GRAND ROUNDS IN UROLOGY PRESENTS

IPCU

34th INTERNATIONAL PROSTATE CANCER UPDATE™

February 11–14, 2024

Poster Abstracts

CONTENTS

CONTENTS

Abstract 001

Real-World Clinical Outcomes by Risk Classification in Medicare Patients with Localized Prostate Cancer Treated with Radical Prostatectomy

Lawrence Karsh[1], Shawn Du[2], Jinghua He[2], Erik Muser[2], Neal Shore[3]

[1]The Urology Center of Colorado, Denver, CO, USA;
[2]Janssen Scientific Affairs, LLC, Horsham, PA, USA;
[3]Carolina Urologic Research Center, Myrtle Beach, SC, USA
*Presenting Author: Lawrence Karsh, larrykarsh@gmail.com

Introduction and Objectives: While radical prostatectomy (RP) is one of the main definitive treatment options for localized prostate cancer (LPC), limited real-world evidence exists on the long-term clinical outcomes of these patients (pts) in more recent years, particularly by risk classification. This study evaluated clinical outcomes in Medicare pts with high risk (HR)-LPC and low/intermediate risk LPC (LIR-LPC), respectively.

Methods: A retrospective cohort study was conducted using Surveillance, Epidemiology, and End Results (SEER)-Medicare linked data. Pts ≥65 years old who were newly diagnosed with LPC between 2012 and 2017 that received RP as initial definitive therapy (index date) were included. LPC risk classification was determined per NCCN criteria. Concurrent ADT use and duration were estimated using the Kaplan–Meier (KM) approach. Time to death, metastasis and initiation of an advanced prostate cancer [PC] treatment were compared between the HR-LPC and LIR-LPC groups using Cox proportional hazards (PH) models adjusting for baseline socio-demographic characteristics, Charlson Comorbidity Index (CCI), and ADT use.

Results: A total of 3,333 HR-LPC and 3,143 LIR-LPC pts were included in the study cohorts. Their baseline socio-demographics and Charlson Comorbidity Index scores appeared similar, and mean follow-up time was >45 months for both groups. Compared to the LIR-LPC cohort, concurrent ADT use with RP in the HR-LPC cohort was more frequent (11.3% vs. 1.5%), and lasted longer (KM median 10.7 months vs. 4.6 months). During the follow-up period, a higher proportion of the HR-LPC cohort experienced metastasis, death, and progression to advanced PC therapies than the LIR-LPC cohort. The Cox PH survival analyses showed higher risk of mortality, metastasis, and advanced PC therapy use for HR-LPC vs LIR-LPC pts after adjusting for all baseline characteristics (Table).

Conclusions: This real-world study in the Medicare setting suggested that HR-LPC is associated with substantially worse clinical outcomes relative to LIR-LPC after RP and highlights the need for additional strategies and treatments to improve clinical outcomes in pts with HR-LPC.

Source of Funding: This study was sponsored by Janssen Scientific Affairs, LLC.

Outcome	HR-LPC Pts with Event	LIR-LPC Pts with Event	Adjusted Hazard Ratio (95% CI) HR-LPC vs. LIR-LPC Pts	P-value
Metastasis or death	25.6%	7.4%	3.72 (3.21, 4.30)	<0.0001
Death	5.3%	2.8%	1.80 (1.38, 2.34)	<0.0001
Advanced PC treatment*	6.9%	0.9%	8.32 (5.57, 12.41)	<0.0001

* Earliest initiation of chemotherapy, PARP inhibitors, radiopharmaceuticals, related immunotherapies, or advanced androgen signaling inhibitors.

Abstract 002

The Forsvall Double Needle – A Future Needle Design Aiming to Improve Tissue Collection in Prostate Biopsy

Andreas Forsvall, MD, PhD, FEBU[1,2] , Jane Fisher, PhD[3,4], Magnus Wagenius, MD, PhD, FEBU [1,2], Adam Linder, MD, PhD[1]

[1]Faculty of Medicine, Department of Clinical Sciences, Infection Medicine, Lund University, Sweden; [2]Department of Urology, Helsingborg Hospital, Sweden; [3]Division of Anesthesiology and Intensive Care, Department of Clinical Sciences Lund, Lund University, Sweden; [4]Division of Dermatology and Venereology, Department of Clinical Sciences Lund, Lund University, Sweden

Introduction: Prostate biopsies that are obtained using Tru-cut needles fill 65% of the biopsy chamber on average. Thus, one-third of the tissue that is targeted for collection at a suspected tumor site is rendered unavailable to pathologists. This may cause understaging and the oversight of a cancer diagnosis.
We examined this suboptimal sampling of biopsies, in relation to needle design. This abstract introduces the Forsvall double needle (FDN), a prototype that constitutes a potential improvement in prostate biopsy. The construction of the FDN maintains the infection-preventive features and on-target technology of the Forsvall biopsy system.

Method: Development: We performed a technical analysis of the limited filling of Tru-cut biopsy needle chambers. Of the approximately 30 factors that were identified, 'air' was particularly influential. The chamber in current biopsy needles is filled with air that must be evacuated quickly during a biopsy. To test our hypothesis that substandard biopsy core lengths may result from air blockage we invented the FDN, which comprises 2 inner needles; this double-needle design allows the chamber to form while firing of the gun, eliminating air-induced blockage and creating low negative pressure, enhancing filling of the chamber.

Next, we performed a small ex vivo study: Four prostates were biopsied in the operating room immediately after prostatectomy, from which 10 samples each were obtained with the FDN and Tru-cut needle (Bard); both needles were 18G and stainless steel, and both chambers had the same maximum length (19 mm) and depth (0.5 mm). The biopsies were taken from base to apex—3 laterally, 1 centrally, and 1 that was angled from the peripheral to central zone bilaterally. The biopsies were transferred to graph paper and measured. The cores from 1 prostate were also weighed.

