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Comparative Analysis of Different Methods of Disease Progression Data Capture in Patients with Metastatic Castration-Resistant Prostate Cancer

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KEY FINDINGS & CONCLUSIONS

- Different real-world prostate cancer datasets capture disease progression in different ways
- In this analysis, few differences were observed between the all PDP (physician-documented progression) definition and the PDP associated with treatment change definition
  - Across the different definitions, HRs for the association between disease progression and mortality were similar
  - There was also no notable difference across definitions for any measure of model association or discrimination
  - However, the PDP ±14 days and ±28 days definitions provided better estimates of some measures of model fit and higher chi-square and Pearson correlation values
- Overall, these findings suggest that in real-world datasets, evaluating PDP events associated with treatment changes leads to findings that are clinically more relevant than evaluating all PDP events
- Given the lack of standardization across different prostate cancer datasets, the findings support the feasibility of comparing disease progression outcomes across different data sources using only progressions associated with treatment changes
- For the PRECISION data platform, which is incorporating datasets from multiple sources, this analysis indicates that evaluating disease progressions that are within 14 days of a treatment change is a suitable approach

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INTRODUCTION

- The PRECISION (PRostatE Cancer dISease observatION) data platform is a comprehensive, longitudinal, patient-level dataset on advanced prostate cancer patients from multiple treatment settings in the United States (US)
- To create PRECISION, real-world data from several heterogenous datasets are being harmonized into a common data model[1]
- One key variable that is being standardized into the common data model is disease progression, a component of progression-free survival (PFS)
  - Progression is being captured across prostate cancer datasets within PRECISION in two different ways:
    - All physician-documented progression (PDP) events
    - Only PDP events associated with a treatment change (e.g. treatment initiation, discontinuation, or switch)
- In order to standardize the definition of disease progression, this study utilized the ConcertAI dataset, which has all PDP events so it can be analyzed based on either definition, to determine which definition is clinically more relevant

METHODS

- This was a retrospective cohort study using the ConcertAI Patient360 dataset from the PRECISION data platform. ConcertAI is a longitudinal dataset comprised of electronic health records from >900 US practices[2]
- The study period was December 1, 1994, to May 1, 2023. Adult men with metastatic castration-resistant prostate cancer (mCRPC) were included and the index date was the date of mCRPC diagnosis
- Patient characteristics, as well as Kaplan–Meier PFS and overall survival (OS), were described for the cohort
- In the PFS analyses, three definitions of disease progression were compared: 1) all PDP; 2) PDP ±14 days of a treatment change (commonly used in real-world datasets); and 3) PDP ±28 days of a treatment change (sensitivity analysis based on double the amount of time around treatment changes as definition 2)
- To identify the most clinically relevant definition of disease progression, an extended Cox model was used to analyze the relationship between the different definitions of disease progression and mortality (e.g., OS); model fit was evaluated in terms of concordance, log-likelihood, and Akaike information criterion (AIC)[3]
- To further explore the clinical relevance of each progression definition, the chi-square test and Pearson correlation were performed

RESULTS

Patient population

- A total of 3,855 patients with mCRPC were identified in the ConcertAI database
- Patients had a mean age of 71.7 years, 76% were White, 85% were treated in a community setting, and 68% had a Gleason score ≥7 (**Table 1**)

Table 1. Patient characteristics

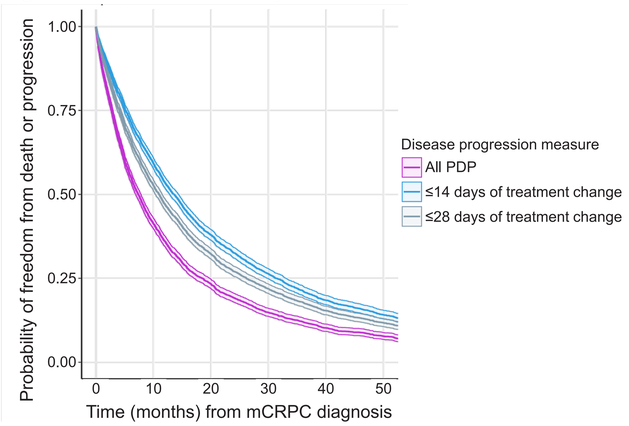
Characteristic	Patient population (N=3,855)
Age, years	
Mean (SD)	71.7 (8.75)
Median (Min, Max)	72.2 (39.8, 87.9)
Race	
White	2,915 (75.6%)
Black or African American	540 (14.0%)
American Indian or Alaska Native	43 (1.1%)
Asian	42 (1.1%)
Native Hawaiian or Other Pacific Islander	2 (0.1%)
Other/unknown	313 (8.1%)
Ethnicity	
Hispanic or Latino	151 (3.9%)
Not Hispanic or Latino	727 (18.9%)
Unknown	2,977 (77.2%)
Practice type	
Community	3,275 (85.0%)
Academic	558 (14.5%)
Unknown	22 (0.5%)
US geographic region	
South	1,448 (37.6%)
Midwest	1,087 (28.2%)
Northeast	659 (17.1%)
West	624 (16.2%)
Multiple	14 (0.4%)
Unknown	23 (0.6%)
Tumor stage	
0–I	60 (1.6%)
II	288 (7.5%)
III	222 (5.8%)
IV	2,419 (62.7%)
Unknown	866 (22.5%)
Gleason score	
≥7	2,617 (67.9%)
<7	467 (12.1%)
Unknown	771 (20.0%)

