ARTERA

ArteraAI Prostate Test Report

PATIENT
Name: **John Doe**
Date of Birth: **08/08/1964**
Condition: **Prostate Cancer**

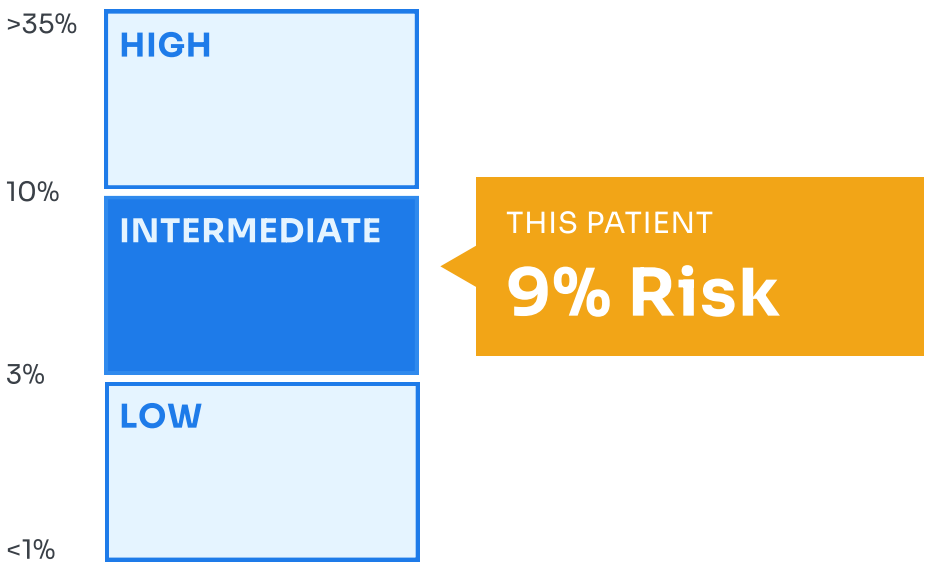
PHYSICIAN
Name: **Adam Smith, MD**
Clinic Name: **Artera Hospital**

ORDER
Order Date: **07/01/2023**
Artera ID: **AM-4Y-VRD-005K**

PROGNOSTIC RISK

INTERMEDIATE

10-YEAR RISK OF DISTANT METASTASIS
(With RT +/- systemic therapy)



95% CI: 7%–11%

5-YEAR RISK OF DISTANT METASTASIS
(With RT +/- systemic therapy)

3%
95% CI: 1%–7%

10-YEAR RISK OF PROSTATE CANCER SPECIFIC MORTALITY
(With RT +/- systemic therapy)

10%
95% CI: <3%–14%

ArteraAI Prognostic Raw Score=0.50

ST-ADT BIOMARKER

Positive

On average, patients with this result had **significant risk reduction** in distant metastasis with the addition of short-term androgen deprivation therapy.[1]

CLINICAL INTERPRETATION

- This patient has a 9% risk of developing metastasis within 10 years based on analysis of data from clinical studies of patients who have had curative intent therapy
- In a clinical study of patients who have been treated with RT +/- ST-ADT, NCCN intermediate-risk patients in the ST-ADT biomarker (+) group
  - Had an average 2.9-fold (95% CI: 1.4–8.8) decrease in risk of distant metastasis within 15 years when treated with radiation therapy plus short-term androgen deprivation therapy compared with radiation therapy alone (Figure 1A)[1]
  - Had an average metastasis risk reduction of 10% at 15 years[1]

The ArteraAI Prostate Test results are provided to support risk-based decisions within the recommended guidelines. Separate AI algorithms are used to estimate prognostic risk and predict benefit from short-term androgen deprivation therapy.

