

Speedy response can be achieved from palliative radiotherapy in the treatment of painful uncomplicated bone metastases

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The 2012 update on the systematic review of palliative radiotherapy trials for bone metastases identified 25 randomized controlled trials comparing single fraction versus multiple fraction schedules for the palliation of painful uncomplicated bone metastases. For intention-to-treat analysis, the overall response rate and complete response (CR) rate in patients receiving single fractions were 60% (1,696 of 2,818 patients) and 23% (620 of 2,641 patients), respectively (1).

In a recently published secondary analysis of the NCIC Clinical Trials Group Symptom Control Trial SC.23 (a double-blind randomized controlled trial investigating dexamethasone for the prophylaxis of pain flare following radiotherapy) (2), McDonald *et al.* examined how soon following radiotherapy one can expect an improvement in pain. A total of 298 patients were enrolled in the study. At day 10 after the delivery of a single 8 Gy fraction for palliation of painful bone metastases, 122 patients responded to radiotherapy [37 with CR and 85 with partial response (PR)]. For intention-to-treat analysis, the overall response rate and CR rate at day 10 in patients receiving single fraction radiation therapy were 41% (122 of 298) and 12% (37 of 298), respectively (3).

Putting the result of the secondary analysis in the context of 2012 update on the systematic review, 68% (41% of 60%) and 52% (12% of 23%) who were destined to have overall response and CR, respectively, experienced pain relief as early as day 10 following a single 8 Gy palliative radiotherapy fraction in the treatment of painful uncomplicated bone metastases.

In the secondary analysis, pain response was assessed

according to the International Bone Metastases Consensus Endpoint Definitions, which account for both changes in pain as well as analgesic intake. CR was defined as a pain score of zero without an increase in analgesic intake. PR was defined as either a reduction of ≥ 2 in the pain score without an increase in analgesic intake or no increase in pain with a $\geq 25\%$ reduction in analgesic intake. Overall response was the sum of CR and PR (4,5).

A previous study compared the magnitude of pain relief achieved from palliative radiation treatment of bone metastases employing the international consensus endpoints with the traditionally reported rates using pain score only. Patients with bone metastases were asked to rate their pain intensity on a categorical scale of 0–10 (0= absence of pain; 10= worst pain possible). Five hundred and eighteen patients were analyzed for radiation therapy outcomes. Analgesic intake during the preceding 24 hours was recorded and converted into total daily dose of oral morphine equivalent. Follow-up was conducted at weeks 1, 2, 4, 8, and 12 after treatment to evaluate pain level and analgesic consumption. Pain score alone was used first to assess the outcome. CR was defined as a pain score of 0, and PR was defined as a reduction of score ≥ 2 of the pretreatment pain score. The response rates were then reported employing international consensus endpoints. When response evaluation was by pain score alone, the PR rates at 1, 2, 4, 8, and 12 weeks were 41%, 41%, 39%, 35%, and 41%, respectively, and the CR rates were 21%, 30%, 32%, 35%, and 32%, respectively. Using the international consensus endpoints, the PR rates at 1, 2, 4, 8, and 12 weeks were 32%, 28%, 26%, 22%, and 28%, respectively, and the CR rates were 17%, 23%, 24%,

25%, and 23%, respectively. The international consensus endpoints take into account both the pain score and the analgesic consumption, hence leading to lower CR and PR rates when compared with the pain-only endpoints (6).

Most of the previously reported randomized trials employed pain-only endpoints. Despite using the more stringent international consensus endpoints, the secondary analysis found that over two-thirds and one-half of those who were destined to have overall response and CR, respectively, experienced pain relief as early as day 10 following a single 8 Gy palliative radiotherapy fraction in the treatment of painful uncomplicated bone metastases. These new findings underscore that a speedy response can be achieved from palliative radiotherapy in the treatment of painful uncomplicated bone metastases, and this analysis can help to inform patient and provider management decisions when discussing palliative radiotherapy.

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Footnote

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