Results: The average core length when using the FDN was 19.9 mm (95% confidence interval [CI] 18.2–21.6) versus 16.4 mm (95% CI 14.5–18.2) with the Tru-cut system, representing a 14% improvement (p=0.0061, t-test). Some stretching occurred when the core was removed from the chamber, resulting in longer-than-expected cores in both groups. The average weight of the cores using the FDN was 0.00460 g (95% CI 0.00344–0.00576) versus 0.00304 g (95% CI 0.00226–0.00382) with the Tru-cut needle (p=0.021, t-test). The FDN visually amassed more liquid. The dry weight of the cores was not determined; thus, the recorded weights could have been affected by varying amounts of liquid in the cores.

Discussion: Trapped air may explain arbitrary filling of biopsy chambers. Our findings on the FDN support the benefit of improvements in needle design. Current Tru-cut needles can be modified to incorporate the simple design of the FDN. The double-needle construction allows for biopsies of any length to be obtained. This preliminary study supports the development and in vivo studies of the FDN. The increased collection of fluid by this needle, however, requires additional evaluation in vivo.

Disclosure: AF holds patent for the Forsvall biopsy needle and pending patent for the FDN.

Abstract 003

Testosterone Nadir and Clinical Outcomes In Patients Treated With Triptorelin Pamoate: A Retrospective Pooled Analysis Of Three Phase III Studies

Laurence Klotz[1], Tri Tat[2]

[1]Division of Urology, Sunnybrook Health Sciences Centre, University of Toronto, Toronto, Canada; [2]Debiopharm International, Lausanne, Switzerland

Background: A correlation between low serum testosterone levels and improved clinical outcomes has been observed in men with advanced prostate cancer. This retrospective study evaluated whether low nadir testosterone during treatment with triptorelin pamoate, an LHRH agonist, is associated with improved clinical outcomes.

Methods: Data were pooled from three prospective, 9–12-month, phase III studies of triptorelin in patients with advanced prostate cancer. The serum testosterone concentration suppression targets evaluated were <0.347 nmol/L (<10 ng/dL), <0.694 nmol/L (<20 ng/dL), and <1.735 nmol/L (<50 ng/dL). Overall survival (OS) and disease-specific survival (DSS) by testosterone suppression group were assessed by Kaplan-Meier analysis, with log rank test. The time frame for the primary analysis was days 1–518 and for the sensitivity analyses was days 1–262. Supplementary analyses combined the ≥0.694- to <1.735-nmol/L and ≥1.735-nmol/L groups.

Results: The sample size comprised 592 patients. Nadir testosterone of <0.347, ≥0.347 to <0.694, ≥0.694 to <1.735, and ≥1.735 nmol/L was achieved by 96.3%, 3.2%, 0.3%, and 0.2% of patients, respectively. Better OS with decreasing level of nadir testosterone was observed (P<0.0001, Figure 1) and this persisted after sensitivity/supplemental analyses (all P<0.0001). A trend for better DSS with decreasing level of nadir testosterone in the primary analysis did not reach significance. Sensitivity/supplemental analysis showed better DSS with decreasing level of nadir testosterone (days 1–262: P=0.0135; combined groups days 1–518: P=0.0339; combined groups days 1–262: P=0.0047).

Conclusion: Low nadir testosterone achieved during treatment with the LHRH agonist triptorelin was associated with improved OS and DSS in patients with advanced prostate cancer.

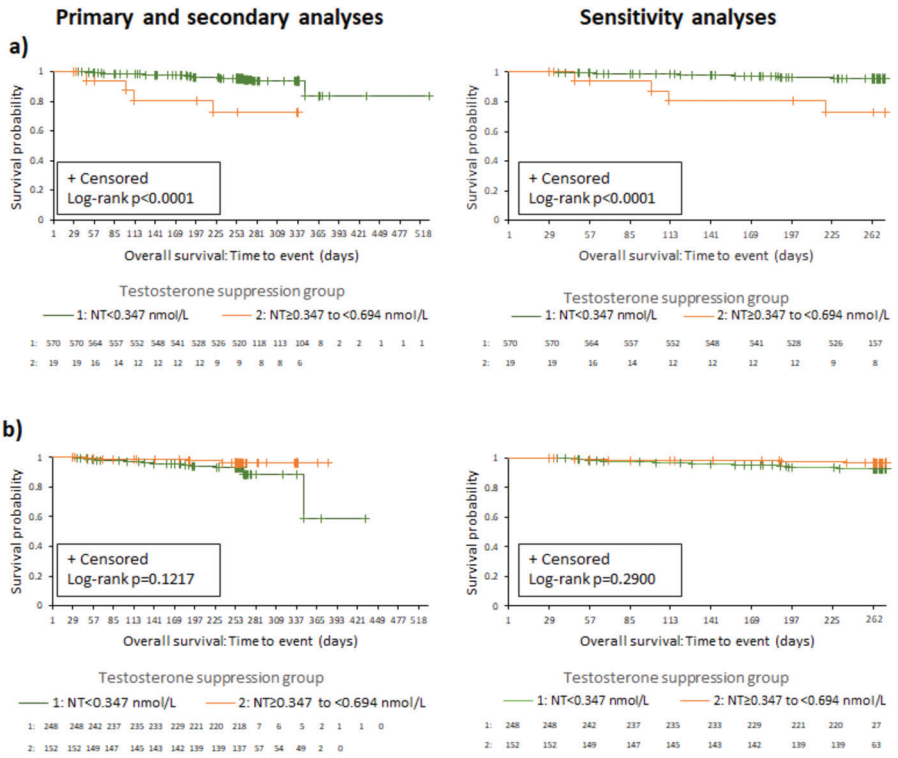


Figure 1

Abstract 004

Performance Of FDA-Approved PSMA-Targeted Radiopharmaceuticals for The Detection Of Recurrent Prostate Cancer: A Systematic Literature Review

Soroush Rais-Bahrami[1,2,3], Phillip Davis[4], Sandra Cuscó[5], Albert Chau[5], Brian F. Chapin[6], David M. Schuster[7], and Catriona M. Turnbull[5]

[1]Department of Urology, University of Alabama at Birmingham, Birmingham, AL, USA; [2]Department of Radiology, University of Alabama at Birmingham, Birmingham, AL, USA; [3]O'Neal Comprehensive Cancer Center, University of Alabama at Birmingham, Birmingham, AL, USA; [4]Blue Earth Diagnostics Inc., Monroe Township, NJ, USA; [5]Blue Earth Diagnostics Ltd, Oxford, UK; [6]Department of Urology, The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [7]Division of Nuclear Medicine and Molecular Imaging, Department of Radiology and Imaging Sciences, Emory University, Atlanta, GA, USA.

