AI-enabled analysis of H&E-stained prostate cancer tissue images: Assessing risk for metastasis prior to apalutamide (APA) treatment of patients with non-metastatic castration-resistant prostate cancer (nmCRPC)

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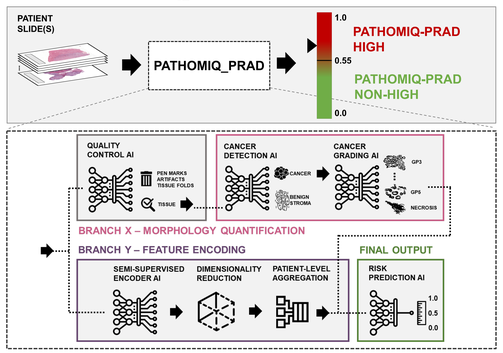
BACKGROUND

- APA has been approved for the treatment of nmCRPC and metastatic castration sensitive prostate cancer (mCSPC) [1].
- PATHOMIQ_PRAD was developed as an AI-enabled prognostic algorithm [2, 3] that predicts the risk of metastasis from Whole Slide Images (WSIs) of H&E-stained core biopsies or radical prostatectomy specimens.
- The objective of this study is to determine the risk for metastasis in nmCRPC patients based on PATHOMIQ_PRAD risk categories.

METHODS

- **Training Data:** The model was previously developed [2, 3] to predict time-to-metastasis. Metastasis was defined as first evidence of radiographically detectable disease in bone or soft tissue. No patient received perioperative treatment with androgen deprivation therapy (ADT) or adjuvant radiotherapy +/- ADT. These data were sourced from University of Wisconsin-Madison and the Icahn School of Medicine Mount Sinai, and the publicly available dataset, TCGA.
- **Test Data:** Patients with available H&E-stained slides from their primary diagnosis in SPARTAN clinical trial [1] were included for validation.
- The PATHOMIQ_PRAD scores (between 0 and 1) were generated for each patient; higher values representing increased risk of metastasis.
- A pre-determined cut-off was previously developed to provide the best predictive accuracy with respect to time-to-metastasis on multiple clinical cohorts and was applied to this dataset to generate PATHOMIQ_PRAD high and low categories.
- Kaplan-Meier analysis was performed on Metastasis-free-survival (MFS).

FIGURE 1: PATHOMIQ_PRAD model pipeline



RESULTS

- WSIs were collected from 467 pts (APA+ADT (n=311); placebo+ADT (n=156)); 35 pts were excluded due to lack of tumor or poor image quality.
- PATHOMIQ_PRAD scores were generated for 436 (93%) pts.
- All pts receiving APA+ADT had improved outcomes compared with pts receiving ADT alone, independent of PATHOMIQ_PRAD risk score category.
- 47% were assigned non-high PATHOMIQ_PRAD risk; also in this cohort, treatment with APA+ADT resulted in a significantly improved MFS (hazard ratio, 0.39; 95% CI, 0.17 – 0.86; P = 0.02) (TABLE 2 & FIGURE 2).
- 53% of pts had high PATHOMIQ_PRAD scores and significantly benefited from treatment with APA+ADT compared to placebo+ADT with regard to MFS (hazard ratio, 0.19; 95% CI, 0.1 – 0.37; P < 0.005) (TABLE 2 & FIGURE 3).

FIGURE 2: MFS by treatment arm in PATHOMIQ_PRAD non-high risk group

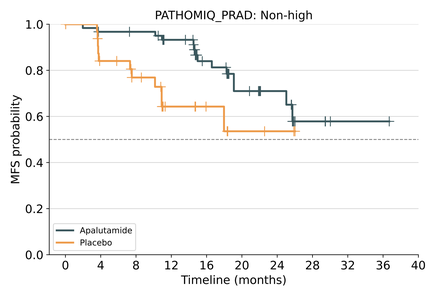


FIGURE 3: MFS by treatment arm in PATHOMIQ_PRAD high risk group

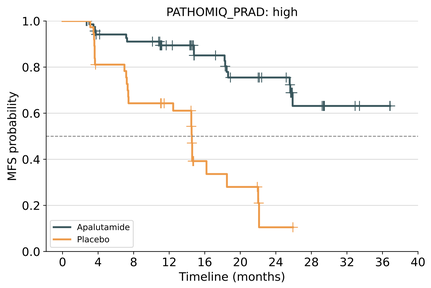


TABLE 1: Baseline Patient Characteristics

		Apalutamide + ADT	Placebo + ADT
n		311	156
Median age		74.0	73.5
PSA (ng/mL), mean (sd)		15.9 (23.6)	16.6 (19.6)
AJCC Tumor Stage, No. (%)	**T1**	52 (16.9)	27 (17.8)
	T2	110 (35.8)	43 (28.3)
	T3	107 (34.9)	69 (45.4)
	T4	12 (3.9)	8 (5.3)
	TX	26 (8.5)	5 (3.3)
Gleason score, No. (%)	**<7**	37 (11.9)	27 (17.3)
	=7	124 (39.9)	64 (41.0)
	>7	145 (46.6)	65 (41.7)
Local or regional nodal disease No. (%)	**N0**	216 (69.9)	100 (65.4)
	N1	47 (15.2)	27 (17.6)
	NX	46 (14.9)	26 (17.0)
Median metastasis-free survival (95% CI), months		NR* (29.1, NR)	14.6 (12.5, 19.0)
Median overall survival (95% CI), months		65.1 (59.8, NR)	58.6 (49.6, NR)

*** NR: Not reached**

TABLE 2: hazard ratios between treatment arms inside PATHOMIQ_PRAD risk groups

PATHOMIQ_PRAD risk groups	Patients (%)	HR	CI	P-value
Non-high	47%	0.39	0.17-0.86	0.02
High	53%	0.19	0.10-0.37	<0.005

KEY TAKEAWAY

- In the present cohort, PATHOMIQ_PRAD stratified patients with nmCRPC based on their risk of metastatic progression.
- H&E-based AI might be a tool for prognostic risk stratification in nmCRPC patients

CONCLUSIONS

- Independent of PATHOMIQ_PRAD risk score category, all pts receiving APA+ADT had improved outcomes compared with pts receiving ADT alone [1].
- For MFS, in PATHOMIQ_PRAD high risk patients there was a bigger separation between treatment arms compared to non-high risk patients (HR = 0.19 vs 0.39)
- Although, there are limitations related to sample size, H&E-based AI could be a tool to risk-stratify patients with nmCRPC based on their prognosis..

REFERENCE

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