of E+LD-H possesses good antitumor activity, with limited cardiotoxicity. The Protocol Committee recommended to enter the second step of the study, maintaining the dose of H at 1 mg/Kg weekly. Accrual is continuing; an update will be presented at the meeting.

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Final results of the HERMINE cohort: a retrospective and prospective, longitudinal French cohort study of 623 metastatic breast cancer women treated by trastuzumab

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Background: The efficacy and safety of trastuzumab (T) in combination with taxanes have been documented in clinical trials of HER2-positive metastatic breast cancer (MBC), particularly in terms of overall survival (OS) and time to progression (TTP) in first-line therapy. The aim of the study was to understand treatment use and outcomes in a large patient population under real-life conditions.
Methods: HERMINE is a longitudinal, observational study by 102 oncologists in France. Eligible patients (pts) $\geqslant$ 18 yrs all had MBC and started T treatment in 2002. Initial data were collected retrospectively (ESMO 2004), with a *2-year follow-up. All data were collected from patient files and reviewed by an independent scientific committee. Study endpoints included duration of T treatment, TTP, OS and cardiac safety.
Results: A total of 623 of 643 pts were analysed with a median follow-up of 23 months. Pts had a median age of 56 years (27–85 years), with median time from first diagnosis of 4.5 years and median disease-free interval of 2.0 years; 20% had MBC at first diagnosis, 71% had visceral metastases and 23% had past cardiac history. Tumour characteristics are as follows: ductal carcinoma = 91%, HER2-positive (IHC 3+) = 93%; SBR III = 56%; ER-positive and/or PR-positive = 6%; ER and PR-positive = 33%. Pts previously had surgery (88%), radiotherapy (82%), chemotherapy (90%) and/or hormonal therapy (58%). T treatment was once-weekly (89%), in combination with other treatment (94%) (paclitaxel = 61%, vinorelbine = 35%, docetaxel = 25%, capecitabine = 9%, or others). There were 19 heart failures (3% of pts) but no death was related to T adverse events. Table 1 presents the median T treatment duration, TTP and OS, according to T treatment lines (Kaplan-Meier method).

Table 1: Comparison of median T treatment duration, TTP and OS

T treatment (lines)	Median [95%CI] T treatment duration (months)*	Median [95%CI] TTP (months)*	Median [95%CI] OS (months)*
1st line (n = 221, 37%)	16.2 [13.2; 18.6]	10.3 [9.3; 12.5]	30.4 [25.4]
2nd line (n = 138, 23%)	15.9 [13.2; 19.4]	9.0 [7.2; 10.6]	27.2 [22.7; 33.0]
$\geqslant$3rd line (n = 243, 40%)	8.9 [7.3; 12.2]	6.3 [5.6; 7.8]	23.3 [20.3; 26.2]
All (n = 623)	13.4 [11.1; 15.5]	8.6 [7.7; 9.3]	26.0 [23.4; 29.0]

* $p < 0.05$

Conclusion: Two-year results confirm that heart failure frequency is similar to results of previous pivotal trials. Results confirm the efficacy data from the M77001 trial in terms of TTP (11.7 months) and OS (31.2 months).

References

[1] ESMO abstract 109PD, 2004.

415 POSTER

Biological and clinical concordance during chemotherapy in metastatic breast cancer

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Background: Frequently in clinical practice, the anatomic standard response evaluation to chemotherapy (CT) becomes difficult, mainly due to cases of non measurable disease and limitations in imaging availability. The usefulness of circulating tumour markers (CTM) in monitoring CT in Metastatic Breast Cancer (MBC) remains under investigation. We try to analyse the biological (bio) and clinical (clin) concordance during CT in MBC.
Material and methods: In 106 consecutive courses of different schedules of CT given along 3 years to 55 patients with progressive MBC, we conducted a prospective trial analysing 4 CTM – oncofetal, 2 mucin related and cytokeratin (CK) – every 3 weeks before CT infusions and performed CTM concentration / time curves. Clinical responses (Cl R) were measured every 2 months according to UICC criteria (measurable disease, 84% of the courses) and Eagan criteria (evaluable disease, 16%). Bio kinetic change has been defined as a lineal slope that includes 2 early and consecutive changes of at least 25% of CTM start value. The analysis covered 604 cycles, 405 curves and 2417 marker determinations. Statistical was performed by SPSS 11.
Results: The sensibilities of CTM at start values of treatment were:
CEA: 72/106 (67.9%)
CA 15.3: 87/106 (82.1%)
CA 549: 76/94 (80.9%)
TPA: 82/97 (84.5%)
Clinical responses were: CR: 15; PR: 41; SD: 25; PD: 21; NE: 4. In CTM expressing diseases, 3 biological patterns during CT can be detected corresponding to directional possibilities: progressive elevation (Pbio), progressive download (Rbio) and stabilization (without bio kinetic criteria of change (Sbio). Considering 2 types of bio responses, progression (Pbio) versus biological control (Cbio = Rbio+Sbio), the cross matching with corresponding clinical responses, i.e., clinical progression (Pclin) versus clinical control (Cclin = CR+PR+SD) shows an excellent concordance between clin and bio behaviours for any expressing marker: 97% for CEA; 97.5% for CA 15.3; 95.7% for CA 549 and 98.7% for TPA(CK 18–19), Tables shows results of circulating CA 15.3 and Cytokeratin 18–19 (TPA). Tables showing other CTM results, as patterns of curves, will be presented as a poster at the meeting.