Background: Three prostate-specific membrane antigen (PSMA)-targeted radiopharmaceuticals (^{68}Ga-PSMA-11, ^{18}F-piflufolastat [^{18}F-DCFPyL], and ^{18}F-flotufolastat [^{18}F-rhPSMA-7.3]) are FDA-approved for PET scanning of PSMA-positive lesions in patients with prostate cancer. In this systematic literature review, we investigate the performance of these radiopharmaceuticals in patients experiencing biochemical recurrence.

Methods: MEDLINE, ScienceDirect, and Cochrane Libraries were searched using: "(positron emission tomography OR PET) AND (prostate specific membrane antigen OR PSMA OR rhPSMA) AND (prostate malignancy OR prostatic carcinoma OR prostate cancer OR prostatic neoplasm OR lymph node) AND (detection OR rate OR sensitivity OR specificity OR PPV)", as part of a wider review. Searches were conducted up to 3-October-2023 and limited to 10 years.
Two individuals systematically reviewed all results independently to identify studies reporting overall (patient-level) detection rates (DR) of 68Ga-PSMA-11, ^{18}F-DCFPyL, or ^{18}F-flotufolastat in ≥100 evaluable patients with prostate cancer recurrence following curative-intent treatment (primarily radical prostatectomy [RP] or radiotherapy). Populations including PSA persistence were excluded, as were secondary or duplicate publications from already-selected populations. Sample-weighted means (SWM) were calculated where appropriate.

Results: Of 4086 published studies, 37 met our inclusion criteria: 1 ambispective, 12 prospective, and 24 retrospective studies reporting relevant data for ^{68}Ga-PSMA-11 (n=28), ^{18}F-DCFPyL (n=7) and ^{18}F-flotufolastat (n=2).
In total, 11239 patients with evaluable data were analyzed. Some heterogeneity was noted in the enrolled populations; most studies recruited a mixed population of patients initially treated with RP and/or radiotherapy. Median PSA levels were reported in 29/37 (73%) studies. ^{68}Ga-PSMA-11 and ^{18}F-DCFPyL studies recruited patients with higher median PSA levels than ^{18}F-flotufolastat studies (reported median PSA ranged from 0.1-10.7, 0.5-2.5 and 0.6-1.1, respectively).
Across all studies, reported overall DR ranged from 25-91% for ^{68}Ga-PSMA-11, 58-86% for ^{18}F-DCFPyL, and 73-83% for ^{18}F-flotufolastat, with SWM of 69%, 75%, and 79%, respectively. Across studies reporting DR for post-RP patients, a SWM DR of 67% was seen for ^{68}Ga-PSMA-11 (n=11 studies), compared with 76% for ^{18}F-DCFPyL (n=1 study) and a SWM of 76% for ^{18}F-flotufolastat (n=2 studies). Across studies reporting DR for post-radiotherapy patients, 68Ga-PSMA-11 achieved a SWM DR of 88% (n=2 studies) compared with 92% for ^{18}F-DCFPyL (n=1 study) and 99% for ^{18}F-flotufolastat (n=1 study).
Reported DR at PSA ≤1 ng/mL ranged from 30-73% for ^{68}Ga-PSMA-11 (n=15 studies), 39-64% for ^{18}F-DCFPyL (n=5 studies), and 64-68% for ^{18}F-flotufolastat (n=2 studies), giving SWM of 57%, 51% and 66%, respectively.
Limitations of these data include the heterogeneity across included populations, and the paucity of ^{18}F-DCFPyL and ^{18}F-flotufolastat studies compared with ^{68}Ga-PSMA-11.

Conclusions: This systematic review of 37 studies highlights considerable heterogeneity in the reported populations of studies of diagnostic PET radiopharmaceuticals, with ^{68}Ga-PSMA-11 and ^{18}F-DCFPyL studies typically recruiting patients with higher median PSA levels than ^{18}F-flotufolastat studies.
When restricting to analyses across similar data sets, the data show that, irrespective of prior treatment, ^{68}Ga-PSMA-11 showed a lower DR than the ^{18}F-labelled PSMA radiopharmaceuticals. Equivalent DR were shown for ^{18}F-DCFPyL and ^{18}F-flotufolastat in post-RP patients, while ^{18}F-flotufolastat was reported to have the highest DR in the post-radiotherapy setting, and amongst patients with low PSA values.

Abstract 005

Physical Isolation of Tumor-Associated ctDNA Fragments For Novel Prostate Cancer Liquid Biopsy

D. Pamart, J-V. Turatsinze, B. Cuvelier, M. Herzog, J. Micallef

VolitionRx Ltd. 1489 West Warm Springs Road Ste 110, Henderson, NV 89014.

Introduction: CTCF transcription factor binding is altered in cancer including both gain and loss of CTCF binding site occupancy. We hypothesised that chromatin immunoprecipitation (ChIP) of circulating cell free CTCF-DNA (cfCTCF-DNA) nucleoproteins from plasma might isolate cancer associated gain of occupancy CTCF binding site sequences from all non-cancer derived plasma cfDNA of the same sequences which would be nucleosome covered and washed away.
We describe a novel method for ctDNA analysis in which tumor derived plasma cfCTCF-DNA is chemically isolated from all non-tumor nucleoproteins comprising cfDNA of the same sequences. This facilitates a simple, low cost rapid ChIP/PCR ctDNA analysis that obviates cfDNA library preparation, next-generation sequencing (NGS) and bioinformatics.