Reviewed by Laboratory Director
Joshua B. Kish, MD

07/07/2023 12:00PM
Review Date and Time (EST)

ARTERA

Name: **John Doe**
Date of Birth: **08/08/1964**

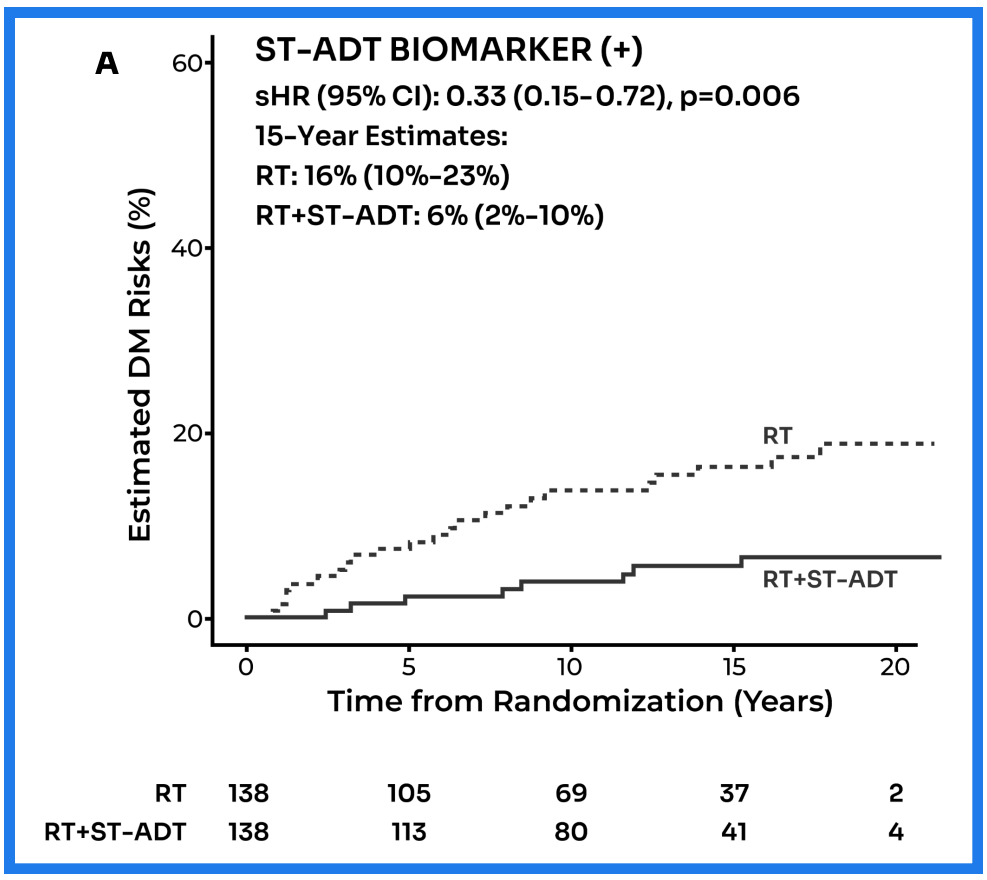
ArteraAI Prostate Test Report

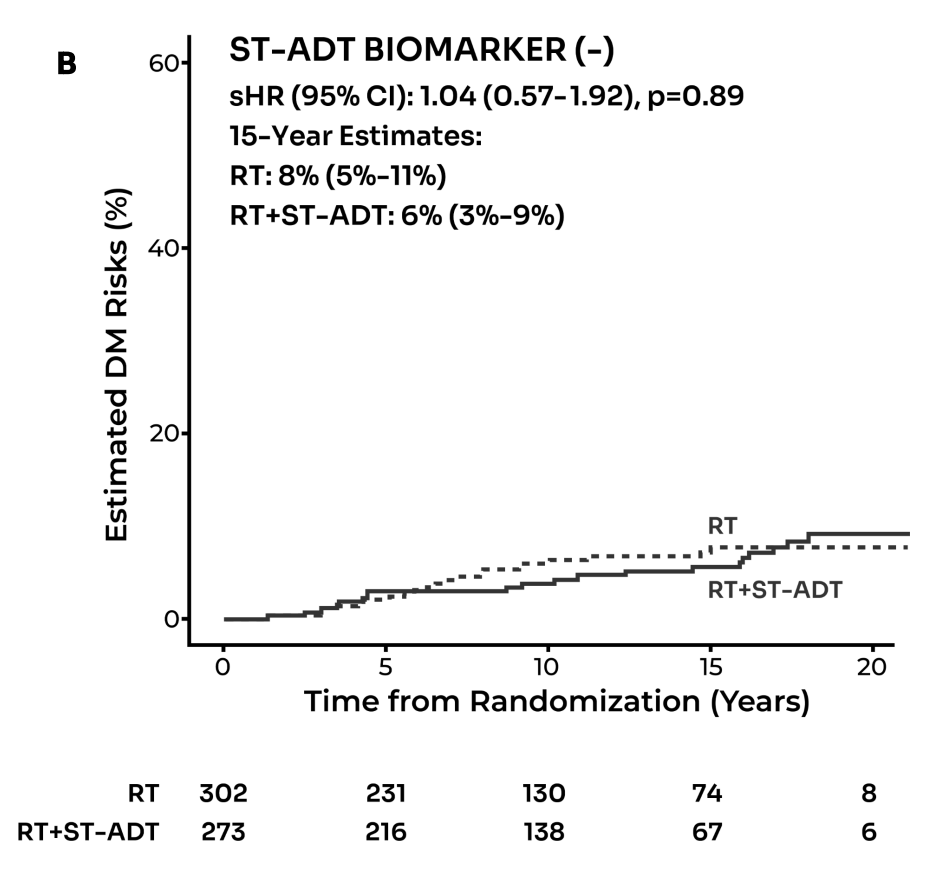
CLINICAL AND PATHOLOGY DETAILS (AS PROVIDED BY THE ORDERING PHYSICIAN)

