Clinical Validation of a Multimodal Artificial Intelligence Prognostic Model in Localized and Advanced Disease

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ARTERA
Precision oncology, powered by AI

BACKGROUND

Introduction

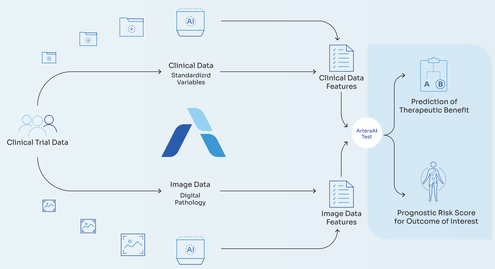
Need for improved tools to personalize therapy in patients with prostate cancer

- Prostate cancer is the second most common cancer among men, with over 375,000 deaths worldwide[1]
- Improved prognostic and predictive tools are needed to avoid over- and undertreatment and minimize prostate cancer-associated morbidity[2,3]

Artificial intelligence (AI) to aid in personalization of prostate cancer treatment

- Artera has developed multimodal AI (MMAI)-enabled predictive and prognostic biomarkers for patients with prostate cancer using large datasets from thousands of patients enrolled in Phase 3 randomized clinical trials[4,5]
- It is important to understand the broader utility of the MMAI biomarkers by validating these models across a spectrum of prostate cancer disease states
- Here, we present data on the validation of the prognostic and predictive MMAI biomarkers for use in a broader range of prostate cancer settings, including in patients with high risk and metastatic disease

ArteraAI Multimodal Architecture



Clinical Trial Data

Distant metastasis

AI to estimate long-term outcomes and predict therapeutic benefit

Model Development and Validation Cohorts

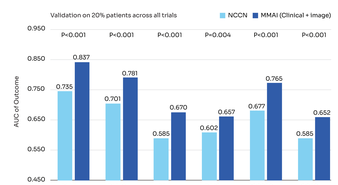
	Prognostic Biomarker[4]	Risk Stratification Analysis[4]	External Validation in High-Risk Disease[6]	Meta-Analysis of High-Risk Patients[7]	Risk Stratification in nmCRPC[8]	High-Risk Localized and Metastatic Disease[9]	ST-ADT Predictive Biomarker[5]	LT-ADT Predictive Biomarker[10]
Studies used for training	NRG/RTOG-9202, 9408, 9413, 9910, and 0126	NRG/RTOG-9202, 9408, 9413, 9910, and 0126	NRG/RTOG-9202, 9408, 9413, 9910, and 0126	NRG/RTOG-9202, 9408, 9413, 9910, and 0126	NRG/RTOG-9202, 9408, 9413, 9910, and 0126	NRG/RTOG-9202, 9408, 9413, 9910, and 0126	NRG/RTOG-9202, 9408, 9413, 9910, and 0126	NRG/RTOG-9408, 9413, 9902, 9910, and 0521
Training set, n	4522	4581	4581	4581	4581	4581	2024	2641
Studies used for validation	NRG/RTOG-9202, 9408, 9413, 9910, 0126	NRG/RTOG-9202, 9408, 9413, 9902, 9910, 0126, 0415, 0521	NRG/RTOG-9902	NRG/RTOG 0521, 9202, 9408, 9413, 9902, 9910	SPARTAN (NCT01946204)	STAMPEDE (NCT00268476)	NRG/RTOG-9408	NRG/RTOG-9202
Validation set, n	1132	2486	318	1088	467	3167	1594	1192

[a]Manuscript in preparation

PROGNOSTIC

Prognostic Biomarker Outperformed Standard Risk Stratification Tool[4]

MMAI Model Outperformed NCCN For All Endpoints



Full Model, Including Pathology Images and Clinical Variables, Yielded the Best Prognostic Performance

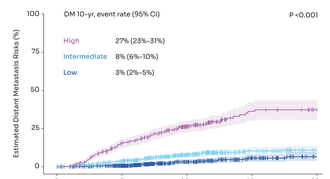
Ablation Study
Evaluation of the incremental benefit of various data components