Methods: We first developed a ChIP-Seq method for isolating and sequencing plasma cfCTCF-DNA nucleoproteins. Anti-CTCF ChIP-Seq was performed on 4 patients diagnosed with Acute Myeloid Leukaemia (AML), 5 patients with inflammatory conditions and 5 healthy volunteers. We identified 29 cfCTCF-DNA cancer associated gain of occupancy binding site sequences that were present in the ChIP isolates of cancer patients, but not present in isolates from healthy subjects or subjects with inflammatory conditions.

We next developed qPCR assays for 10 of the 29 DNA sequences identified as cancer associated gain of occupancy CTCF binding sites. The 10 qPCR assays derived using an AML model were investigated as liquid biopsy assays for detection of AML and prostate cancer in a preliminary proof-of-concept study. ChIP isolates from plasma samples obtained from AML patients (n=31), prostate cancer patients (n=10) and from control subjects that were either healthy (n=35), or had an inflammatory condition (n=15) were tested by qPCR for the presence of the 10 CTCF-bound binding site sequences selectively occupied in cancer.

Results: The qPCR assays developed for CTCF binding site gain of occupancy biomarkers identified by discovery using AML samples were effective for detection of AML. A single qPCR assay detected 19 of 31 AML cases (61%) using a simple +/- cutoff with 1 false positive result among 50 control samples (98% specificity). Interestingly, the same single qPCR assay with the same cutoff was also effective for the detection of solid cancers including the detection of 5 of 10 prostate cancer cases tested (98% specificity). Another single qPCR assay detected of 7 of 10 prostate cancer cases tested (90% specificity).

Conclusions: cfCTCF-DNA binding site occupancy biomarkers represent a new class of untapped cancer biomarkers. ChIP/PCR of plasma nucleoproteins is rapid, low cost, suitable for automation and may provide a useful novel liquid biopsy method. Further discovery studies using prostate cancer samples rather than AML samples are required to identify prostate specific markers followed by clinical studies to ascertain clinical accuracy.

Abstract 006

MYB Exhibits Racially Disparate Expression and Clinicopathologic Association In Prostate Cancer: Significance As A Predictor Of Biochemical Recurrence

Mohammad Aslam Khan[1,2]*, Srijan Acharya[1,2], Shashi Anand[1,2], Fnu Sameeta[1], Paramahansa Pramanik [3], Christopher Keel[4], Seema Singh[1,2,5], James Elliot Carter[1], Santanu Dasgupta[1,2,5] and Ajay Pratap Singh[1, 2,5]*

[1]Department of Pathology, College of Medicine, University of South Alabama, Mobile, AL; [2]Cancer Biology Program, Mitchell Cancer Institute, University of South Alabama, Mobile, AL; [3]Department of Mathematics and Statistics, University of South Alabama, Mobile, AL; [4]Department of Urology, Whiddon P. Frederick College of Medicine, University of South Alabama, Mobile, AL; [5]Department of Biochemistry and Molecular Biology, Whiddon P. Frederick College of Medicine, University of South Alabama, Mobile, AL

MYB acts as a potentiator of aggressiveness and castration-resistance in prostate cancer (PCa) through aberrant activation of androgen-receptor (AR) signaling. Since Black men experience higher PCa incidence and mortality than White men, we examined if MYB was differentially expressed in prostate tumors from patients of these racial backgrounds. The data reveal that aberrant MYB expression starts early in precancerous high-grade prostate intraepithelial neoplastic lesions and increases progressively in malignant cells. PCa tissues from Black patients exhibit higher MYB expression than Whites in overall and grade-wise comparisons. MYB also exhibits a positive correlation with AR and both display higher expression in advanced tumor stages. Notably, we find that MYB is a better predictor of biochemical recurrence than AR, pre-treatment PSA, or Gleason's grades. These findings establish MYB as a promising molecular target in PCa that could be used for improved risk prediction and therapeutic planning.

Correspondence to:
Ajay Pratap Singh, PhD
Department of Pathology
Whiddon P. Frederick College of Medicine
USA Health Mitchell Cancer Institute
University of South Alabama
1660 Springhill Avenue, Mobile, AL 36604
Tel: 251-445-9843, Fax: 251-460-6994
Email: asingh@southalabama.edu

Mohammad Aslam Khan, PhD
Department of Pathology
Whiddon P. Frederick College of Medicine
USA Health Mitchell Cancer Institute
University of South Alabama
1660 Springhill Avenue, Mobile, AL 36604
Tel: 251-445-9874, Fax: 251-460-6994
Email: makhan@southalabama.edu

Abstract 007

Treatment Of Metastatic Castrate-Resistant Prostate Cancer Patient with Two Cycles Of ^{67}Cu SAR-bisPSMA (8 GBq) Leads To Undetectable PSA Level: A Case Report

Luke Nordquist, MD[1]

[1] XCancer – Omaha. drluke@xcancer.com

Prostate cancer (PC) is the second most frequent malignancy in men worldwide. Despite recent advances in treatment options, patients with metastatic disease still have poor outcomes, warranting the development of new effective therapies in this setting. Prostate-specific membrane antigen (PSMA) is a type II transmembrane glycoprotein that is expressed in normal and benign prostate tissues, and overexpressed in prostate tumor cells. PSMA-targeting agents have been used to both image and treat PC patients with PSMA-expressing tumors. The bivalent structure of SAR-bisPSMA in ^{64}Cu-SAR-bisPSMA (imaging) and ^{67}Cu-SAR-bisPSMA (therapy) may offer advantages (including higher uptake and retention in lesions) compared to currently used single-target PSMA agents. We report the administration of two cycles of ^{67}Cu-SAR-bisPSMA (8 GBq) in a 74-year-old male patient with metastatic castrate-resistant PC leading to an excellent response. The patient was diagnosed in 2017 (PC Localized, Gleason 9, PSA 20.5 ng/ml) and underwent definitive therapy with external beam radiation therapy in addition to neo-adjuvant docetaxel and 2 years of androgen deprivation therapy (ADT). ADT was resumed in 2020 due to PSA recurrence. The patient first had evidence of metastatic disease in 2022 and underwent several lines of systemic therapies including ADT, abiraterone, enzalutamide and a clinical trial with a novel PARP inhibitor. At the time of disease progression, he was enrolled in the phase I/IIa SECuRE clinical trial (May 2023, NCT04868604), in which he received one cycle of ^{67}Cu-SAR-bisPSMA (8 GBq, Jun 2023). After a considerable decrease in PSA levels observed over the period of 3 months (99.4% reduction), the patient received a second dose of ^{67}Cu-SAR-bisPSMA (8 GBq) under the Food and Drug Administration Expanded Access Program (Sep 2023). This second dose led to a further reduction of PSA to undetectable levels (lower level of detection 0.05 ng/ml, confirmed by two consecutive tests). The patient also had a near complete response assessed by RECIST v1.1. Two lesions showed complete response, and a third (lymph node) missed the complete response criteria by 2 mm. No PSMA uptake was observed in any of the lesions using ^{64}Cu-SAR-bisPSMA at the last follow-up. No adverse events related to ^{64}Cu-SAR-bisPSMA were reported. Adverse events related to ^{67}Cu-SAR-bisPSMA included the following dry mouth (grade 1), altered taste (grade 1) and fatigue (grade 2). Both the dry mouth and altered taste improved but continue intermittently. The fatigue resolved. The patient has reported excellent quality of life and he continues in follow-up. At the time of submission of this abstract, the SECuRE clinical trial is enrolling patients for its highest dose cohort of ^{67}Cu-SAR-bisPSMA (12 GBq, single cycle).

