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The ProBio trial: molecular biomarkers for advancing personalized treatment decision in patients with metastatic castration-resistant prostate cancer

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Abstract

Background: Multiple therapies exist for patients with metastatic castration-resistant prostate cancer (mCRPC). However, their improvement on progression-free survival (PFS) remains modest, potentially explained by tumor molecular heterogeneity. Several prognostic molecular biomarkers have been identified for mCRPC that may have predictive potential to guide treatment selection and prolong PFS. We designed a platform trial to test this hypothesis.

Methods: The Prostate-Biomarker (ProBio) study is a multi-center, outcome-adaptive, multi-arm, biomarker-driven platform trial for tailoring treatment decisions for men with mCRPC. Treatment decisions in the experimental arms are based on biomarker signatures defined as mutations in certain genes/pathways suggested in the scientific literature to be important for treatment response in mCRPC. The biomarker signatures are determined by targeted sequencing of circulating tumor and germline DNA using a panel specifically designed for mCRPC.

Discussion: Patients are stratified based on the sequencing results and randomized to either current clinical practice (control), where the treating physician decides treatment, or to molecularly driven treatment selection based on the biomarker profile. Outcome-adaptive randomization is implemented to early identify promising treatments for a biomarker signature. Biomarker signature-treatment combinations graduate from the platform when they demonstrate 85% probability of improving PFS compared to the control arm. Graduated combinations are further evaluated in a seamless confirmatory trial with fixed randomization. The platform design allows for new drugs and biomarkers to be introduced in the study.

Conclusions: The ProBio design allows promising treatment-biomarker combinations to quickly graduate from the platform and be confirmed for rapid implementation in clinical care.

Trial registration: ClinicalTrials.gov Identifier [NCT03903835](#). Date of registration: April 4, 2019. Status: Recruiting.

Keywords: Clinical trial platform; Genetic biomarker; Precision medicine; Prostate cancer.

Conflict of interest statement

Henrik Grönberg has received honoraria for giving talks at Janssen, Bayer, and Astellas. All other authors declare no conflict of interest.

Figures

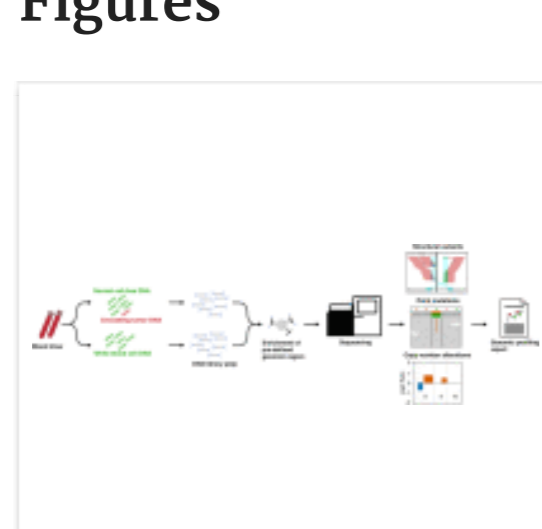


Fig. 1 5 Genomic profiling in the ProBio...

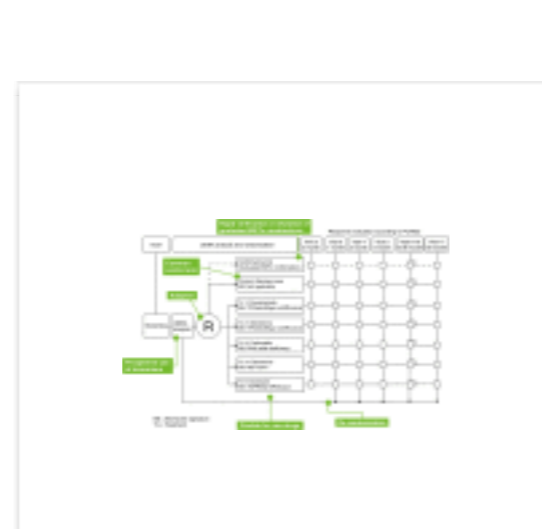


Fig. 2 5 Study design of the ProBio...

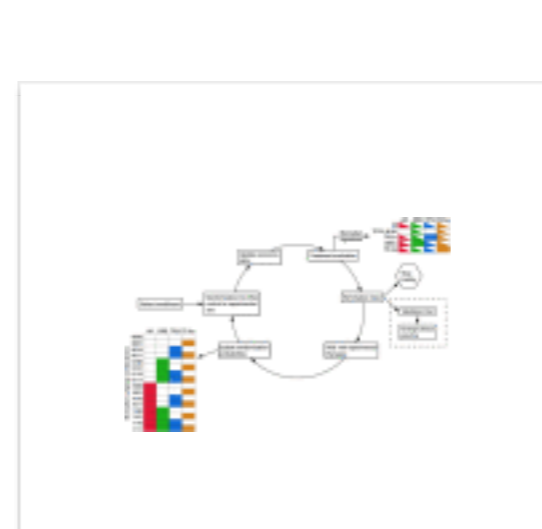


Fig. 3 5 Life cycle of the ProBio...

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