Model	DM 5-yr	DM 10-yr	BF 5-yr	BF 10-yr	PCSS 10-yr	OS 10 yr
NCCN*	0.735	0.701	0.585	0.602	0.677	0.585
Images	0.779	0.728	0.646	0.612	0.766	0.587
Images+NCCN*	0.827	0.782	0.666	0.660	0.761	0.615
MMAI → Images+NCCN+3**	0.837	0.781	0.670	0.657	0.765	0.652

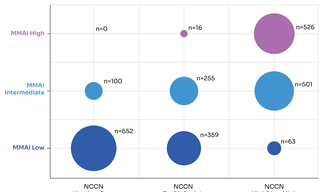
*NCCN = Gleason combined + baseline PSA + T-stage
**Pathology images + NCCN + Gleason primary + Gleason secondary + age

Prognostic Biomarker Identified a Greater Proportion of Low-Risk Patients Than NCCN

MMAI Risk Groups Demonstrated Prognostic Ability for Distant Metastasis



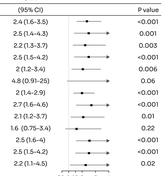
MMAI Identified More Low Risk Patients Than NCCN



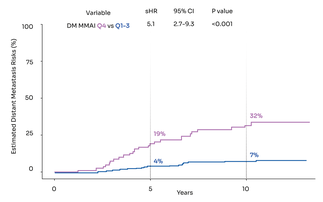
External Validation in High-Risk Disease[6]

Consistent Prognostic Performance of MMAI for Distant Metastasis by Subgroups

Variable	Subgroups	No. of patients (no. of events)	sHR (95% CI)	P value
Total		318 (42)	2.4 (1.6–3.5)	<0.001
Arm	RT+ADT	161 (23)	2.5 (1.4–4.3)	0.001
	RT+ADT+CT	157 (19)	2.2 (1.3–3.7)	0.003
Age	<65	132 (22)	2.5 (1.5–4.2)	<0.001
	65+	186 (20)	2 (1.2–3.4)	0.006
Race	African American	83 (5)	4.8 (0.91–25)	0.06
	Non-African American	234 (37)	2 (1.4–2.9)	<0.001
Baseline PSA (ng/ml)	<20	135 (20)	2.7 (1.6–4.6)	<0.001
	20+	183 (22)	2.1 (1.2–3.7)	0.01
Gleason	7	105 (9)	1.6 (0.75–3.4)	0.22
	8–10	213 (33)	2.5 (1.6–4)	<0.001
Clinical T Stage	T1-T2	215 (25)	2.5 (1.5–4.2)	<0.001
	T3-T4	102 (17)	2.2 (1.1–4.5)	0.02

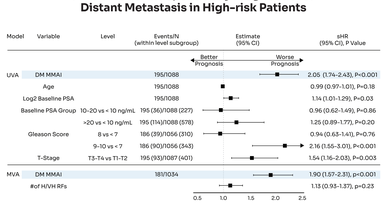


Estimated Risk of Distant Metastasis by MMAI Quartile

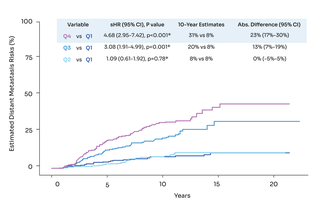


Meta-Analysis of High-Risk Patients Demonstrated Consistent Prognostic Performance[7]

MMAI Model Independently Prognostic for Distant Metastasis in High-risk Patients

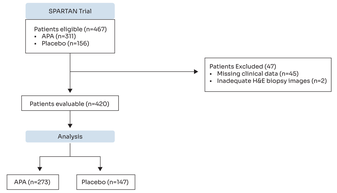


MMAI Model Identified Substantial Differences in Absolute Risk of Distant Metastasis in High-risk Patients

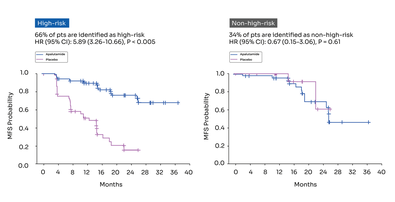


Prognostic Risk Stratification in Non-Metastatic Castration-Resistant Prostate Cancer (nmCRPC)[8]

