

ABSTRACT

The treatments for prostate cancer becomes complex since it is with progression of the natural history of the disease and response to treatment. The initial diagnosis of prostate cancer either localized or metastatic disease can progress to metastatic hormone sensitive prostate cancer (mHSPC) or castration-resistant prostate cancer (CRPC) and ultimately leading to metastatic CRPC. This paper briefly describes the Oncology statistics analysis in clinical trial studies at Pfizer to prostate cancer based on Prostate Cancer Working Group (PCWG) criteria, which can be considered as valuable approaches for related studies to meet the analysis need in clinical trial studies.

INTRODUCTION

The PCWG3 is an international working group of clinical and translational experts in prostate cancer in light of a changing therapeutic landscape and advances in the understanding of the disease, which provides recommendations on baseline disease assessments, biomarker assessments, criteria for PSA progression, defining and reporting outcomes related to circulating tumor cell (CTC) enumeration, the assessment of patient reported outcomes (PRO), defining progression in relation to bone metastases, defining other bone-related outcomes such as time to skeletal related events, treatment beyond progression, and the assessment of time to no longer clinically benefiting (NLCB).

A Revised Clinical States Model to Account for the Effect of Prior Therapies on Disease Biology

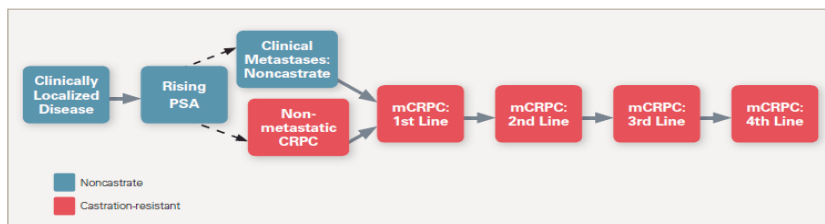


Figure 1. Prostate Cancer Clinical States Model as Updated by the Prostate Cancer Clinical Trials Working Group 3 (PCWG3) Guidelines[14]. CRPC = castration-resistant prostate cancer; mCRPC = metastatic castration-resistant prostate cancer; PSA = prostate-specific antigen.

- **Action:** Detail prior therapies in the order administered, including start/stop dates and response if applicable
- **Blood-based diagnostics:** Testosterone (ultra-sensitive), CTC, cfDNA, immune
- **Rebiopsy:** Histology (adenocarcinoma, small cell, intermediate phenotypes), biologic characterisation

cfDNA: cell-free DNA; CTC: circulating tumour cells; mCRPC: metastatic castration-resistant prostate cancer; PSA: prostate-specific antigen.

1. Scher HI et al. *J Clin Oncol*. 2016;34:1402-1418.

EXAMPLES OF ANALYSIS METHODS

Criteria for Evidence of Bone Progression

Date Progression Detected (Visit)	Criteria for Progression	Criteria to Confirm Progression	Criteria to Document Disease Progression on Confirmatory Scan
Week 8	2 or more new lesions compared to <u>baseline bone scan</u>	Timing: at least 6 weeks after progression identified or at week 16 visit	Persistence of at least 2 lesions seen at week 8 AND 2 or more new bone lesions on bone scan compared to week 8 scan
Week 16 or later	2 or more new lesions on bone scan compared to <u>week 8 bone scan</u>	Timing: at least 6 weeks after progression identified or at next imaging time point [2]	Persistence of at least 2 of the lesions identified as new compared to week 8

Incorporation of Bone Progression into Best Overall Response

Example Number	Timepoint	Soft Tissue Response	Bone Assessment	Overall Soft Tissue Response#
1	Week 9	CR	Progression criteria met (PD)	PD
	Week 17	CR	Progression criteria confirmed	PD
2	Week 9	CR	Progression criteria met (unconfirmed PD)	CR
	Week 17	CR	Progression criteria NOT confirmed	CR
3	Week 9	SD	Non PD	SD
	Week 17	PR	Progression criteria met (PD)	PD
	Week 25	PR	Progression criteria confirmed	PD
4	Week 9	SD	Non PD	SD
	Week 17	PR	Not Evaluable	PR
	Week 25	PR	Progression criteria met but not yet confirmed (unconfirmed PD)	PR

#Considering bone progression (derived)

Prostate Specific Endpoints

1. Prostate-Specific Antigen (PSA): Response and progression
2. Time to First Symptomatic Skeletal Related Events
3. Time to castration resistance
4. Time to Initiation of Antineoplastic Therapy and Time to Initiation of Cytotoxic Chemotherapy
5. Time to Deterioration in Patient Reported Pain and other PRO analysis
6. CTC and CTC0 count conversions
7. Metastatic Free Survival

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AUTHOR CONTACT INFORMATION

Email: tony.tian@Pfizer.com