Safety and clinical validity of tumor genomic testing for guiding active surveillance selection in men with NCCN intermediate-risk prostate cancer

Abstract No. 336

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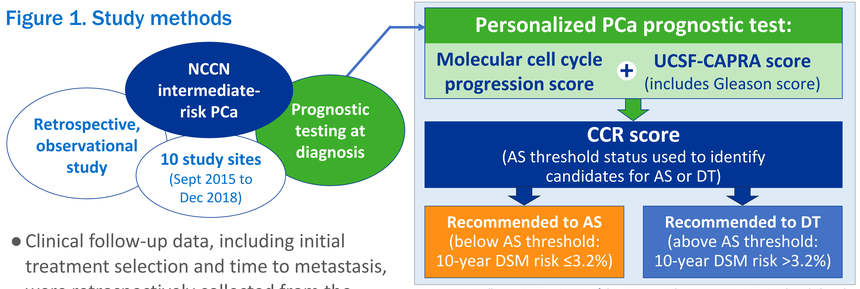
Background

- Clinicopathologic features are considered the gold standard for predicting prostate cancer (PCa) disease severity and guiding decisions on the use of active surveillance (AS) or definitive treatment (DT).
- However, tumor genomic testing has been shown to provide valuable information as an addition to clinical risk stratification measures, allowing for more accurate identification of AS candidates.
- **Primary objective:** To evaluate the safety of genomic testing for guiding AS selection in patients with National Comprehensive Cancer Network (NCCN) intermediate-risk PCa.

Methods

Figure 1. Study methods



AS, active surveillance; CAPRA, Cancer of the Prostate Risk Assessment; CCR, Combined Clinical Risk; DSM, disease-specific mortality; DT, definitive treatment; NCCN, National Comprehensive Cancer Network; PCa, prostate cancer; UCSF, University of California, San Francisco.

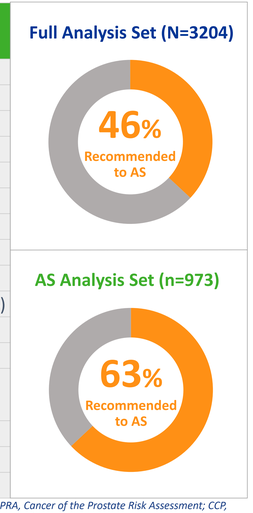
- Clinical follow-up data, including initial treatment selection and time to metastasis, were retrospectively collected from the treating clinics.
- Kaplan-Meier estimates were used to evaluate the safety of AS in patients who initially selected AS.
- Cox proportional hazards models were used to evaluate CCR as a predictor of metastasis.

Results

- In total, 3204 patients were included in this analysis, with 1468 (45.8%) recommended to pursue AS, and 1736 (54.2%) recommended to DT (**Table 1**).
  - Among the 973 (30.4%) patients who initially selected AS (AS analysis set), 613 (63.0%) were recommended to AS and 360 (37.0%) were recommended to DT.

Table 1. Patient characteristics

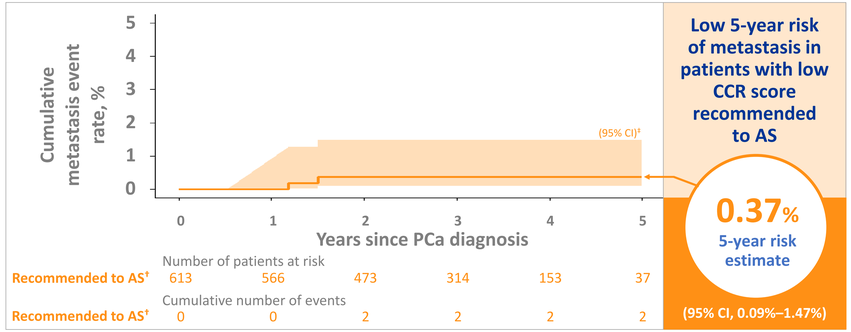
	Full Analysis Set N = 3204	AS Analysis Set n = 973
Initially on AS, n (%)	973 (30.4)	973 (100)
Age, median (IQR)	67 (61, 72)	68 (62, 73)
Gleason 3+3, n (%)	331 (10.3)	183 (18.8)
Gleason 3+4, n (%)	2216 (69.2)	711 (73.1)
Gleason 4+3, n (%)	657 (20.5)	79 (8.1)
NCCN favorable int. , n (%)	1785 (55.7)	720 (74.0)
NCCN unfavorable int. , n (%)	1419 (44.3)	253 (26.0)
CAPRA, median (IQR)	3 (2, 4)	3 (2, 3)
CCP, median (IQR)	-0.6 (-1.0, -0.1)	-0.8 (-1.2, -0.3)
CCR, median (IQR)	0.933 (0.495, 1.446)	0.657 (0.324, 1.056)
Below AS threshold, n (%)	1468 (45.8)	613 (63.0)
Above AS threshold, n (%)	1736 (54.2)	360 (37.0)
Time to last follow up, yrs, median (IQR)	3.0 (2.0, 3.9)	3.0 (2.0, 3.9)
Recorded metastasis events, n	23	5
Below AS threshold	3	2
Above AS threshold	20	3



