Methods: Three international, multicenter, randomized, double-blind, placebo-controlled trials over a 96-week treatment period were conducted. In a trial of intravenous (i.v.) ibandronate, patients were randomized to receive i.v. ibandronate 6mg (n=154) or placebo (n=158), infused over 12 hours every 34 weeks. In two trials of oral ibandronate, patients received a 50mg daily dose (n=287) or placebo (n=277). Pooled data from the oral trials were analysed for efficacy. Patients were required to report their level of bone pain on a 7-point scale (from 0=none to 6=requiring >100mg/day morphine or equivalent) . Quality of life (QoL) was also evaluated using the EORTC QLQ-C30, a 30-item questionnaire that produces QoL scores for global health status and five functional domains.

Results: Patients receiving i.v. ibandronate 6mg or oral ibandronate 50mg experienced a rapid initial reduction in bone pain score that remained below baseline levels over 2 years of treatment. The mean reduction in baseline bone pain score with i.v. ibandronate 6mg was 0.28, compared with an increase of +0.21 with placebo ($p<0.001$). In the pooled oral studies, oral ibandronate 50mg reduced mean baseline bone pain scores by 0.10, compared with an increase of +0.20 with placebo (p=0.001). Analgesic use scores were also significantly lower with oral ibandronate 50mg compared with placebo (p=0.019). Pain reductions with i.v. ibandronate 6mg and oral ibandronate 50mg were accompanied by significant improvements in global QoL compared with placebo (p=0.004 and p=0.03, respectively). Ibandronate 6mg i.v. significantly improved functional domain scores for physical function (p=0.034), emotional function (p=0.025) and social function (p=0.008), while oral ibandronate 50mg significantly improved physical function ($p<0.05$) and role function ($p<0.01$) domain scores compared with placebo.

Conclusions: Treatment with i.v. ibandronate 6mg and oral ibandronate 50mg relieves bone pain in patients with MBD from breast cancer. Unlike other bisphosphonates for MBD, pain reductions with oral and i.v. ibandronate are maintained below baseline levels over 2 years of treatment, and are accompanied by significant improvements in QoL.

449 POSTER

Capecitabine monotherapy is active, well tolerated and provides convenient outpatient therapy for patients with taxane-pretreated advanced breast cancer: findings from an expanded access program

M. Venturini[1], R. Bell[2], R. Paridaens[3], D. Rossner[4], M. Vaslamatzis[5], J.W.R. Nortier[6], H. Rodrigues[7]. [1] *Istituto Nazionale per la Ricerca sul Cancro, Division of Medical Oncology, Genova, Italy;* [2] *Geelong Hospital, Andrew Love Cancer Centre, Geelong, Australia;* [3] *Katholieke Universiteit Leuven, University Hospital Gasthuisberg, Leuven, Belgium;* [4] *Medical University of Hannover, Department of Gynecologic Oncology, Hannover, Germany;* [5] *Evangelismos Hospital, Department of Medical Oncology, Athens, Greece;* [6] *Leids University Medical Center, Department of Clinical Oncology, Leiden, The Netherlands;* [7] *Instituto Portugues de Oncologia, Porto, Portugal*

Background: Phase II/III trials have shown the oral fluoropyrimidine capecitabine (Xeloda®) to be active and well tolerated in patients with advanced breast cancer progressing after failure of previous taxane- and anthracycline-based therapy. An expanded access program was initiated to provide access to capecitabine for patients who were not eligible for other capecitabine investigative protocols.

Methods: All patients had progressive disease after having received at least two chemotherapy regimens, one of which contained paclitaxel or docetaxel for metastatic disease. Data are currently available on 631 patients who received outpatient treatment with the standard dose of oral capecitabine (1250 mg/m^2 twice daily on days 1-14 of a 21-day treatment cycle) up to a maximum of 16 cycles.

