1263 POSTER DISCUSSION

Phase III study of liposome-encapsulated doxorubicin (TLC D-99) and cyclophosphamide (CPA) vs. epirubicin (EPI) and CPA in first-line treatment of metastatic breast cancer (MBC)

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Purpose: To compare the efficacy and toxicity of TLC D-99 and EPI when used in combination with CPA.

Methods: 160 patients with MBC and no prior anthracycline therapy were randomised to receive either D-99 (75 mg/m^2) or EPI (75 mg/m^2), in combination with CPA (600 mg/m^2) every 3 weeks as first line treatment for their MBC. The primary efficacy endpoints were response rates and progression-free survival. Responses were assessed using WHO criteria. Cardiac function was monitored by echocardiography. Patients were removed from study if LVEF declined ≥20% from baseline to a final value of ≥50%, or by ≥10% to <50%.

Results: Median age was 53 years on both treatment groups. Other prognostic factors were also balanced.

	TLC D-99 (n = 80)	Epirubicin (n = 80)	p-value
Response rate (CR + PR)	46%	39%	NS
Progression-free survival	7.7 mon.	6.0 mon.	0.04
Grade 3 Stomatitis/Mucositis	7%	0%	0.03
Protocol-defined LVEF changes	11%	9%	NS

No dermatitis was reported with this liposome encapsulated doxombicin.

Conclusion: In this randomised prospective study the comparator TLC D-99 was superior to EPI in terms of time to disease progression when combined with CPA, but EPI may have less acute toxicity in terms of stomatitis/mucositis.

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Promising activity with eniluracil (776C85) and oral 5-fluorouracil in patients with anthracycline-refractory of anthracycline- and taxane-refractory advanced breast cancer: A phase II study

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Introduction: Eniluracil (776C85) is a potent inactivator of dihydropyrimidine dehydrogenase, the most important enzyme in 5-FU catabolism. Coadministration of eniluracil allows low dose 5-FU to be given orally with plasma levels comparable to those reported in the literature with continuous infusional 5-FU.

Method: Patients with refractory advanced breast cancer (ABC), were enrolled into a multicentre, phase II study of eniluracil/5-FU. Patients were stratified as anthracycline-refractory (AR) and anthracycline-and taxane-refractory (ATR) which were strictly defined. Patients had to have measurable disease, a Karnofsky Performance Status (KPS) ≥ 70, an estimated creatinine clearance >50 mL/min and no more than 2 prior chemotherapies. Oral 5-FU 1 mg/m^2 and eniluracil 10 mg/m^2 together, were given twice daily for 28 days of each 35-day course

Results: 106 patients entered the study, 61 with AR and 45 with ATR ABC. Median age was 54 years (range 31–77). Currently 85 patients are evaluable for response. The response rate in AR and ATR patients was 11/49 (22%) and 8/36 (22%), respectively. Treatment was well-tolerated with a low incidence of treatment-related grade 3/4 toxicities: thrombocytopenia (8%), granulocytopenia (8%), nausea (2%) and fatigue/asthenia (2%).

Conclusion: Oral 5-FU plus eniluracil is an active, well-tolerated, convenient outpatient therapy in refractory-advanced breast cancer.

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Quality of life audit of 161 anthracycline pretreated metastatic breast cancer patients treated with docetaxel

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Introduction: 55 oncologists in 39 UK centres are participating in a British national breast cancer Quality of Life (QoL) audit programme. EORTC QLQ-C30 data, together with clinical response data and Karnofsky performance status (KPS) have been collected before, during and after docetaxel (D) treatment of patients (pts) with metastatic breast cancer (MBC) who have failed anthracycline treatment. The aim is to monitor QoL prospectively, using a recognised instrument, together with KPS and response data, in an unselected population of pts with MBC treated with D.

Procedures: At baseline, after each alternate cycle of D and at the end of chemotherapy, pts completed a QLQ-C30 questionnaire which was analysed together with tumour response data and changes in KPS.

Data: 161 (160 F, 1 M) evaluable pts provided data before, during and after chemotherapy. The median number of cycles administered was 5 (range [r] 2–9) and pts completed a median of 3 (r 2–5) assessments. Mean age was 49.1 years (r 27–76) and mean KPS at entry was 79.9 (r 40–100) and at end of chemotherapy 78.5 (r 35–100). Intent-to-treat response rates were 6 (4%) complete responses, 51 (32%) partial responses and 45 (28%) disease stabilisation. A further 34 (21%) pts were not assessable for response. Comparing total cohort changes (n = 161) in QoL domains between baseline and end of chemotherapy, there were significant beneficial changes in the constructs for pain (mean change [m] = 10.1, p = 0.0001), emotional function (m = 6.1, p = 0.001), constipation (m = 8.6, p = 0.002) and insomnia (m = 6.3, p = 0.04), while there were detrimental changes in the constructs for diarrhea (m = 7.7, p = 0.002) and fatigue (m = 5.5, p = 0.02.) Notably, in the 59 pts not clinically responding to chemotherapy, there were beneficial changes in the domains of constipation, pain and emotional function, though nausea/vomiting and diarrhea were worse.

Conclusion: This instrument has the sensitivity, in a real-life setting, to detect both positive and negative changes in individual QoL parameters. There was no evidence that overall QoL is impaired during treatment of MBC with docetaxel.

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Outpatient sequential alkylating regimen with stem cell support for patients with breast cancer

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Purpose: The objective of this study was to evaluate the feasibility to administer as outpatient a sequential high dose alkylating regimen with hematopoietic growth factor (HGF) and stem cell support to patients with an advanced breast cancer who had received at least one chemotherapy regimen.

Methods: Prior to the entry in the study, peripheral blood stem cells (PBSC) were collected after high dose of chemotherapy and HGF. Two consecutive cycles of chemotherapy were planned: Thiotepa (T) then 15 days after BiCNU. Three consecutive dose levels had to be studied: 400 mg/m^2, 500 mg/m^2 and 600 mg/m^2. The administration of HGF and reinfusion of PBSC followed both cycles. Toxicity and response were evaluated according the WHO recommendations.

Results: From 04/96 to 08/98, 30 females entered in this study: 8 in the 1st dose level, 12 in the 2nd and 10 in the 3rd dose level. In all cases, B was administered after T in a median delay of 25 days [20–45] because of grade 3 and/or 4 hematological toxicity. 4 pts did not receive B because of previous lung radiotherapy, persistent tricytopenia, and insufficient PBSC collection. There was no statistically difference in terms of hematological and non-hematological ≥ 2 toxicity between the three steps. 19 pts had measurable lesions and were considered for the response. The objective response rate was 48% (11% CR, 37% PR).

Conclusion: In the absence of difference in the toxicity between the three doses and with this encouraging response rate, we choose the last dose level, i.e. T and B at a dose of 600 mg/m^2 to conduct a phase II study in metastatic breast cancer.