Source of funding: Clarity Pharmaceuticals Ltd – SECuRE clinical trial sponsor (NCT04868604), provision of ^{64}Cu-SAR-bisPSMA and ^{67}Cu-SAR-bisPSMA under Expanded Access Program (FDA), medical writing support.

Abstract 008

Evaluating the mtDNA Copy Number in Prostate Cancer Samples

Adeline M. Bray, Presley A. Mekeel, Jack Petroski, Benjamin Brisman, Raj Patel, Justin Rosales, Vasudeva Kamath

Touro College of Osteopathic Medicine. Middletown, NY, USA

Context/Background: Mitochondrial DNA (mtDNA) has been shown to be increased in several cancerous tissues. It is suggested that when DNA is damaged, mtDNA increases. Moore et. al 2017. used peripheral blood leukocytes to demonstrate that increased mtDNA copy number was associated with non-aggressive prostate cancer (PCa) as well as a higher Prostate Specific Antigen level (PSA), but was not associated with aggressive PCa. Our research utilized human prostate cancer tissue samples to examine this relationship between mtDNA copy number changes in comparison with normal prostate tissue.

Objective: The objective of this study is to confirm that cancerous prostate tissue has an increased mtDNA copy number when compared to non cancerous prostate tissue.

Methods:
A study was conducted on ten human paraffin-embedded prostate samples from biopsy curls obtained from Precision for Medicine Massachusetts, USA, not requiring IRB approval. All research was conducted in the Touro College of Osteopathic Middletown Campus laboratory. Thermo Scientific GeneJET FFPE DNA Purification kit was used to isolate DNA. Next, the nuclear and mtDNA was amplified via PCR using the Absolute Human Mitochondrial DNA Copy Number Quantification qPCR Assay Kit (AHMQ). From this data, the mtDNA copy number was calculated. MtDNA from the cancerous and normal prorate samples were then compared.

Results: The results showed that mtDNA copy number was significantly increased in cancerous prostate tissue when compared to the normal tissue. The mtDNA copy number from the cancerous samples was 61% higher compared to the normal tissue.

Conclusion: This study confirms that mtDNA copy number increases in prostate cancer samples. It is possible that mtDNA copy number could serve as a possible marker for prostate cancer screening and targets for therapeutic measurements. In the future, this study also hopes to contribute to the understanding of TFAM and Twinkle genes as they pertain to change in mtDNA copy number in prostate cancer. Further research also includes examining the mtDNA copy number as it pertains to the varying grades of PCa.

Abstract 009

Impact Of a Rash Management Guide On Incidence And Severity Of Rash With Apalutamide: Experience from The Apa-RP Study In High-Risk Localized Prostate Cancer

Neal Shore,[1] Jason Hafron,[2] Daniel Saltzstein,[3] Amitabha Bhaumik,[4] Pankaj Aggarwal,[5] Rushikesh Potdar,[5] Jennifer Phillips,[5] Tracy McGowan[5]

[1]Carolina Urologic Research Center, Myrtle Beach, SC, USA
[2]Michigan Institute of Urology, West Bloomfield, MI, USA
[3]Urology San Antonio, San Antonio, TX, USA
[4]Janssen Research and Development, Titusville, NJ, USA
[5]Janssen Medical Affairs, Horsham, PA, USA

Background: Apa-RP is a multicenter, open-label, single-arm Phase 2 study of adjuvant treatment with apalutamide and androgen deprivation therapy (ADT) in treatment-naïve patients with high-risk localized prostate cancer who underwent radical prostatectomy (NCT04523207). A rash management guide was implemented to improve dermatologic adverse events (AEs) that included proactive patient education on appropriate skin care and monitoring for rash, and frequent outreach through patient phone calls. We present rash-related safety data from Apa-RP compared with data from two Phase 3 apalutamide registrational studies.

Methods: 108 patients were treated with apalutamide 240 mg once daily with ADT for 12 28-day cycles. Rash occurrence was monitored and skin-related AEs were defined by Common Terminology Criteria for Adverse Events (CTCAE) v5.0 grading scale. These factors were collated and compared with data from the North American population from SPARTAN (non-metastatic castration-resistant prostate cancer; NCT01946204) and TITAN (metastatic castration-sensitive prostate cancer; NCT02489318).

Results: Of 108 patients in Apa-RP, 21.3% developed rash vs 28.3% in SPARTAN and 33.3% in TITAN. Information on rash severity, median time to onset of first rash, the proportion of patients with rash resolution, median time to resolution and the treatment administered for rash are provided in Table 1.

Conclusions: The Apa-RP rash management protocol demonstrates a proactive and patient-empowered approach to monitoring and managing patients on apalutamide who develop skin rash. With increased vigilance from the care team and appropriate patient education, it may be possible to reduce the incidence, severity, and median time to resolution of skin rash.

