ARTERA

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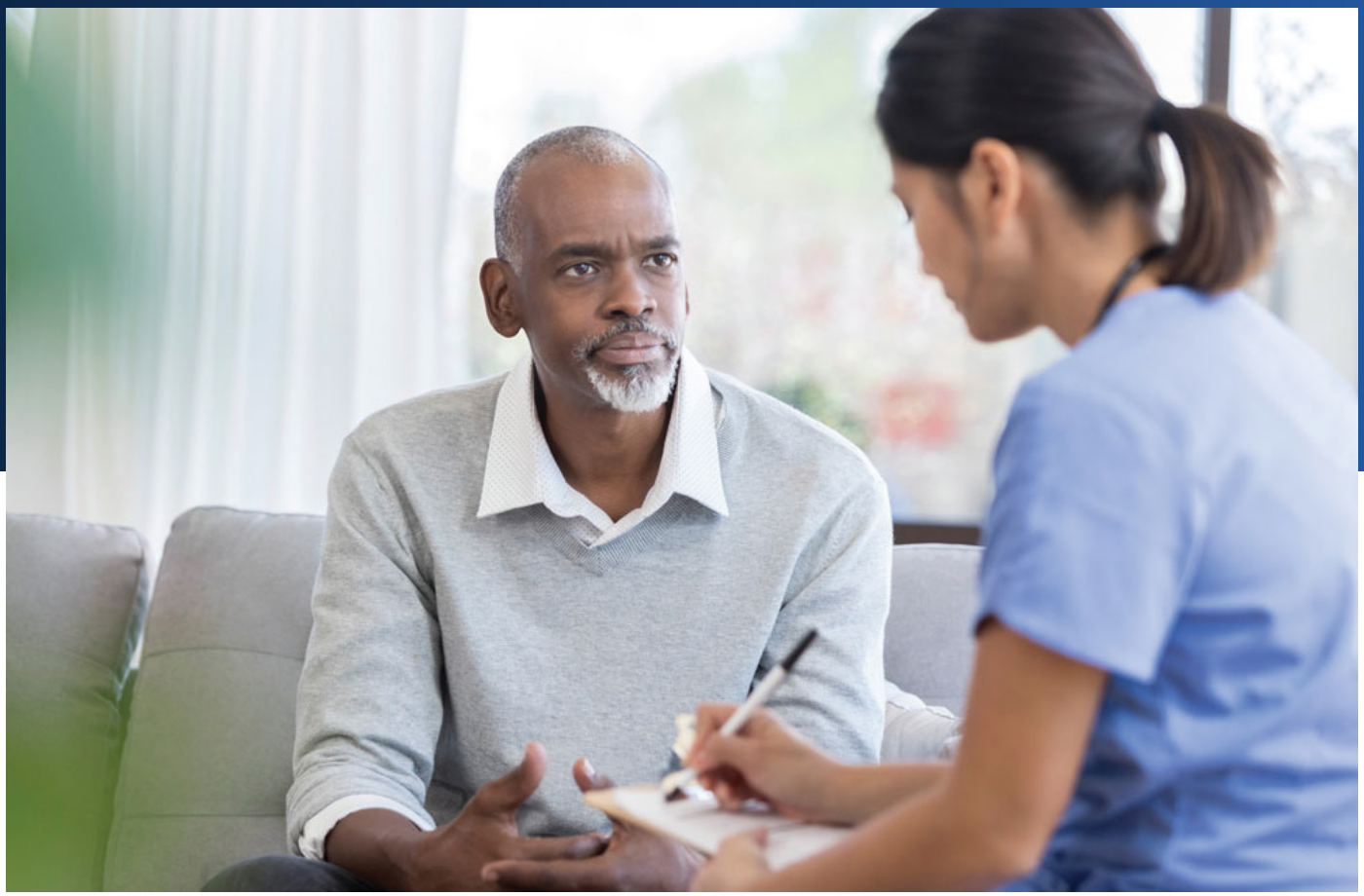


White Paper

Supporting Active Surveillance Decision-Making: Insights from the ArteraAI Prostate Test

The ArteraAI Prostate Test is a Laboratory Developed Test that is now clinically available through a single CLIA-certified laboratory in Jacksonville, FL. This test has not been cleared or approved by the U.S. Food and Drug Administration.

