



mutations significantly responded to 800 mg daily of imatinib vs 400 mg as compared to those with exon 11 mutations ($p < 0.0013$).

PANCREATIC ADENOCARCINOMA

Erlotinib is the first drug to be approved in combination with gemcitabine for the treatment of pancreas cancer. In a Canadian study reported last year by M. Moore on behalf of the NCIC-CTG investigators), 569 patients were randomized between gemcitabine or gemcitabine + erlotinib. While the overall survival was statistically significantly increased from 6.0 to 6.4 months ($p < 0.028$), one could debate whether this was "clinically significant". As in colorectal cancer, the development of a rash portends efficacy with those patients with a grade 2 rash had a median survival of 10.5 months (1-yr survival of 43%) vs 5.3 months (1-yr survival of 11%) for those with no rash. While the pharmacoeconomic aspects of the combined regimen could be debated (S. Grubbs, et al., PASCO 2006), it seems an empiric trial of the combination may be of benefit and continue erlotinib should a

"significant" cutaneous reaction occur.

BISPHOSPHONATES IN METASTATIC BREAST CANCER THERAPY

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Complications from bone metastases are a common problem in oncology. In the placebo arm of two large phase III trials at 2 years of follow-up, 70% had ≥ 1 skeletal complication and 50% had a pathologic fracture. These issues contribute to significant morbidity for our patients.

Bisphosphonates bind preferentially to bone at sites of active bone metabolism and inhibit osteoclast activity and survival. Two generations of bisphosphonates are available, with the aminobisphosphonates being more potent. In nine studies of more than 2000 women with bone metastases, bisphosphonates reduced the risk of a skeletal event by 17% ($RR = 0.83$, $p = 0.00001$). The optimal duration of therapy is unclear however data supports at least 2 years of therapy. The most commonly used bisphosphonates for patients with bone

metastases in the U.S. are pamidronate (P) and zoledronic acid (ZA). These two agents have been compared to each other in a phase III multicenter trial. In patients with breast cancer and ≥ 1 lytic lesion to bone, ZA reduced the risk of a skeletal complication an additional 20% over P. This effect was more significant in patients receiving endocrine therapy. Trials are ongoing evaluating the use of bisphosphonates in the adjuvant setting. In general, the bisphosphonates are well tolerated. Approximately 1% of breast cancer patients developed an increased creatinine after 2 years of ZA. A recent FDA labeling change has led to reduced dosages of ZA for patients with a baseline CrCl of ≤ 60 ml/min. Osteonecrosis of the jaw is a rare complication of bisphosphonate use in cancer patients and should be suspected in a patient complaining of tooth or jaw pain while on bisphosphonate therapy.

In summary, bisphosphonates are now an integral part of the therapy of metastatic breast cancer with lytic metastases to bone. Ongoing trials are exploring the utility of these agents in the adjuvant setting. **OA**