Table 1. Rash-related data from apalutamide-treated groups in Apa-RP, SPARTAN, and TITAN (safety populations)

	Apa-RP (N=108)	SPARTAN (N=283)	TITAN (N=63)
Treatment-emergent rash*			
Any Grade, N (%)	23 (21.3)	80 (28.3)	21 (33.3)
Grade 1, n (%)†	14 (60.9)	32 (40.0)	6 (28.6)
Grade 2, n (%)†	6 (26.1)	30 (37.5)	8 (38.1)
Grade 3, n (%)†	3 (13.0)	18 (22.5)	7 (33.3)
Median time to onset of first skin rash, days‡	79.0	97.5	84.0
Resolved, n (%)†,¶	22 (95.7)	75 (93.8)	12 (57.1)
Median time to resolution, days	45.5	60.0	142.0
Treatment received for rash, n (%)†	11 (47.8)	–	–
Topical corticosteroid, n (%)†	10 (43.5)	21 (26.3)	11 (52.4)
Oral antihistamine, n (%)†	5 (21.7)	22 (27.5)	2 (9.5)
Systemic corticosteroid, n (%)†	3 (13.0)	17 (21.3)	3 (14.3)

*Rash is a grouped term including MedDRA Preferred Terms related to general term 'rash'.
†Proportion of patients with any Grade rash (n/N).
‡Regardless of Grade. Starting time for median calculation is the date of first dose of study drug.
¶Defined as all skin rashes being reported as resolved (regardless of initial or worst Grade). Starting time for median calculation is the date of first skin rash.

Abstract 010

Effect Of Rapid Ultra-Low Prostate-Specific Antigen Decline (UL PSA) In TITAN Patients (pts) With Metastatic Castration-Sensitive Prostate Cancer (mCSPC) who Received Apalutamide (APA) Plus Androgen Deprivation Therapy (ADT)

Axel S. Merseburger,[1] Neeraj Agarwal,[2] Anders Bjartell,[3] Hirotsugu Uemura,[4] Alvaro Juarez Soto,[5] Amitabha Bhaumik,[6] Jürgen Böhm,[7] Nguyen Tran,[7] Nils Krochmann,[7] Mehregan Nematian-Samani,[7] Suneel D. Mundle,[8] Sabine D. Brookman-May,[9,10] Sharon A. McCarthy,[8] Kim Chi,[11] Simon Chowdhury[12]

[1]University Hospital Schleswig-Holstein, Campus Lübeck, Department of Urology, Lübeck, Germany
[2]Huntsman Cancer Institute, University of Utah, Department of Genitourinary Oncology, Salt Lake City, UT, USA
[3]Skåne University Hospital, Lund University, Department of Urological Cancer, Malmö, Sweden
[4]Kindai University Faculty of Medicine, Department of Medicine, Osaka, Japan
[5]Hospital Universitario de Jerez de la Frontera, Department of Urology, Cadiz, Spain
[6]Janssen Research & Development, Titusville, NJ, USA
[7]Janssen-Cilag GmbH, Neuss, Germany
[8]Janssen Research & Development, Raritan, NJ, USA
[9]Janssen Research & Development, Spring House, PA, USA
[10]Ludwig-Maximilians-University, München, Germany
[11]BC Cancer and Vancouver Prostate Centre, Department of Medicine, Vancouver, BC, Canada
[12]Guy's, King's, and St Thomas' Hospitals and Sarah Cannon Research Institute, Department of Urological Cancer, London, UK

Background: In TITAN mCSPC pts, 3 mos' APA + ADT produced rapid and deep ≤0.2 ng/mL PSA decline that was associated with improved overall survival (OS) (Chowdhury et al, Ann Oncol. 2023). Here we evaluate the effect of UL PSA on outcomes.

Methods: 525 and 527 pts receiving 240 mg/d APA or placebo (PBO) + ADT were analyzed. Two groups of UL PSA, >0.02 to ≤0.2 ng/mL (UL1) and ≤0.02 ng/mL (UL2), were assessed for association with OS, radiographic progression-free survival, time to castration resistance, and time to PSA progression using landmark analysis, Kaplan-Meier method, and Cox proportional hazards model.

Results:
Of 515 APA and 520 PBO pts with evaluable UL PSA values, 49% and 17%, respectively, achieved UL2 PSA during the study. By 3 mos, UL1 and UL2 were achieved in 38% and 23% of APA and 15% and 5% of PBO pts. By 6 mos, these values were 29% and 36% (APA), and 17% and 6% (PBO). APA pts with UL1/UL2 at 3 mos had lower baseline PSA and higher % of low-volume disease vs PSA>0.2 ng/mL. Pts with UL1/UL2 at 3 or 6 mos had improved long-term outcomes irrespective of volume. Volume-adjusted outcomes were significantly improved in pts with UL1/UL2 achieved at 3 mos (Table) or at 6 mos. At 42 mos' follow-up post landmark, survival rate (% [95% CI]) was 89 (81-94), 81 (75-85), and 34 (26-43) when UL2 was achieved at 3 mos, after 3 mos, or never after 3 mos and was 89 (83-93), 77 (70-83), and 34 (26-43) when UL2 was achieved at 6 mos, after 6 mos, or never after 6 mos. Survival rate at 42 mos with UL1, UL2, or none achieved at any time was 59 (48-68), 92 (88-95), and 33 (26-41). APA safety profile across subgroups was consistent with previous reports.

Conclusions: More TITAN mCSPC pts achieved UL PSA with APA vs PBO. Rapid and deep UL PSA was associated with significantly improved survival outcomes regardless of disease volume, most notably UL2. Data may guide design of future treatment escalation/de-escalation trials in mCSPC.

