National Cancer Institute's Working Group on Biochemically Recurrent Prostate Cancer: Clinical Trial Design Considerations

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Background: Biochemically recurrent prostate cancer (BCR) after definitive surgery and/or radiation (including salvage strategies) is a burgeoning area of clinical research inspired by ultrasensitive next-generation imaging. Most phase 3 trials in prostate cancer (PCa) have focused on metastatic disease, defined by conventional imaging (CI). Despite the emergence of new imaging, clinical trial principles from metastatic studies will not optimize future BCR trials.

Methods: A Working Group convened at the National Cancer Institute on November 13, 2024 (NCI BCR WG). Key areas of discussion included nomenclature, baseline criteria for data capture, imaging considerations, delineation of high-risk populations to be targeted for trial development, requirements of metastasis-directed therapy (MDT) or hormonal therapy, quality-of life-considerations, and potential study end points.

Results: The NCI BCR WG defined the novel term "PSMA+BCR" to identify the emerging concept of recurrent PCa identifiable only on PSMA PET, overlapping with BCR and distinct from metastatic hormone-sensitive PCa as traditionally defined by CI. The WG suggested defining high-risk BCR with a PSA doubling time ≤6 months, regardless of PET findings. The WG provided recommendations for baseline data capture and imaging requirements. Neither systemic therapy nor MDT were considered mandatory for control arms. The WG also discussed novel endpoints and quality-of-life metrics in this disease space.

Conclusions: These discussions should inform future clinical BCR trials in this distinct disease space relative to metastatic disease defined by CI. The NCI BCR WG strongly advocates that future trials explore de-intensification of treatment to minimize toxicity in this relatively indolent disease state.

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