Please consult with your health care provider for personalized medical advice and determine if the ArteraAI Prostate Test is appropriate for you.

For general questions, please contact Artera® at: **info@artera.ai**
For billing questions, please call: **1-650-239-7018**

The ArteraAI Prostate Test

For many patients with lower-risk localized prostate cancer, forgoing or delaying definitive therapy through active surveillance (AS) can help them avoid significant side effects associated with surgery or radiation.[1] Some patients who opt for upfront definitive therapy over AS later experience decision-regret, often due to these side effects.[2,3] This is particularly true for patients with lower-risk prostate cancer, who are most likely to regret choosing treatment over AS.[3] Therefore, there is a growing need for reliable tools that can accurately identify patients who are good candidates for AS, enabling clinicians and patients to make more informed, shared decisions to ensure the best possible care.

The ArteraAI Prostate Test is a guideline-recommended, multimodal artificial intelligence (MMAI)-derived biomarker test designed to support risk-based clinical decision-making for patients with localized prostate cancer.[4–6] By analyzing an individual's clinical data and histopathology images, the MMAI algorithm generates a prognostic score that can be used to estimate the risk of metastasis or death from prostate cancer, as well as provide insights into the suitability of AS as a management option.

The MMAI prognostic biomarker was trained and validated using data from thousands of patients with localized prostate cancer who were enrolled in large-scale, randomized phase 3 clinical trials with follow-up periods of up to 20 years.[6] Additional studies have validated the prognostic performance of and risk stratification using the MMAI biomarker across a broad range of patients with localized prostate cancer.[7–12] Further research has also validated the prognostic performance of the MMAI biomarker in patients with metastatic prostate cancer,[8,13–16] though this falls outside the intended use of the test.

The test can be applied across all NCCN risk groups, with additional insights available for certain patients (Figure 1). For patients with intermediate-risk disease, the test provides predictive results regarding the potential benefit of adding short-term androgen deprivation therapy to radiation (RT).[5] For patients with very-low-, low-, or favorable intermediate-risk disease, additional insights help guide AS decisions. Accurate risk stratification is essential in determining whether patients can safely pursue AS or require more immediate definitive therapy. This white paper provides additional context regarding the use of the ArteraAI Prostate Test in patients eligible for AS. In addition, case studies are provided to further illustrate how the ArteraAI Prostate Test can be used to guide AS shared decision-making.

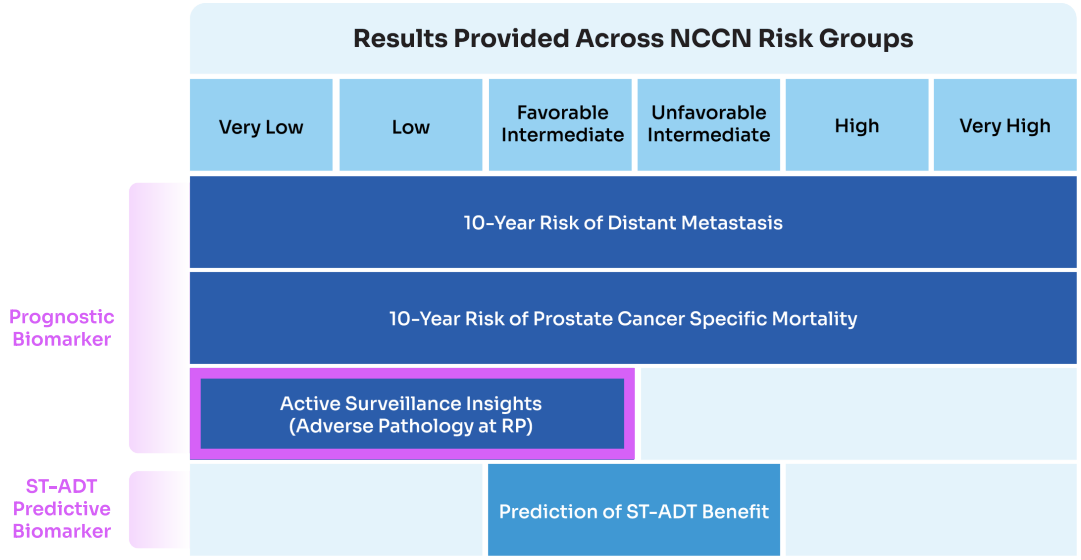


Figure 1. ArteraAI Prostate Test results provided by NCCN risk group. MMAI, multimodal artificial intelligence; RP, radical prostatectomy; ST-ADT, short-term androgen deprivation therapy.

