Bone-strengthening drug gives pain relief in prostate cancer bone metastases

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Stockholm, Sweden: Many prostate cancer patients develop bone metastases, and controlling the pain these cause can be difficult. Now the first large randomised Phase III trial of a bisphosphonate drug in these patients has shown that a single dose of the drug is as good for pain relief as single dose radiotherapy, the standard treatment for bone metastases. Results of the trial were presented today at the 2011 European Multidisciplinary Cancer Congress.

Professor Peter Hoskin, consultant clinical oncologist at the Mount Vernon Cancer Centre, Northwood, UK, and Professor of Clinical Oncology at University College, London, and colleagues, randomised 470 patients with primary prostate cancer and painful bone metastases to receive either a single dose of radiation or a single intravenous infusion of the bisphosphonate ibandronate (IB). Patients reported their primary site of pain at entry into the trial, and then at four, eight, twelve, 26 and 52 weeks after treatment.

Those who had not responded to the first treatment at four weeks crossed over to the alternative therapy and received their second treatment no later than week eight. Pain levels were measured at four and twelve weeks by examining analgesic use, using a combination of scoring via the WHO pain ladder and the Mercadante method, which defines analgesic use in morphine equivalents.

"We found that using IB was as good as single dose radiotherapy in controlling pain," said Prof Hoskin. "Although there were more patients

in the IB group with worse Mercadante scores at four weeks who needed re-treatment, at six and twelve months there was no long-term difference in pain relief between the two groups."

Side effects were few; short-lived nausea and stomach upsets if radiotherapy passes through the abdomen and flu-like symptoms with IB. The patients in the trial were well balanced as to age, site of pain, prior treatment and performance status. The median survival of the four groups was 11.8 months (radiotherapy only), 11.4 months (IB only), 12.7 months (radiotherapy then IB), and 16.8 months (IB then radiotherapy).

"We hope to analyse these survival differences further in the hope that it can give us further pointers as to how and whether we should use a combination of treatments," Prof Hoskin said. "Currently we are unsure about the optimal timing and scheduling of treatment for these patients."

The constant turnover of bone is kept in balance by the interaction of osteoblasts, which form bone, and osteoclasts, which beak it down. Bisphosphonates work by sticking to calcium and binding to it, thus preventing bone loss through inhibiting the activity of osteoclasts.

Bone metastases are common in many primary cancers. "They are a serious problem for many men with prostate cancer, and can cause intense pain as well as fractures and spinal cord compression," Prof Hoskin said. "But there are also patients who have bone metastases and only mild or moderate pain, which can be readily controlled by analgesics. Others have multiple metastatic sites, but only one causes significant pain. There are many questions still to be answered in this field."

The researchers intend to follow up their work with a study looking at biomarkers for bone resorption. "If we can correlate these markers with response to both radiotherapy and IB we will be able to see whether they

can predict which patients would respond best to which treatment," said Prof Hoskin. "Currently we don't know exactly how radiotherapy works in bone metastases – we just know that it does. We hope to be able to shed more light on this in our follow-up study.

"It is important to stress that radiotherapy still has a crucial role to play and is a highly effective treatment for many cancer patients. For patients with solitary metastases, pathological fracture, where the bone breaks due to weakness, and neurological complications of bone metastases, it remains the treatment of choice. Our research adds to the arsenal of the many effective treatments now available, and we believe that the findings will also be applicable to other primary cancers that can lead to bone metastases, for example breast cancer, where they are very common," he concluded.

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