Clinical trial identification (trial protocol number, NIH or European equivalent, and release date):
56021927PCR3002, 16 March 2020

Source of Funding: Janssen Research & Development

Table. Clinical outcomes in patients according to ultra-low PSA values at 3 months

HR (95% CI)	PSA values achieved at landmark 3 mos vs PSA >0.2 ng/mL (ref) in APA group[a]	
	UL1 (>0.02 to ≤0.2 ng/mL)	UL2 (≤0.02 ng/mL)
OS[b]	0.46 (0.31–0.67)	0.24 (0.13–0.43)
Radiographic progression-free survival[c]	0.54 (0.35–0.83)	0.28 (0.14–0.54)
Time to castration resistance[b]	0.56 (0.39–0.80)	0.20 (0.11–0.38)
Time to PSA progression[b]	0.51 (0.34–0.76)	0.11 (0.04–0.27)

[a]Stratified by disease volume at baseline. [b]44.0 mos follow-up. [c]22.7 mos follow-up.

Abstract 011

The Effect of Prior Docetaxel (DOC) Treatment On Efficacy And Safety Of Apalutamide (APA) Plus Androgen Deprivation Therapy (ADT) In Patients (pts) With Metastatic Castration-Sensitive Prostate Cancer (mCSPC) From TITAN

Kim N. Chi[1], Axel S. Merseburger[2], Mustafa Ozguroglu[3], Simon Chowdhury[4], Anders Bjartell[5], Byung Chung[6], Andrea Juliana Pereira de Santana Gomes[7], Robert Given[8], Álvaro Juárez[9], Hirotsugu Uemura[10], Dingwei Ye[11], Lawrence Ivan Karsh[12], Benjamin Adam Gartrell[13], Sabine D. Brookman-May[14], Suneel Mundle[15], Sharon Anne McCarthy[16], Florence Lefresne[15], Oliver Brendan Rooney[17], Amitabha Bhaumik[18], Neeraj Agarwal[19]

[1]BC Cancer and Vancouver Prostate Centre, Vancouver, BC, Canada; [2]Universitätsklinikum Schleswig-Holstein, Campus Lüebeck, Lüebeck, Germany; [3]Istanbul University-Cerrahpaşa, Cerrahpaşa School of Medicine, Istanbul, Turkey; [4]Guy's, King's, and St. Thomas' Hospitals, and Sarah Cannon Research Institute, London, United Kingdom; 5Skåne University Hospital, Lund University, Malmö, Sweden; [6]Yonsei University College of Medicine and Gangnam Severance Hospital, Seoul, South Korea; [7]Liga Norte Riograndense Contra O Câncer, Natal, Brazil; [8]Urology of Virginia, Eastern Virginia Medical School, Norfolk, VA; [9]Hospital Universitario de Jerez de la Frontera, Cadiz, Spain; [10]Kindai University Hospital Faculty of Medicine, Osaka, Japan; [11]Fudan University Shanghai Cancer Center, Shanghai, China; [12]The Urology Center of Colorado, Denver, CO; [13]Montefiore Medical Center, Bronx, NY; [14]Ludwig-Maximilians-University (LMU), Munich, Germany; [15]Janssen Research & Development, Los Angeles, CA, USA; [16]Janssen Research & Development, Raritan, NJ, USA; [17]Janssen Research & Development, High Wycombe, UK; [18]Janssen Research & Development, Titusville, NJ, USA; [19]Huntsman Cancer Institute, University of Utah, Salt Lake City, UT, USA

Background: Addition of androgen receptor signaling inhibitors to ADT + DOC has been shown to improve clinical outcomes in pts with mCSPC. TITAN, a placebo-controlled phase 3 study, showed that APA + ADT improved overall survival (OS) and other clinical outcomes in mCSPC (Chi, J Clin Oncol 2021). This post hoc analysis of TITAN evaluated outcomes in pts who had received DOC prior to treatment with APA + ADT versus those who did not.

Methods: In TITAN, 1052 pts were randomized 1:1 to APA (240 mg QD) or placebo added to ongoing ADT. We assessed radiographic progression-free survival (rPFS), OS, and time to prostate-specific antigen (PSA) progression in pts receiving DOC and ADT prior to adding APA vs those receiving only ADT plus APA. Outcomes by prior DOC were also assessed in pts with high- or low-volume disease at randomization (baseline [BL]) per adapted CHAARTED criteria, or those with matched BL characteristics. A Cox proportional hazards model was used to derive hazard ratios (HRs) and p values. rPFS was assessed using the first interim analysis cutoff (23 mo median follow-up); OS and time to PSA progression were assessed using the final analysis cutoff (44 mo median follow-up).

Results: A total of 58/525 (11%) pts from the APA + ADT group had received DOC prior to randomization: 76% (n = 44) had high-volume disease, 62% (n = 36) had bone-only metastases, 16% (n = 9) had visceral metastases, and 59% (n = 34) had > 10 bone lesions. In the overall APA-treated population and in the subset of pts with high-volume disease, OS, rPFS, and time to PSA progression were similar in those who received prior DOC and those who did not (Table). Pts with low-volume disease also had similar results, although the number of pts was small. Clinical outcomes in pts with matched BL characteristics (including PSA and time from initial diagnosis to randomization, among others) were similar regardless of prior use of DOC (Table). The safety profile of APA was not substantially different between pts with or without prior DOC. Limitations of this analysis include lack of data on tumor volume and other disease characteristics at the initiation of prior DOC treatment; interpretation was based on small number of pts with prior DOC (only 11% of TITAN pts), most notably in the rPFS analysis.

Conclusions: Prior use of DOC in pts with mCSPC did not further improve clinical benefits of APA + ADT in TITAN.

