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Prophylactic Radiation Therapy Versus Standard of Care for Patients With High-Risk Asymptomatic Bone Metastases: A Multicenter, Randomized Phase II Clinical Trial

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Purpose: External-beam radiation therapy (RT) is standard of care (SOC) for pain relief of symptomatic bone metastases. We aimed to evaluate the efficacy of radiation to asymptomatic bone metastases in preventing skeletal-related events (SRE).

Methods: In a multicenter randomized controlled trial, adult patients with widely metastatic solid tumor malignancies were stratified by histology and planned SOC (systemic therapy or observation) and randomly assigned in a 1:1 ratio to receive RT to asymptomatic high-risk bone metastases or SOC alone. The primary outcome of the trial was SRE. Secondary outcomes included hospitalizations for SRE and overall survival (OS).

Results: A total of 78 patients with 122 high-risk bone metastases were enrolled between May 8, 2018, and August 9, 2021, at three institutions across an affiliated cancer network in the United States. Seventy-three patients were evaluable for the primary end point. The most common primary cancer types were lung (27%), breast (24%), and prostate (22%). At 1 year, SRE occurred in one of 62 bone metastases (1.6%) in the RT arm and 14 of 49 bone metastases (29%) in the SOC arm ($P < .001$). There were significantly fewer patients hospitalized for SRE in the RT arm compared with the SOC arm (0 v 4, $P = .045$). At a median follow-up of 2.5 years, OS was significantly longer in the RT arm (hazard ratio [HR], 0.49; 95% CI, 0.27 to 0.89; $P = .018$), which persisted on multivariable Cox regression analysis (HR, 0.46; 95% CI, 0.23 to 0.85; $P = .01$).

Conclusion: Radiation delivered prophylactically to asymptomatic, high-risk bone metastases reduced SRE and hospitalizations. We also observed an improvement in OS with prophylactic radiation, although a confirmatory phase III trial is warranted.

Trial registration: ClinicalTrials.gov [NCT03523351](#).