other event necessitating withdrawal. Tumour response was assessed monthly using Union Internationale Contre le Cancer criteria. Time to progression (TTP) was defined from start of treatment until objective disease progression. Duration of response (DOR) was defined, for responding patients only, as the time from treatment initiation to disease progression.

Results: Between 8/2001 and 10/2003 a total of 44 patients (median age 63 years [range 39–91 years]) were treated in our centre and the median follow-up was 28 weeks (range 12–104 weeks). 86% of patients had ER-positive and/or PgR-positive disease. All had received prior endocrine treatment for advanced disease and 50% had received adjuvant endocrine treatment. Thirty patients (68%) had also received prior chemotherapy. Most patients (75%) were receiving fulvestrant as their 3rd- or 4th-line endocrine treatment for advanced disease. Three patients (7%) had a partial response (PR); all responses were ongoing at the time of analysis (currently of 40, 76 and 104 weeks duration). Twenty patients (45%) had stable disease (SD) ⩾24 weeks giving a clinical benefit rate (PR + SD ⩾ 24 weeks) of 52%. The median TTP was 22 weeks. Fulvestrant 250 mg was well tolerated and no WHO grade III/IV toxicities were observed.

Conclusion: Fulvestrant 250 mg is a promising endocrine agent with demonstrable efficacy and a very favourable tolerability profile in patients with advanced, breast cancer. The monthly injection schedule supports both close patient monitoring and good compliance. Fulvestrant offers clinicians a new option for the treatment of postmenopausal women with advanced breast cancer progressing on prior endocrine therapy.

265 POSTER

Intensive intravenous ibandronate treatment significantly relieves opioid-resistant bone pain and improves quality of life in patients with skeletal metastases

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Background: Bone metastases are associated with severe and sometimes intractable pain, leading to poor quality of life. A phase III placebo-controlled trial demonstrated that treatment with intravenous (i.v.) ibandronate 6 mg every 3–4 weeks significantly reduced the risk of bone events ($p=0.003$) and reduced bone pain below baseline for 2 years of treatment in metastatic breast cancer ($p<0.001$) [1]. Ibandronate has a renal event profile similar to placebo, supporting the use of higher doses to achieve bone pain relief. This open-label pilot study investigated the effects of intensive "loading dose" treatment with i.v. ibandronate for opioid-resistant bone pain.

Patients and methods: Eighteen patients with resistant pain from bone metastases due to various advanced tumor types (10 breast, 8 miscellaneous) received ibandronate 4 mg by 2-hour infusion for 4 consecutive days (16 mg total dose). Mean baseline opioid analgesic-use was equivalent to 400 mg/day morphine. Patients were assessed for 6 weeks or until death. Study assessments included bone pain (visual analog scale [VAS] from 0=no pain to 10=maximum pain), opioid consumption (morphine equivalent daily dose [MEDD]), patient functioning (EFAT scale), quality of life (VAS from 0=good to 10=poor), and performance status (ECOG scale). Renal function was assessed by serum urea and creatinine measurement.

Results: Intensive "loading dose" ibandronate treatment significantly reduced mean bone pain scores within 7 days ($p<0.001$) and maintained them below baseline levels throughout the study. Ibandronate significantly improved quality of life, patient functioning and performance status ($p<0.05$). Bone-pain relief was not due to increased use of opioids: mean MEDD was unchanged from baseline to endpoint. Ibandronate was well tolerated, with no changes in renal functioning.

Conclusions: Intensive "loading dose" treatment with i.v. ibandronate had a marked analgesic effect in patients with opioid-resistant bone pain, with benefits for patient quality of life and functioning. Despite the high dosing schedule, ibandronate did not lead to dose-limiting renal toxicity. Ibandronate may therefore provide a useful adjuvant to more commonly-used palliative treatments for bone pain, such as opioids, non-opioid analgesics and radiotherapy. The positive effects of intensive ibandronate treatment in this pilot study warrant further investigation in controlled clinical trials.

References

[1] Body JJ, et al. Ann Oncol 2003;14:1399–405.

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Phase I intrapatient dose escalation study of weekly epirubicin and docetaxel as first line chemotherapy in metastatic breast cancer

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Anthracyclines in combination with docetaxel are amongst the most active combination therapies for the treatment of advanced breast cancer but are associated with high incidence of myelotoxicity. Weekly combination with these agents has the potential to produce less haematological toxicity than standard 3-weekly regimens at recommended doses. We conducted a Phase I study to define the maximum tolerated dose (MTD) when epirubicin and docetaxel are combined and delivered as a weekly treatment in patients with advanced breast cancer. Treatment comprised epirubicin and docetaxel administered every seven days for 6 doses. Following a two week interval patients tolerating treatment were given a further twelve treatments at the next dose level. The MTD for docetaxel was determined before escalating the dose of epirubicin.

Eleven patients were entered with median age 55 years (range 35 to 67) and performance status 0 to 1. One patient (with extensive bone disease) was unable to tolerate dose level 1 due to repeated grade 3 neutropenia. Three patients completed 6 weeks at dose level 1 and 12 weeks at dose level 2. Of the three patients starting at dose level 3, two experienced dose limiting toxicity (DLT) with grade 3 neutropenia and one patient died from progressive disease after 3 doses, without treatment toxicity. Of the four patients commencing at dose level 2A, one patient completed 17 weeks of treatment and one underwent further escalation of docetaxel dose. Two patients at dose level 2A had DLT due to neutropenia. No grade 4 neutropenia and no febrile episodes occurred. 1 patient required admission for non-neutropenic, non-febrile infection. MTD was defined by dose limiting grade 3 neutropenia, at dose level 3 and 2A. Worst non-haematological toxicities were alopecia, mucositis, nausea, diarrhea, nail changes, asthenia and skin changes (all grade 2). Cardiac function was unaffected. Tumour reduction was seen in all but 2 patients. Formal response evaluation CR 1, PR 3, SD/Not assessable 7. This schedule confers the ability to deliver combination docetaxel and epirubicin at a dose density in excess of standard 3-weekly dosing schedule without significant myelosuppression and acceptable non-haematological toxicity. The schedule is active with responses seen at all dose levels. The recommended dose level for phase II study is epirubicin 30 mg/m^2 and docetaxel 30 mg/m^2 with dose descalation to 25 mg/m^2, 30 mg/m^2 in the event of grade 3 neutropenia.

Dose escalation schedule

Schedule			Number of patients	
Dose level	Epirubicin (mg/m^2)	Docetaxel (mg/m^2)	Entered	Escalated to
1	25	25	4	
2	25	30		3
3	25	35	3	
2A	30	30	4	
3B	30	35		1

267 POSTER

Fulvestrant: an effective second-line treatment for postmenopausal women with advanced breast cancer

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Background: Fulvestrant ('Faslodex') is an estrogen receptor (ER) antagonist that has no agonist effects. Two randomised, Phase III clinical trials including postmenopausal women with advanced breast cancer who have progressed following prior endocrine therapy have shown that fulvestrant is at least as effective as anastrozole in terms of time to progression (TTP), objective response (OR) and clinical benefit (CB) rates. More recently, survival data have also become available.

Methods: Literature review and indirect comparison of efficacy data from second-line trials including fulvestrant, anastrozole, letrozole, and exemestane.

Results: Fulvestrant is at least as effective as anastrozole in terms of survival and indirect comparisons with other second-line treatment trials show that fulvestrant is comparable in terms of efficacy (including survival) to letrozole and exemestane. Efficacy data across second-line treatment trials using these agents is summarised in Table 1.