Prognostic Validation of MMAI Model for the Endpoint of Adverse Pathology at Radical Prostatectomy in Patients Managed With AS

Background and Endpoint Selection

The initial training and validation of the MMAI prognostic model was conducted using phase 3 randomized clinical trial data from patients treated with definitive RT.[6] Additional validation was performed in a cohort of patients (n=3337) managed with AS or treated with definitive therapy (including radical prostatectomy [RP] or RT), from the NRG/RTOG 9202, -9408, -9413, -9902, -9910, -0126, -0415, and -0521 studies, as well as additional datasets.[6,17–19] In this broader cohort, the MMAI prognostic score was significantly associated with risk of distant metastasis (DM; HR 2.59 [95% CI: 2.28-2.94]; p<0.001).[19] However, it is still of interest to investigate the association between the MMAI prognostic score and AS-relevant outcomes in patients managed with AS.

Adverse pathology (AP) at RP is a recognized proxy for long-term prostate cancer outcomes and is associated with an increased risk of future metastasis.[20] Understanding the risk of AP at RP is relevant for patients considering AS because it provides insight into the likelihood of the cancer developing more aggressive features over time.[20] AP endpoints are commonly used in studies evaluating patients managed with AS to determine its appropriateness as a management strategy for those with lower-risk localized prostate cancer.[17,18] In a study of patients from the real-world Swedish UPCA cohort, the MMAI biomarker was found to be prognostic for AP at RP (OR 3.92 [95% CI:1.76-10.87]; p=0.002) in an analysis of 49 patients who were eligible for AS (ie, NCCN low- or favorable intermediate-risk disease) but received radical prostatectomy.[7] The next line of inquiry is to then assess whether the MMAI prognostic score correlates with AP at RP in a cohort of patients *managed* with AS.

Methodology

Validation of the MMAI prognostic model was performed in a cohort of patients who were eligible for (NCCN very low-, low-, or favorable intermediate-risk disease) and managed with AS who underwent RP.[17,18] The objective was to determine whether the MMAI prognostic score correlated with **AP at RP, defined as the presence of any of the following: Grade Group 3 or higher, pT3b or higher, and/or N1 disease.** A logistic regression model was used to evaluate the association between the MMAI score and AP at RP.

Results

A total of 292 patients who were eligible for and managed with AS who underwent RP were included in this analysis (Table 1). Of these patients, 26% (77/292) had AP at RP.

MMAI prognostic score at diagnostic or first available positive biopsy was associated with AP at RP in this AS-managed cohort (n=292; OR 1.31 [95% CI: 1.02-1.68]; p=0.036, reporting unit = 1 standard deviation of the score).

Table 1. Characteristic of patients who were eligible for and managed with AS who underwent RP (N=292)

Variable	Value
Median age, y	62
Median PSA at diagnosis, ng/mL	4.9
Clinical Gleason Score, n (%)	
≤6	267 (91)
7 (3+4)	25 (9)
NCCN Risk Group, n (%)	
Low	259 (89)
Favorable Intermediate	33 (11)
ArteraAI Risk Group, n (%)	
Low	232 (79)
Intermediate/High	60 (21)

AS, active surveillance; PSA, prostate-specific antigen; RP, radical prostatectomy.

Overview of AS Insights on the ArteraAI Prostate Test Report

Understanding the relative risk of AP at RP can assist both patients and clinicians in making more informed decisions about whether AS is an appropriate management option. Alternatively, definitive therapy may be considered to prevent the cancer from developing more aggressive features.[20] To support shared AS decision-making, the patient's risk of AP at RP, relative to those in the AS-managed cohort from the validation study, is provided on the ArteraAI Prostate Test report based on the MMAI prognostic score (Figure 2). Patients with a relatively low risk of AP at RP may consider AS an appropriate management strategy, whereas those with a higher risk may weight the additional option of definitive therapy. Specifically, patients in the ArteraAI low-risk group will see a suggestion to "Consider AS," whereas those in the ArteraAI intermediate- or high-risk groups will see a suggestion to "Consider AS or Definitive Therapy."