SPARTAN Trial: CONSORT Diagram

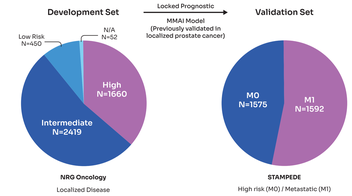


MMAI High Risk Patients Demonstrated Improvement in Metastasis-Free Survival With Apalutamide

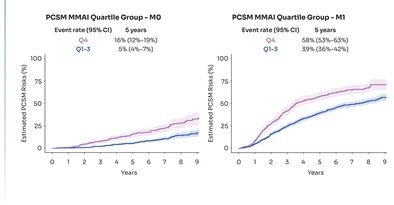


Prognostic Risk Stratification in High-Risk Localized and Metastatic Disease[9]

STAMPEDE Study Design



MMAI Identified a Patient Population With Poorer Prognosis



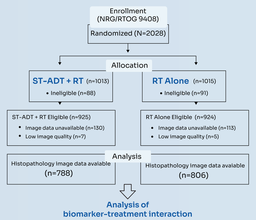
Localized | Localized | High Risk Localized | High Risk Localized | nmCRPC | High-Risk Localized/Metastatic

Manuscript in preparation

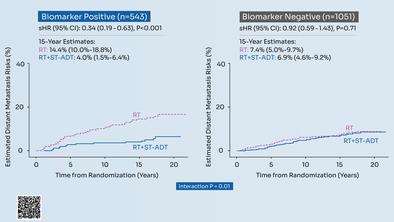
PREDICTIVE

ST-ADT Biomarker Identified 66% of Patients Who May Not Need Hormone Therapy, Avoiding Potential Toxicities Associated with ADT[5]

CONSORT Diagram for NRG/RTOG 9408 (Validation Set)



MMAI Identifies Patients Who Could Avoid Treatment Intensification With ST-ADT



LT-ADT Biomarker Identified 34% of Patients Who Could Safely Avoid Long-Term Hormone Therapy[10]

- An MMAI predictive biomarker was developed to predict additional benefit from long-term ADT (LT-ADT) over short-term ADT (ST-ADT) in men with high-risk localized prostate cancer receiving radiotherapy (RT)
- The model was trained on data from 2641 men enrolled in six phase III NRG/RTOG randomized clinical trials and validated using data from 1192 men participating in RTOG 9202
- LT-ADT biomarker (+) patients had reduced risk of distant metastases with LT-ADT over ST-ADT (subdistribution hazard ratio [sHR], 0.55; 95% confidence interval [CI], 0.41–0.73; P=0.001; n=785); no benefit was observed in LT-ADT biomarker (-) patients (sHR, 1.06; 95% CI, 0.61–1.84; P=0.84; n=407)
- A statistically significant biomarker-treatment interaction was observed (P=0.04)
- The biomarker identified 34% of men with localized high-risk prostate cancer who could derive similar benefit to LT-ADT with ST- ADT

Conclusions

- The MMAI prognostic biomarker for localized prostate cancer demonstrated improved prognostication over the standard NCCN risk stratification tool[4]
- The MMAI prognostic model identified a greater proportion of patients with low-risk of distant metastasis compared to the NCCN risk stratification tool
- Similarly, the MMAI prognostic biomarker outperformed clinical and pathological variables in men at high risk for disease progression[6,7]
- Using data from the phase 3 SPARTAN and STAMPEDE clinical trials, the MMAI prognostic biomarker was externally validated in patients with non-metastatic castrate-resistant prostate cancer and high-risk localized/metastatic prostate cancer, respectively[8,9]
- The MMAI predictive biomarker identified patients who may benefit from the addition of ST-ADT to RT[5]
- Additionally, MMAI biomarkers were shown to predict benefit with LT-ADT over ST-ADT[10]
- Robust clinical validation of the prognostic model using clinical trial data in patients with localized and advanced prostate cancer exemplifies its use to accurately risk stratify disease, contributing to shared decision-making between patients and clinicians

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