Results: At study entry, the mean age of patients was 54.1 ± 10.3 years, 79% had a KPS of 7090, and the majority (94%) had metastatic disease. The mean duration of capecitabine treatment was 3.9 ± 3.6 (range 0-24.8) months, given at a mean daily total dose of 4116 ± 593 mg. In the 349 patients evaluable for efficacy, an objective response rate of 35% (CR 3%, PR 32%) and disease stabilization in 47% of patients was recorded. The estimated median time to treatment failure and median overall survival were 3.0 months (n=592; 95% CI, 2.8-3.5 months) and 10.2 months (n=569; 95% CI, 8.6-15.6 months), respectively. Overall, 528/631 (84%) patients experienced at least one adverse event, the majority of which were mild to moderate and affected the gastrointestinal tract (58%) or skin and subcutaneous tissue (44%). The most common treatment-related grade 3/4 adverse events were diarrhea (9%), vomiting (3%) and hand-foot syndrome (8%). Grade 3/4 myelosuppression was rare (neutropenia, 1%; thrombocytopenia, 2%) and no grade 3 alopecia was reported (grade 2, 0.3%). Dose modification due to adverse events was reported for 180 (29%) patients.

Conclusions: The results achieved in this heavily pretreated population confirm previous findings that capecitabine monotherapy is active, well tolerated and provides convenient outpatient therapy for patients with advanced and/or metastatic breast cancer refractory to previous treatment, including taxanes.

450 POSTER

Improving clinical outcomes and treatment convenience with oral ibandronate for metastatic bone disease

R. Bell[1], R. Coleman[2], B. Bergstrom[3]. [1] *The Andrew Love Cancer Centre, Cancer Services Medical Oncology, Victoria, Australia;* [2] *Weston Park Hospital, Academic Unit of Clinical Oncology, Sheffield, UK;* [3] *F. Hoffmann-LaRoche Inc, Nutley, USA*

Background: Standard therapy for metastatic bone disease (MBD) currently involves intravenous (i.v.) infusion of bisphosphonates, which target the underlying pathological processes of osteclast-mediated bone resorption to reduce skeletal complications. However, the requirement to visit hospital regularly for i.v. administration of a supportive care agent is inconvenient for patients, and may impact upon their quality of life. The clinical usefulness of i.v. bisphosphonates may occasionally be limited by a deterioration in renal function which, if patients are not closely monitored, can rarely progress to renal failure. Additionally, parenteral administration costs and staff time requirements add to treatment costs. Although oral bisphosphonate therapy is available, its use in practice is limited by concerns with regard to efficacy and the potential for gastrointestinal adverse effects. To improve clinical outcomes and treatment convenience for patients with MBD, there is a clinical need for an oral bisphosphonate that would allow ambulatory at-home administration, without compromise of efficacy or safety. The efficacy and safety of the oral formulation of ibandronate, a highly-potent, third-generation bisphosphonate, has been evaluated in phase III clinical trials of patients with metastatic breast cancer.

Patients and methods: In two randomized, multicenter studies, patients with MBD from breast cancer were randomized to treatment with oral ibandronate 50mg (n=287) or placebo (n=277). A multivariate Poisson regression analysis of pooled data from these studies assessed the number of skeletal related events arising in each treatment group during the 96-week treatment period. Metastatic bone pain was assessed on 7-point scale (from 0=none to 6=requiring >100mg/day morphine or equivalent), and patient quality of life was assessed using the EORTC QLQ-C30 questionnaire. Treatment-related adverse events were continually monitored.

Results: Oral ibandronate 50mg provided a significant (38%) reduction in the risk of new skeletal events compared with placebo (p=0.0001). Bone pain scores were significantly reduced from baseline (p=0.001) and maintained below baseline for the two-year study duration. Quality of life deterioration over time (commonly seen with MBD) was significantly reduced with oral ibandronate (p=0.03 vs placebo). Oral ibandronate was well-tolerated, with few gastrointestinal side effects and renal toxicity similar to placebo.

Conclusions: Oral ibandronate 50mg significantly improves clinical outcomes in patients with MBD, with efficacy comparable to zoledronate. As was demonstrated in a trial of i.v. ibandronate 6mg i.v. [1], statistically significant reductions in the risk of skeletal complications and bone pain with oral ibandronate were accompanied by quality of life benefits. Patients receiving oral ibandronate do not require hospital visits solely for administration of bisphosphonate therapy, resulting in improved treatment convenience for patients who have completed chemotherapy. Oral ibandronate would also permit convenient at-home administration in conjunction with other oral therapies (including hormonal therapy) and would ameliorate the bone mineral loss associated with some of these treatment strategies. The efficacy of oral ibandronate in reducing symptoms and complications of MBD, coupled with low gastrointestinal and no significant renal toxicity risk, provides effective therapy with reduced management costs, particularly for patients who are likely to receive bisphosphonate therapy for more than 6 months.

Reference

[1] Body et al. Ann Oncol in press.