Design and end points of clinical trials for patients with progressive prostate cancer and castrate levels of testosterone: recommendations of the Prostate Cancer Clinical Trials Working Group.


Abstract

PURPOSE: To update eligibility and outcome measures in trials that evaluate systemic treatment for patients with progressive prostate cancer and castrate levels of testosterone.

METHODS: A committee of investigators experienced in conducting trials for prostate cancer defined new consensus criteria by reviewing previous criteria, Response Evaluation Criteria in Solid Tumors (RECIST), and emerging trial data.

RESULTS: The Prostate Cancer Clinical Trials Working Group (PCWG2) recommends a two-objective paradigm: (1) controlling, relieving, or eliminating disease manifestations that are present when treatment is initiated and (2) preventing or delaying disease manifestations expected to occur. Prostate cancers progressing despite castrate levels of testosterone are considered castration resistant and not hormone refractory. Eligibility is defined using standard disease assessments to authenticate disease progression, prior treatment, distinct clinical subtypes, and predictive models. Outcomes are reported independently for prostate-specific antigen (PSA), imaging, and clinical measures, avoiding grouped categorizations such as complete or partial response. In most trials, early changes in PSA and/or pain are not acted on without other evidence of disease progression, and treatment should be continued for at least 12 weeks to ensure adequate drug exposure. Bone scans are reported as "new lesions" or "no new lesions," changes in soft-tissue disease assessed by RECIST, and pain using validated scales. Defining eligibility for prevent/delay end points requires attention to estimated event frequency and/or random assignment to a control group.

CONCLUSION: PCWG2 recommends increasing emphasis on time-to-event end points (ie, failure to progress) as decision aids in proceeding from phase II to phase III trials. Recommendations will evolve as data are generated on the utility of intermediate end points to predict clinical benefit.

Comment in

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Trial design for metastatic castration-resistant prostate cancer.  [J Clin Oncol. 2008]


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