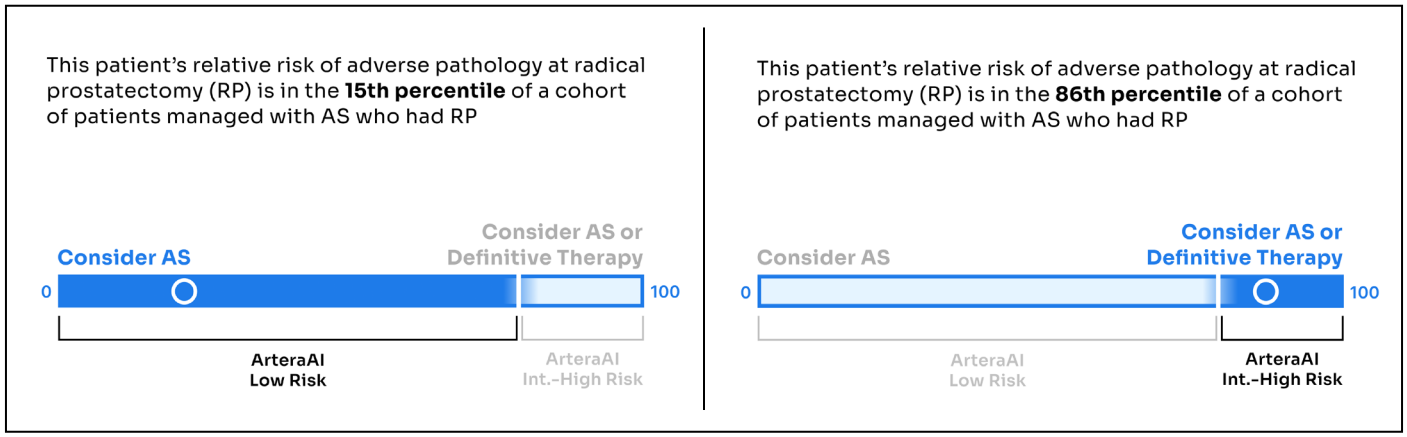


Figure 2. ArteraAI Prostate Test AS Insights. AS insights are only reported for those who have NCCN very low-, low-, or favorable intermediate-risk disease. MMAI, multimodal artificial intelligence; RP, radical prostatectomy; ST-ADT, short-term androgen deprivation therapy.

Case Studies

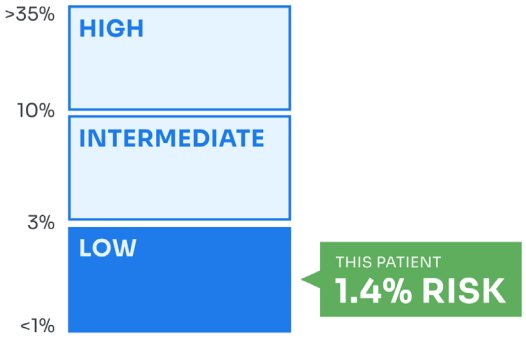
Provided by:
Dr. Zachary Horne (Radiation Oncology, Allegheny Health Network) and
Dr. Zachary Klaassen (Urologic Oncology, Medical College of Georgia)

Patient 1

Clinical Tumor Stage	cT1c
Prebiopsy PSA	1.6 ng/mL
Gleason Score	6 (3+3)
Patient Age at Order Date	65
NCCN Risk	Low

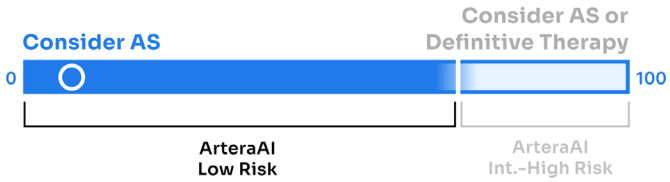
ArteraAI Prostate Test Results

10-YEAR RISK OF DISTANT METASTASIS



ACTIVE SURVEILLANCE (AS) INSIGHTS

This patient's relative risk of adverse pathology at radical prostatectomy (RP) is in the **8th percentile** of a cohort of patients managed with AS who had RP