Data are n (%) unless otherwise indicated.
SD: standard deviation; Min: minimum; Max: maximum.

Progression-free survival

- When PFS was examined using the three different definitions of disease progression, all PDP definition captured the most events post-mCRPC diagnosis
- The time to progression or death was shorter with the all PDP definition compared with the two treatment-anchored definitions (**Figure 1**)
  - The median PFS was 7.4 months (95% confidence interval [CI] 6.9–7.8 months) with the all PDP definition, compared with 13.5 months (95% CI 12.8–14.4 months) with the PDP ±14 days of a treatment change definition, and 11.0 months (95% CI 10.3–11.5 months) with the PDP ±28 days of a treatment change definition
- However, by 50 months of follow-up, the proportion of patients who were free from progression or death was similar with all three definitions used to capture disease progression

Figure 1. Kaplan-Meier analysis of PFS

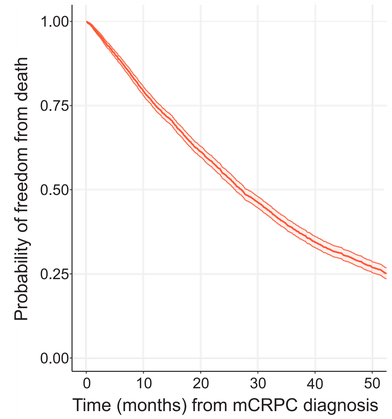


mCRPC: metastatic castration-resistant prostate cancer; PFS: progression-free survival.

Overall survival

- Median OS for patients post-mCRPC diagnosis was 27.1 months (95% CI 26.0–28.2 months) (**Figure 2**)
- The rate of death was approximately constant throughout the follow-up period

Figure 2. Kaplan-Meier analysis of OS



mCRPC: metastatic castration-resistant prostate cancer; OS: overall survival.

Analysis of measures of disease progression

Relationship between progression and mortality

- Using an extended Cox model to analyze the relationship between disease progression and mortality, the all PDP definition for capturing disease progression produced a hazard ratio (HR) of 0.68 (95% CI 0.55–0.83), while PDP ±14 days of a treatment change resulted in an HR of 0.63 (95% CI 0.51–0.78) and PDP ±28 days resulted in an HR of 0.65 (95% CI 0.53–0.80) (**Table 2**)

Model fit

- Across the three different definitions, no notable difference was observed in any measure of association or discrimination in model fit (concordance, log-likelihood, and AIC) between patients who died and those who did not die (**Table 2**)
- However, linking progression to treatment changes resulted in better estimates of model fit (i.e., higher log-likelihood and lower AIC)

Clinical relevance

- In examining the correlation between any disease progression and death at any time, linking progression to treatment changes also resulted in higher chi-square and Pearson correlation values (**Table 2**)

Table 2. Analysis of measures of disease progression in predicting mortality

Measure	All PDP	PDP ±14 days of treatment change	PDP ±28 days of treatment change
HR	0.68 (0.55–0.83)	0.63 (0.51–0.78)	0.65 (0.53–0.80)
Concordance	0.51 (0.50–0.52)	0.52 (0.51–0.53)	0.52 (0.51–0.53)
Log-likelihood ×10⁴	–1.65 (–1.71 to –1.59)	–1.12 (–1.16 to –1.08)	–1.33 (–1.39 to –1.28)
AIC ×10⁴	3.30 (3.18–3.41)	2.24 (2.16–2.23)	2.67 (2.57–2.77)
Chi-square test statistic	35.47 (14.61–67.29)	43.82 (19.09–78.49)	42.32 (18.21–76.57)
Pearson correlation coefficient (r)	0.11 (0.07–0.15)	0.14 (0.09–0.19)	0.13 (0.08–0.17)

Data values are shown with 95% confidence intervals. Higher values preferred for concordance, log-likelihood, chi-square test, and Pearson correlation; lower values preferred for AIC.
AIC: Akaike information criterion; HR: hazard ratio; PDP: physician-documented progression.

References

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Disclosures

JN and JP are employees of Novartis Pharmaceuticals Corporation. CB and JT are consultants engaged by Novartis Pharmaceuticals Corporation to conduct this study.