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Denosumab delays metastasis in prostate cancer patients

The monoclonal antibody denosumab (XGEVA) can impede the onset of bone metastases in men with hormone-refractory prostate cancer by just over 4 months, found a phase III study presented at the congress. These results held across all demographic and disease-related subgroups.

Up to 90% of men with prostate cancer resistant to hormone treatment will have their primary tumour metastasize to the bone, placing the patient at risk of serious skeletal-related events. Denosumab is a fully human monoclonal antibody that inhibits RANKL, a protein key to formation of osteoclasts. If formation of osteoclasts can be impeded, the bone can continue to resist development of metastases, explained study presenter Professor Stéphane Oudard, from Georges Pompidou Hospital, Paris, France.

In the study, 1432 men with castrate-resistant prostate cancer considered at high risk for bone metastasis were randomized to denosumab 120 mg subcutaneously every 4 weeks (n=716) or placebo subcutaneously every 4 weeks (n=716). The primary end point was time to first bone metastasis (symptomatic or asymptomatic) or death on study. Exclusion criteria included bone metastasis detected radiographically, metastatic involvement of distant organs and intravenous bisphosphonates.

Bone metastasis-free survival was 29.5 months in those randomized to denosumab *vs* 25.2 months in those receiving placebo (hazard ratio 0.85, 95% confidence interval 0.73–0.98; P=0.028). The results held across all subgroups, with hazard ratios ranging from 0.58 to 0.87. 'Subgroup analysis showed that whatever the patient's age, race, histology, or patient characteristics they all benefitted from denosumab,' said Professor Oudard.

Adverse effects were relatively similar between patients randomized to denosumab and placebo, although low blood calcium levels and jaw osteonecrosis were slightly more frequent among the denosumab group.

Janet Fricker

Ipilimumab improves survival from melanoma metastases

Ipilimumab shows similar antitumour activity in patients with malignant melanoma and brain metastases as in those without brain disease, show 2-year results from prospective studies.

Dr Kim Margolin, from the University of Washington, Seattle, USA, reported results for the prospective CA184-042 study, including patients with malignant melanoma and active, measurable brain metastasis that was stable without steroid therapy or required steroids for CNS symptoms. They were treated with ipilimumab 10 mg/kg every 3 weeks for four doses. She also reported on the expanded access programme CA184-045 with ipilimumab 3 or 10 mg/kg every 3 weeks for four doses.

Ipilimumab augments T-cell-mediated antitumour responses. Activated T-cells cross the blood–brain barrier, supporting a trial of ipilimumab in patients with brain metastases. One in three metastatic melanoma patients (30%) have brain metastases at diagnosis, and a further 30% develop these within 1–2 years of diagnosis. Only 10% of patients respond to current therapy (radiation) and median survival is 3–6 months.

Patients with brain metastases not requiring steroids had 12-month overall survival of 31% after treatment with ipilimumab, sustained at 26% out to 2 years. The 12-month overall survival in patients with symptomatic brain metastases was 10%, but they had more advanced disease.

Dr Margolin concluded: 'Ipilimumab prolonged survival and achieved durable responses in patients with malignant melanoma and brain metastases.'

Sue Mayor

Synchronous chemoradiation reduces breast cancer recurrence

Giving radiotherapy between or during chemotherapy cycles significantly reduces the risk of recurrence in women with early breast cancer, according to a major UK study.

The Sequencing of Chemotherapy and Radiotherapy in Adjuvant Breast cancer study randomized 2296 women who had undergone breast-conserving surgery or mastectomy to sequential chemotherapy and radiotherapy or synchronous treatment, where radiotherapy was given in the gaps between chemotherapy cycles. More than 60% of patients received 40 Gy in 15 fractions over 3 weeks.

'Synchronous chemoradiation reduces the risk of local cancer recurrence by 35%,' reported Dr Indrajit Fernando, consultant clinical oncologist at University Hospitals Birmingham NHS Foundation Trust, UK.

The 5-year local recurrence rates were 2.8% in the synchronous chemoradiation group and 5.1% in the sequential group. The 2.3% difference between groups was statistically significant.

Dr Fernando suggested that the reduction in recurrence would significantly improve survival: 'even a 2.3% reduction in local recurrence rates will have an impact because this is such a common cancer.' He said his clinic has switched to giving synchronous chemoradiation based on the findings.

More patients undergoing synchronous chemoradiation showed acute skin toxicity with radiotherapy treatment, but only 4% had a severe reaction, which took several weeks to heal.

Sue Mayor