

Circulating Tumor Cells and Ra-223 Response in Metastatic Castration-Resistant Prostate Cancer

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Background: The radiopharmaceutical Ra-223 improves survival and prevents skeletal-related events in men with metastatic castration-resistant prostate cancer (mCRPC). However, biomarkers of its activity are lacking. We recently developed a digital RNA expression signature of circulating tumor cells (CTCs) that predicts response to abiraterone in men with mCRPC. Here we provide an update of our efforts to develop CTC-based molecular biomarkers of response to Ra-223.

Methods: Patients were enrolled in a prospective single-arm open label biomarker study of standard-of-care Ra-223 for mCRPC, which allowed for biospecimen collection including blood for CTC analyses. Eligible patients were men with bone-predominant mCRPC with at least two skeletal metastases on bone scan and no visceral or brain metastases, who were planned for clinical standard-of-care Ra-223 treatment administered every 4 weeks for up to 6 cycles. Patients donated 20 mL blood prior to initiation of therapy and at several follow-up time points (2 and 6 months). CTCs were isolated using the CTC-iChip negative selection microfluidic device, and quantitation of CTC RNA expression was performed for a panel of genes using a multiplex droplet digital PCR assay. A previously defined CTC-M score was calculated for each time point and compared to clinical outcomes.

Results: Molecular CTC analyses were performed prospectively in 22 mCRPC patients treated with Ra-223. Initial analyses suggest that baseline CTC-M scores are correlated with bone scan progression during Ra-223 treatment. Additional analyses are in progress.

Conclusion: Molecular CTC signatures in the blood may serve as potential biomarkers of response to Ra-223 therapy. Further analyses and long-term follow up of patients are ongoing.

Conflict of Interest Statement: MGH has applied for patent protection for the CTC-iChip

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