Date of Biopsy: **05/23/2022**
Procedure: **Biopsy**
Clinical Tumor Stage: **T1c**
Baseline PSA: **5.5 ng/mL**
Gleason Score: **7 (4+3)**
Patient Age at Order Date: **60**
Specimen Site: **Prostate**
Specimen ID: **22-00130**
NCCN Risk: **Intermediate Unfavorable**

This patient has an estimated 10-year risk of metastasis that is **higher than 75%** of patients in the same NCCN intermediate risk group.

ST-ADT BIOMARKER SUPPLEMENTAL INFORMATION





Population-level data supporting the clinical interpretation on page 1.

Figure 1. Cumulative incidence of distant metastasis in the validation cohort subgroup of NCCN intermediate-risk patients who are (A) ST-ADT biomarker (+) or (B) ST-ADT biomarker (-).

In a clinical study of a subgroup of NCCN intermediate-risk patients who have been treated with curative intent therapy[1]

- 32% (276 patients) were classified as ST-ADT biomarker (+) and predicted to have more benefit with a significant reduction in risk of metastasis from adding ST-ADT to RT (Figure 1A)
- 68% (575 patients) were classified as ST-ADT biomarker (-) and predicted to have less benefit with no clear reduction in risk of metastasis (Figure 1B)

This report was electronically signed by Dr. Joshua B. Kish on 07/07/2023 at 12:00PM.

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TEST DESCRIPTION

The ArteraAI Prostate Test is a multimodal artificial intelligence (MMAI)-based test that leverages a unique algorithm that combines digital image and clinical data to estimate long-term clinical outcomes and predict benefit from short-term androgen-deprivation therapy (ST-ADT). Hematoxylin and eosin (H&E)-stained slides from a prostate biopsy are scanned at 20x magnification to create digital images. Once a pathologist reviews these digital histopathology images and confirms a prostate cancer diagnosis, the images and a limited set of clinical variables–clinical tumor stage, PSA blood test, and patient age–are assessed by the MMAI and test results are calculated through AI-based analysis.

To evaluate a patient's prognostic risk, a score (ranging from 0.0 to 1.0) and corresponding calibrated probability are provided for each of the following clinical endpoints: 5-year and 10-year risk of distant metastasis (DM) and 10-year risk of prostate cancer-specific mortality (PCSM) after first-line treatment. These clinical endpoints are calibrated to a cohort of 1236 localized prostate cancer patients who received radiation therapy (RT) without additional hormone therapy or chemotherapy, RT with hormone therapy, or RT with hormone therapy and chemotherapy from 1992-2009.[1,2] Additional rescaling of the baseline incidence was performed to adjust for shifts in screening and treatment over time with estimates from contemporary cohorts. Confidence ranges of the estimates are provided using 10,000-time bootstrap resampling. Based on the 10-year metastasis risk of ArteraAI scores, patients are categorized into one of three risk groups defined by physician-driven cut-offs.

To evaluate a patient's predicted benefit from adding ST-ADT to RT, a ST-ADT biomarker (+) or (-) result is reported to describe whether the patient is more or less likely to benefit from the addition of ST-ADT. The ST-ADT biomarker (+) or (-) results are calculated for all patients but only reported for those who have NCCN intermediate-risk disease, as ST-ADT is only clinically relevant for this patient population.

