The frequency of use and enrollment impact of patient-centered outcomes in prostate cancer clinical trials

Madison Krischak, **Merrick Bank**, Mary Byrnes, Rishi Sekar, Patrick Lewicki, Lindsey Herrel, Gretchen Piatt, Khurshid Ghani, Ted Skolarus, Kristian Stensland

INTRODUCTION
Cancer treatments should improve patient quantity or quality of life; however, some cancer trial outcomes are not patient-centered and do not correlate with overall survival. Selecting trial endpoints that reflect these goals could improve the discovery process by ensuring trial results are of direct interest to patients and may increase enrollment. How frequently prostate cancer clinical trials use patient-centered outcomes, and how outcome type impacts trial enrollment, is unknown.

METHODS
On October 23, 2022, we queried ClinicalTrials.gov for full text records of phase 2-3 prostate cancer trials started after January 1, 2007. We extracted primary outcomes and trial characteristics with a custom Python script. Two reviewers assigned each outcome into categories (e.g., overall survival, patient-reported measure). As previously studied, the only valid surrogate for overall survival is metastasis-free survival. We considered these two outcomes and outcomes directly noticeable to patients to be patient-centered. For completed or terminated trials, we defined ‘sufficient accrual’ as attaining 85% of goal enrollment. We identified associations between trial outcome types and sufficient trial enrollment with chi-square tests and logistic regression.

RESULTS
Of 1,717 prostate cancer trials, only 37% used a patient-centered outcome, with 6% using overall or metastasis-free survival. Among 318 Phase 3 trials, 49% used a patient-centered outcome and 26% used overall or metastasis-free survival. Of 731 completed or terminated prostate cancer trials, 55% of trials and 68% of phase 3 trials reached sufficient enrollment (85% of goal). On multivariable analysis, trials with an overall survival endpoint had higher odds of sufficient enrollment (OR 8.0 [95% CI 2.2-33.5], $p < 0.01$), but trials with any patient-centered outcome had lower odds of sufficient enrollment (OR 0.25 [95% CI 0.11-0.54], $p < 0.01$).

CONCLUSION
Less than half of prostate cancer trials use an outcome that is patient-centered (i.e., overall survival or outcome noticeable to patients). Further work is needed to clarify the use, understanding, and effect of outcome selection in cancer trials. Realigning trial efforts with patient-centered goals may be critical to achieving our pursuit of patient-centered care.

Table 1. Outcomes used in prostate cancer clinical trials, by phase (trials could have multiple outcome types)

Outcome Type	**Phase I/II N=285 (%)**	**Phase II N=1063 (%)**	**Phase II/III N=51 (%)**	**Phase III N=318 (%)**
Overall survival	4 (1.4)	12 (1.1)	1 (2.0)	66 (20.8)
Progression-free survival	29 (10.2)	188 (17.7)	6 (11.8)	69 (21.7)
Disease-specific survival	0 (0.0)	11 (1.0)	2 (3.9)	14 (4.4)
Outcome specific to disease	12 (4.2)	122 (11.5)	5 (9.8)	53 (16.7)
Adverse events	157 (55.1)	114 (10.7)	3 (5.9)	22 (6.9)
Dose determination	87 (30.5)	15 (1.4)	0 (0.0)	2 (0.6)
Radiographic accuracy	18 (6.3)	60 (5.6)	14 (27.5)	29 (9.1)
Metastasis-free survival	0 (0.0)	4 (0.4)	2 (3.9)	16 (5.0)
Response rate	55 (19.3)	164 (15.4)	2 (3.9)	9 (2.8)
Cellular markers	16 (5.6)	101 (9.5)	1 (2.0)	4 (1.3)
Study parameters	11 (3.9)	26 (2.4)	3 (5.9)	3 (0.9)
Clinical measures	10 (3.5)	24 (2.3)	2 (3.9)	15 (4.7)
Patient-reported measures	4 (1.4)	39 (3.7)	5 (9.8)	14 (4.4)
Freedom from failure	3 (1.1)	24 (2.3)	3 (5.9)	12 (3.8)
Biomarkers	43 (15.1)	272 (25.6)	1 (2.0)	24 (7.5)
Insufficient information	20 (7.0)	55 (5.2)	5 (9.8)	15 (4.7)