Biopsy was performed following symptoms consistent with prostate cancer. Following diagnosis, the patient initially considered brachytherapy as a management option but wanted to avoid RT. To explore whether AS was a viable management option, the ArteraAI Prostate Test was ordered. The test results indicated that the patient's relative risk of AP at RP was in the 8th percentile, suggesting a relatively low risk compared to others in the AS-managed validation cohort. Based on these findings, **the patient chose to proceed with AS.**

Case Studies

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Dr. Zachary Horne (Radiation Oncology, Allegheny Health Network) and
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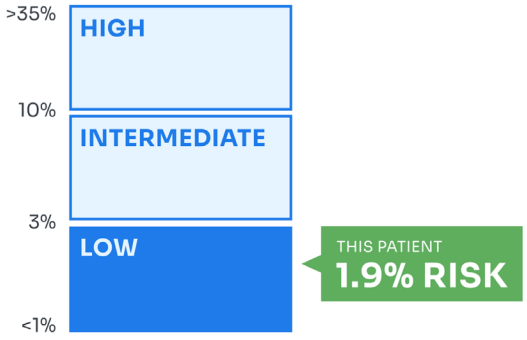
Patient 2

Clinical Tumor Stage	cT1c
Prebiopsy PSA	3.8 ng/mL
Gleason Score	7 (3+4)
Patient Age at Order Date	68
NCCN Risk	Favorable Intermediate

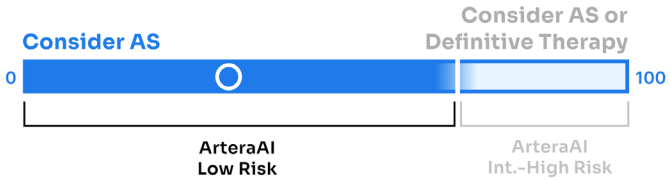
ArteraAI Prostate Test Results

10-YEAR RISK OF DISTANT METASTASIS



ACTIVE SURVEILLANCE (AS) INSINGHTS

This patient's relative risk of adverse pathology at radical prostatectomy (RP) is in the **35th percentile** of a cohort of patients managed with AS who had RP



After initially considering brachytherapy, the patient underwent magnetic resonance imaging, which revealed no PI-RADS 3+ lesions. With a lack of nearby brachytherapy providers and the recent departure of his urologist, the patient sought additional information on active surveillance as a management option. The ArteraAI Prostate Test was ordered, and the results indicated a relatively low risk of AP at RP, placing the patient in the 35th percentile of the AS-managed cohort. Based on these results, **the patient elected to proceed with AS.**

Case Studies

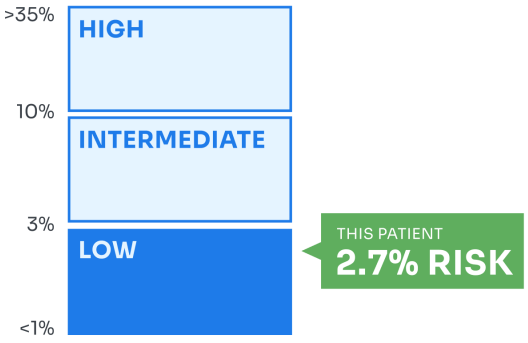
Provided by:
Dr. Zachary Horne (Radiation Oncology, Allegheny Health Network) and
Dr. Zachary Klaassen (Urologic Oncology, Medical College of Georgia)

Patient 3

Clinical Tumor Stage	cT1c
Prebiopsy PSA	9.1 ng/mL
Gleason Score	7 (3+4)
Patient Age at Order Date	68
NCCN Risk	Favorable Intermediate

