The efficacy and safety of oral ibandronate in the treatment of metastatic bone disease in patients with breast cancer

We read with interest D. Tripathy and coworkers’ study [1], published in the May 2004 issue of Annals of Oncology. They concluded that oral ibandronate was well tolerated and an effective treatment for metastatic bone disease in patients with breast cancer. Both oral ibandronate 20 mg and 50 mg significantly reduced the skeletal morbidity period rate when compared with placebo. However, when we look at the incidence of death, it is obvious that both ibandronate 20 mg and 50 mg had a higher incidence of death when compared with placebo, but the differences among groups were not statistically significant at this level. The incidence of death was increased by 42.8% and 58% in the ibandronate 20 mg and 50 mg arms, respectively. This finding is contradictory to the literature. The bisphosphonates did not have a detrimental effect on survival [2]; in fact, in same study, they prolonged survival significantly [3]. Therefore, it is somewhat difficult to conclude that oral ibandronate at the doses given is safe in the treatment of metastatic bone disease in patients with breast cancer, according to the results of the study by D. Tripathy et al.

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References


In response to Dr Utkan and colleagues [1] regarding the mortality incidence we reported with oral ibandronate in a 2-year phase III trial [2], the actual number of deaths was very small (16 in the placebo group compared with 23 in the ibandronate 20 mg and 50 mg groups). Most deaths were due to disease progression, and none were attributed to treatment. The number of events was insufficient to find a statistically significant difference between the groups. Survival was not a primary end point in this trial of patients with established skeletal metastases; in fact, a survival benefit has not been seen with any bisphosphonates in metastatic bone disease using Cochrane review methodology [3]. However, the benefits of bisphosphonates overall in reducing skeletal events and morbidity are now strong enough for them to be uniformly recommended in destructive bone metastases [4]. The clodronate studies referred to by Utkan et al. [5,6] were conducted in the adjuvant patient setting, where improved survival is one of the main aims of bisphosphonate therapy. Atula et al. [6] found only a borderline survival benefit (P = 0.047) of clodronate in breast cancer patients, based on multiple regression analyses of a small number of events. Another long-term randomized trial failed to support these results [7], and clodronate was actually associated with a worse mortality rate. Ibandronate, a highly potent bisphosphonate with anti-tumor efficacy [8], may offer enhanced protection for patients at risk of bone metastases. The results of ongoing adjuvant trials using several bisphosphonates are eagerly awaited.

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References