INTENDED USE

The ArteraAI Prostate Test is intended for use in patients diagnosed with localized prostate cancer who have not yet received RT or ADT prior to biopsy. The ArteraAI Prostate Test results are intended to inform risk-based treatment decisions as an adjunct to conventional clinical risk factors and other diagnostic tools for determining the metastatic potential of the tumor and patient prognosis.

The ArteraAI Prostate Test is not indicated for the following:

- Men in whom the diagnosis of prostate cancer is uncertain
- Men with diagnosed metastatic prostate cancer
- Men with poor health who have a life expectancy less than 10 years due to comorbid conditions
- Men who are not considering receiving treatment for their prostate cancer

MODEL INFORMATION

The AI algorithms used in the ArteraAI Prostate Test were developed using multimodal deep learning trained on digital histopathology data and clinical data from multiple randomized controlled trials (RCTs) to estimate long-term, clinically relevant outcomes and predict benefit from adding ST-ADT to RT. All patients in these trials received definitive external RT, with or without pre-specified use of ADT.

For the prognostic risk model, data from 8 clinical trials (NRG/RTOG 9202, 9408, 9413, 0415, 0521, 9902, 9910, and 0126) were split into training (n=5259) and validation (n=1767) cohorts.[1,2] Prior to deployment in the CLIA laboratory, improvements were made to the published model.[1] Model validation with the final model version (v1.2) yielded a multimodal AI (MMAI) time-dependent area under the curve (tdAUC) of 0.736 (95% CI: 0.686-0.786) vs an NCCN tdAUC of 0.629 (95% CI: 0.586-0.672) for DM at 10-year, an MMAI tdAUC of 0.800 (95% CI: 0.746-0.846) vs an NCCN tdAUC of 0.715 (95% CI: 0.667-0.754) for DM at 5-year, and an MMAI tdAUC of 0.736 (95% CI: 0.679-0.793) vs an NCCN tdAUC of 0.641 (95% CI: 0.594-0.692) for PCSM at 10-year.[1]

ArteraAI Prostate Test Report

For the predictive ST-ADT biomarker model, data from 7 clinical trials (NRT/RTOG 9202, 9413, 9902, 9910, 0126, 0415, and 0521) were used for development (v1.3) and the NRG/RTOG 9408 trial was used for validation.[1,3] Of the NCCN intermediate-risk patients in the validation cohort, 276 (32%) were classified as ST-ADT biomarker (+), where addition of ST-ADT significantly reduced the risk of distant metastasis compared with RT alone (sHR 0.33, 95% CI: 0.15-0.72, p=0.006).[1] In contrast, there was no significant difference between the two treatments for ST-ADT biomarker (-) patients (n=575; sHR 1.04, 95% CI: 0.57-1.93, p=0.89).[1] In this intermediate-risk subgroup, patients who were ST-ADT biomarker (+) had an average 2.9-fold (95% CI: 1.4-8.8) decrease in risk of distant metastasis within 15 years when treated with additional ST-ADT compared with RT alone; patients in the ST-ADT biomarker (-) group had no significant reduction in risk of distant metastasis within 15 years when ST-ADT was added (fold-change=1.4, 95% CI: 0.7-2.9).[1] These data are consistent with analysis of the full validation cohort.[1]

DISCLAIMER

The ArteraAI Prostate Test is a laboratory developed test. Testing is performed by ArteraAI, located at 6800 Southpoint Pkwy., Ste 950, Jacksonville, Florida 32216. The ArteraAI Prostate Test was developed and its performance characteristics were determined by ArteraAI. This Laboratory is certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA ‘88) as qualified to perform high-complexity clinical laboratory testing. This test is used for clinical purposes and should not be regarded as investigational or for research. This test has not been cleared or approved by the U.S. Food and Drug Administration.

References

1. Data on File. Artera, 2023.
2. Esteva A, Feng J, van der Wal D, et al. Prostate cancer therapy personalization via multi-modal deep learning on randomized phase III clinical trials. *NPJ Digit Med.* 2022;5(1):71. doi: 10.1038/s41746-022-00613-w.
3. Spratt DE, Tang S, Sun Y, et al. Artificial intelligence predictive model for hormone therapy use in prostate cancer. *NEJM Evid.* Published 2023 June 29. doi: 10.1056/EVIDoa230002.