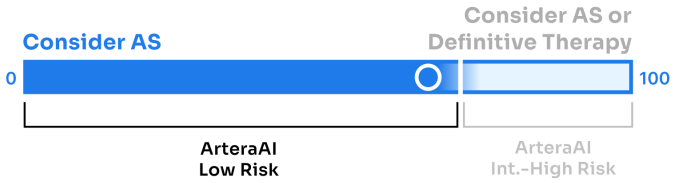
ArteraAI Prostate Test Results

10-YEAR RISK OF DISTANT METASTASIS



ACTIVE SURVEILLANCE (AS) INSINGHTS

This patient's relative risk of adverse pathology at radical prostatectomy (RP) is in the **72nd percentile** of a cohort of patients managed with AS who had RP



The patient was initially hesitant to undergo a prostate biopsy, but given his excellent health and family history of prostate cancer, he proceeded with the biopsy, which revealed Gleason Score 3+4, favorable intermediate-risk prostate cancer. Based on this diagnosis and his family history, the patient considered treatment, but sought additional insight. The ArteraAI Prostate Test placed him in the 72nd percentile for AP at RP with an estimated 2.7% risk of DM at 10 years. While still classified as ArteraAI low-risk, in a shared decision-making discussion with his significant other, the patient reviewed the risks and benefits of AS, RT, and RP. Ultimately, given the higher than anticipated relative risk of AP at RP and his preference to consider treatment, **he decided to proceed with RP.**

Case Studies

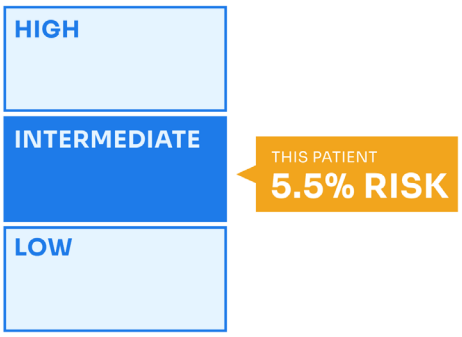
Provided by:
Dr. Zachary Horne (Radiation Oncology, Allegheny Health Network) and
Dr. Zachary Klaassen (Urologic Oncology, Medical College of Georgia)

Patient 4

Clinical Tumor Stage	cT1c
Prebiopsy PSA	9.6 ng/mL
Gleason Score	7 (3+4)
Patient Age at Order Date	60
NCCN Risk	Favorable Intermediate

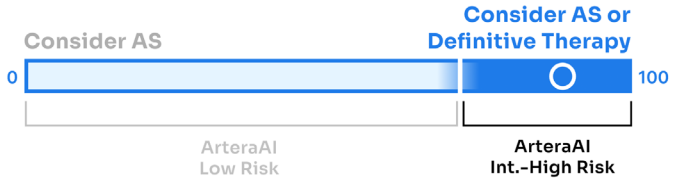
ArteraAI Prostate Test Results

10-YEAR RISK OF DISTANT METASTASIS



ACTIVE SURVEILLANCE (AS) INSIGHTS

This patient's relative risk of adverse pathology at radical prostatectomy (RP) is in the **94th percentile** of a cohort of patients managed with AS who had RP



The patient initially had a strong preference for AS, and the ArteraAI Prostate Test was ordered to further assess his risk. The test results placed him in the 94th percentile for AP at RP, suggesting a relatively high risk compared to others managed with AS. After a shared decision-making discussion with his family, including the risks and benefits of AS and definitive therapy, **the patient opted for RT.** This decision was based on his relatively high risk of AP at RP and, due to comorbidity, desire to avoid a surgery requiring general anesthesia. In addition, the ArteraAI predictive ST-ADT biomarker was negative, suggesting he would not benefit from the addition of short-term androgen deprivation therapy to radiation. The patient decided to proceed with radiation monotherapy, and declined the addition of ST-ADT.

Conclusions

The ArteraAI Prostate Test is a valuable tool for risk stratification of patients with localized prostate cancer across all NCCN risk groups. As demonstrated in this white paper, the MMAI algorithm has been validated in an AS-managed cohort for AP at RP, a critical endpoint for this population. These findings have informed the development of the AS Insights provided by the ArteraAI Prostate Test, offering a data-driven approach to identifying which patients are suitable candidates for AS and which may benefit from definitive therapy.

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