Friday, 2 October 1998 **16:00-18:00**

PARALLEL SESSION

Metastatic disease

404 INVITED

Developments in the palliation of metastatic bone disease

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Rapid developments are occurring in the palliative management of metastatic bone disease with improvements in reconstructive orthopaedic surgery, radiotherapy – particularly through the development of bone-seeking radiopharmaceuticals, new endocrine and cytotoxic treatments, and the increasing use of bisphosphonates to prevent and treat skeletal complications. Acute inhibition of bone resorption by bisphosphonates, given at high dose intravenously, provides the treatment of choice for hypercalcaemia of malignancy and, in about one half of patients, will relieve metastatic bone pain with consequent improvement in quality of life. Long term bisphosphonate treatment clearly reduces skeletal morbidity rates in breast cancer, but a cost-effective strategy to optimise their use is needed. For effective treatment of bone pain, normalisation of bone resorption rates, as measured by modern specific biochemical markers, appears to be necessary for individual patient benefit. For long-term bisphosphonate use, prioritisation of use is suggested based on sites of disease, symptoms, current treatment, past history of skeletal events, and prognostic factors. Patients should continue to receive bisphosphonate treatment for as long as the skeleton is the dominant site of metastases, as all indications suggest the effects of treatment on skeletal metabolism wane within a few months of stopping therapy.

405 ORAL

A new standard treatment for advanced premenopausal breast cancer: A meta-analysis of the Combined Hormonal Agent Trialists Group (CHAT)

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Purpose: Both medical castration by LHRH-agonists and anti-estrogenic treatment with tamoxifen (TAM) are endocrine treatment modalities for premenopausal metastatic breast cancer but with different endocrine effects. Four randomized trials tested the hypothesis that "complete estrogen blockade" by combined LHRH-agonist plus TAM treatment is more effective than medical castration alone. Recently, a meta-analysis of these 4 trials has been performed in order to establish a new standard treatment.

Methods: Individual patient data were collected from 506 patients randomized between LHRH-A + TAM and LHRH-A (goserelin or buserelin) alone in the Zeneca 2302, EORTC 10881, Italian and Japanese trials regarding premenopausal metastatic breast cancer. Treatments were compared with respect to response-rate (RR), progression-free (PFS) and overall survival (OS) according to the intent to treat principle.

Results: There were no major differences between the treatment groups with respect to patient and tumor characteristics. Summary of efficacy results:

	Parameter	LHRH-A	LHRH-A + TAM	OR/HR*	p
1)	RR (CR + PR)	30%	39%	0.67	0.03
2)	PFS (median)	5.4 m	8.7 m	0.70	<0.001
3)	OS (median)	2.5 yrs	2.9 yrs	0.78	0.02

*OR/HR = odds/hazard ratio

Conclusion: Combined LHRH-A + TAM treatment was superior to medical castration alone with respect to all 3 efficacy parameters. Therefore this combined treatment modality has to be proposed as a new standard regimen.

406 ORAL

Phase III trial comparing epirubicin/paclitaxel vs epirubicin/cyclophosphamid as first line treatment in metastatic breast cancer: Preliminary results of a German AGO trial

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Purpose: Previously the Arbeitsgemeinschaft Gynäkologische Onkologie (AGO) study group has demonstrated that a combination of epirubicin/paclitaxel (ET) is effective and safe in patients with metastatic breast cancer. In this prospectively randomized phase III trial this combination is tested against a standard epirubicin/cyclophosphamide (EC) regimen as first line therapy for metastatic disease.

Methods: So far 292 of 422 planned patients with metastatic breast cancer have been recruited since 10/96 from 52 participating centers. 149 patients received ET (E = 60 mg/m″ and T = 175 mg/m″) and 143 received EC (E = 60 mg/m″ and C = 600 mg/m″) in a 3 weeks schedule.

Results: 857 cycles have been evaluated for toxicity. Median number of cycles per patients were 6 for ET and 4 for EC. Application had to be postponed due to toxicity in 4% of the patients with ET and in 18% of the patients with EC, whereas treatment had to be discontinued in 8% and 2% respectively. NCI-CTC grade III/IV was 1% and 0% for anaemia, 27% and 39% for leukopenia, 0% and 2% for thrombopenia respectively. Non-haematological toxicities grade IV were vomiting (1%) and infection (1%) in the ET group and 0% in the EC group. Peripheral neuropathies were more frequent in the ET and arthralgias/myalgias more frequent in the EC group. So far complete remission were observed in 14% and partial remissions in 34% (overall response rate 48%). Data on effectivity per group will be provided after the end of recruitment.

Conclusion: ET and EC as first line treatment in metastatic breast cancer are safe and effective regimens. Differences in effectivity will be provided at the end of the trial in 12/98.

407 ORAL

Epirubicin (E) plus paclitaxel (P) vs epirubicin followed by paclitaxel in metastatic breast cancer (MBC): An ongoing pharmacoeconomic study

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The combination of E (90 mg/sqm bolus i.v.) followed by P (200 mg/sqm 3 hr infusion) is feasible and very active when used as first line therapy in MBC; however pharmacokinetics data might suggested that E interferes with the pharmacodynamic effects of P as demonstrated by the lack of the correlation between the dose of the taxane and the degree of myelosuppression (JCO 1997, 2510–2517). On these premises we designed a phase III randomized trial aimed at evaluating the best schedule of administration of the two drugs in order to reduce any inteference and to improve their antitumor activity. Previously untreated M.B.C. pts are randomized to receive: 8 courses of E + P (arm A, doses and schedule previously reported), or 4 cycles of E 120 mg/sqm bolus iv followed by 4 cycles of P 250 mg/sqm 3 hr infusion (arm B). In light of the lower costs and possibly lower toxicity of the sequential regimen (arm B) this could become the one of choice if associated with a reduction not greater than 15% in the proportion of responses. In order to detect this difference with an 80% power for alpha = .05 (one-side test) 133 patients are needed in each arm. In parallel to the clinical trial a prospective pharmaco-economic study will be performed in order to evaluate the cost-effectiveness (economic efficiency) of the sequential with respect to the combination regimen. The study main hypotesis is that the use of the sequential regimen will lead to a reduction in the use of the health care resources and an improvement in patient's satisfaction due to better side-effect profile of this regimen. The primary perspective of the study will be that of society and will include all health care-releted costs. However, two secondary analises will estimate the costs from a narrowed perspective of the payers: the Italian National Health Service and the hospital. So far 84 pts have been randomized: the study is in progress.