**Most common DTs were radical prostatectomy or radiotherapy ± androgen deprivation therapy. AS, active surveillance; CAPRA, Cancer of the Prostate Risk Assessment; CCP, cell-cycle progression; CCR, Combined Clinical Risk score; int, intermediate risk; IQR, interquartile range; MM, medical management; yrs, years.*

- In patients who were recommended to and pursued AS, the estimated 5-year risk of metastasis was 0.37% (95% CI, 0.09%–1.47%) (**Figure 2**).

Figure 2. Cumulative risk of metastasis within 5 years for NCCN intermediate-risk patients who initially selected AS, with CCR scores below the AS threshold



†CCR-based 10-year DSM risk below the AS threshold (≤3.2%). ‡Shaded area represents the 95% CI.
CAPRA, Cancer of the Prostate Risk Assessment; CCR, Combined Clinical Risk score; CI, confidence interval; DSM, disease-specific mortality; PCa, prostate cancer.

- After adjustment for initial treatment decision (AS vs DT) and CAPRA score in patients who opted for AS (**Table 2**):
  - Patients recommended to DT (above the AS threshold) were at higher risk of metastasis than patients recommended to AS (below the AS threshold).
  - Patients with higher CCR scores were at higher risk of metastasis vs those with lower CCR scores.

Table 2. Secondary analysis: Predictive value of personalized PCa prognostic testing for time to metastasis, after adjustment for initial treatment decision and CAPRA score

Variable	HR (95% CI)	$\Delta\chi^2$	p-value	Variable	HR (95% CI)	$\Delta\chi^2$	p-value
AS threshold status	4.20 (1.41–18.04)	4.85	**0.03**	**Continuous CCR score**	7.11 (4.13–12.49)	16.12	**6.0×10^{-5}**
Initial treatment choice	0.94 (0.30–2.42)	0.015	0.90	**Initial treatment choice**	1.17 (0.38–3.02)	0.083	0.77
CAPRA	1.31 (0.95–1.80)	2.17	0.14	**CAPRA**	0.70 (0.52–0.94)	2.06	0.15

Conclusions

- For patients with NCCN intermediate-risk PCa who were identified by genomic testing as candidates for AS, AS was associated with a very low 5-year risk of metastasis (0.37%), suggesting AS may be a safe approach for these patients.
- Personalized PCa prognostic testing added valuable information to CAPRA.
- CCR score was a strong predictor of metastasis beyond clinicopathologic factors.

Disclosures: *WC, LL, DI, JJ, AG, RF, TS, and TC were employees of Myriad Genetics, Inc. at the time of the study and received salary and stock options.* ***AG*** *has had a prior consulting/advisory role for DermTech.* ***TS*** *has had a consulting/advisory role for and ownership interests in Oncodeo.* ***TM*** *has had consulting/advisory roles for Myriad Genetics, Inc., Terumo, Blue Earth Diagnostics, Stratify Genomics, Myovant Sciences, Tempus, and Foundation Medicine, received research funding from Myriad Genetics, Inc., MDxHealth, and GenomeDx.* ***HK*** *has received research funding from Myriad Genetics, Inc.* ***JH*** *has had consulting/advisory and speaker roles for Myriad Genetics, Inc., Astellas Pharma, Dendreon, Janssen Biotech, Myovant Sciences, and Pfizer; advisory roles for Promaxo, and LynxDx, Lilly; and speaker roles for Amgen, Bayer, Blue Earth Diagnostics, Procept BioRobotics, Tolmar, and UroGen Pharma; and received honoraria for all of the above, as well as Lantheus Medical Imaging and Merck; and research funding from Myriad Genetics, Inc., Astellas Pharma, Dendreon, Janssen Biotech, Myovant Sciences, Pfizer, Merck, Bayer, Lipella Pharmaceuticals, and miR Scientific.* ***RT*** *has had consulting/advisory roles for Exosome Diagnostics, Myovant Sciences, Nymox, and Novartis; speaker roles for Medivation/Astellas, Exosome Diagnostics, and Pfizer; has received research funding from Medivation/Astellas, Janssen Oncology, Bayer, MDxHealth, Genomic Health, Exosome Diagnostics, Advantagene, Merch, POINT Biopharma, Dendreon, and Veru; and has stock/ownership interests in Nymax, Novartis, Myovant Sciences, Veru, Compass Therapeutics, and GlaxoSmithKline.* ***AD, TR, KC,*** *and* ***PY*** *have no conflicts of interest to declare.*