Clinical Trial ID: NCT02489318
Source of Funding: Janssen Research & Development

Table. Clinical outcomes in patients who received prior docetaxel (DOC) and those who did not

	No prior DOC (Ref)/ prior DOC, n/N	Outcome	HR	95% CI	P-value
Overall population (n=525)	467/58	OS Time to PSA progression rPFS	1.20 1.31 0.78	0.76–1.90 0.80–2.15 0.41–1.49	0.425 0.289 0.454
High-volume subgroup (n=325)	281/44	OS Time to PSA progression rPFS	1.04 1.11 0.67	0.63–1.71 0.65–1.88 0.34–1.33	0.883 0.707 0.257
Pts with matched disease characteristics (n=232)	174/58	OS Time to PSA progression rPFS	1.13 1.14 0.77	0.69–1.86 0.66–1.95 0.39–1.54	0.634 0.641 0.465

Abstract 012

Niraparib (NIRA) With Abiraterone Acetate Plus Prednisone (AAP) As First-Line (1L) Therapy In Patients (Pts) with Metastatic Castration-Resistant Prostate Cancer (mCRPC) and Homologous Recombination Repair (HRR) Gene Alterations: Three-Year Update And Final Analysis (FA) Of MAGNITUDE

K. N. Chi[1]*, E. Castro[2], G. Attard[3], M. R. Smith[4], S. Sandhu[5], E. Efstathiou[6], G. Roubaud[7], E. J. Small[8], A. J. Gomes[9], D. Rathkopf[10], M. Saad[11], H. Gurney[12], W. Jung[13], G. Mason[14], S. Dibaj[14], D. Wu[14], B. Diorio[14], A. Lopez-Gitlitz[14], W. Kim[14], D. Olmos[15]

[1]BC Cancer and Vancouver Prostate Centre, University of British Columbia, Vancouver, BC, Canada, [2]Institute of Biomedical Research, Hospital Universitario 12 de Octubre, Madrid, Spain, [3]University College London, UCL Cancer Institute, London, United Kingdom, [4]Massachusetts General Hospital Cancer Center, Harvard Medical School, Boston, MA, United States of America, [5]Department of Medical Oncology, Peter MacCallum Cancer Centre, Melbourne, VIC, Australia, [6]GU Medical Oncology Department, Houston Methodist Cancer Center, Houston, TX, United States of America, [7]Department of Medical Oncology, Institute Bergonie, Bordeaux, France, [8]Helen Diller Family Comprehensive Cancer Center, University of California San Francisco Medical Center, San Francisco, CA, United States of America, [9]Department of Medical Oncology, Liga Norte Riograndense Contra o Cancer, Natal, Brazil, [10]Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, NY, United States of America, [11]Universiti Malaya, University of Malaya Medical Centre, Kuala Lumpur, Malaysia, [12]Department of Oncology, Macquarie University, Sydney, NSW, Australia, [13]Keimyung University School of Medicine, Keimyung University Dongsan Hospital, Daegu, Korea, Republic of, [14]Janssen, Research & Development, Raritan, NJ,

Background: In the phase 3 MAGNITUDE study (NCT03748641), NIRA + AAP significantly improved radiographic progression-free survival in *BRCA*-mutant (*BRCA*+) pts. Here we present the FA of MAGNITUDE, a phase 3 study with the largest population of 1L *BRCA*+ mCRPC pts, reporting mature overall survival (OS) data and prespecified multivariate analysis (MVA) for OS, addressing baseline imbalances.

Methods: Eligible pts (N = 423) with HRR+ mCRPC were randomized 1:1 to NIRA + AAP (n = 212) or placebo (PBO) + AAP (n = 211) as 1L therapy. At this FA, secondary endpoints of OS and time to cytotoxic chemotherapy (TCC) were formally assessed. Updates to time to symptomatic progression (TSP) and patient-reported outcomes (PROs) in *BRCA*+ pts and to safety for all HRR+ pts are also reported.

Results: At FA, 225 *BRCA*+ pts were evaluated; 113 pts received NIRA + AAP. Median follow-up was 35.9 months. In the NIRA + AAP and PBO + AAP arms, 70% and 86% of pts received subsequent post-progression life-prolonging therapy. OS favored NIRA + AAP over PBO + AAP (Table). A prespecified MVA adjusting for baseline imbalances showed an OS benefit for NIRA + AAP. Continued improvement in TSP and a clinically meaningful improvement in TCC were observed with NIRA + AAP. Time to worst pain progression and time to pain interference progression also favored NIRA + AAP. No new safety signals were observed with additional treatment exposure. Pulmonary embolism occurred in 4.7% and 1.4% of pts in NIRA + AAP and PBO + AAP arms, with no cases of myelodysplastic syndrome or acute myeloid leukemia in the NIRA + AAP arm.

Conclusions: OS favored NIRA + AAP for pts with *BRCA*+ mCRPC. NIRA + AAP led to improvements in TSP, TCC, and PROs. The positive benefit-risk profile supports 1L NIRA + AAP as a new standard of care for pts with *BRCA*+ mCRPC.

Clinical trial registration number: NCT03748641

Source of Funding: Janssen

Table 1. Endpoints at FA in pts with BRCA+ mCRPC, NIRA + AAP vs PBO + AAP

	HR	95% CI	Nominal P
OS	0.79	0.55–1.12	0.18
OS with MVA	0.66	0.46–0.95	0.02
TSP	0.56	0.37–0.85	0.01
TCC	0.60	0.39–0.92	0.02
Time to worst pain progression	0.81	0.52–1.25	
Time to pain interference progression	0.77	0.48–1.23	

Abstract 013

Presence Of Somatic/Germline Homologous Recombination Repair (HRR) Mutations And Outcomes In Metastatic Castration-Resistant Prostate Cancer (mCRPC) Patients (Pts) Receiving First-Line (1L) Treatment Stratified By BRCA Status

David Olmos, MD, PhD,[1] David Lorente, MD, PhD,[2] Daniel Alameda, PhD,[3] Carlo Cattrini, MD,[4] Nuria Romero-Laorden, MD, PhD,[5] Rebeca Lozano, MD,[6] Pedro P. Lopez-Casas, PhD,[1] Camille Capone,[7] Anne Marie Vanden Broecke, MPharm[8] Marco Trevisan,[9] Suzy Van Sanden,[10] Alexandra Jürgens,[11] Bernardo Herrera-Imbroda, MD, PhD,[3] Elena Castro, MD, PhD[1,3]

[1]Hospital Universitario 12 de Octubre. Instituto de Investigación Sanitaria Hospital 12 de Octubre, Madrid, Spain; [2]Hospital Provincial de Castellón, Castellón, Spain; [3]Hospital Virgen de la Victoria. Instituto de Investigación Biomédica de Málaga, Málaga, Spain; [4]"Maggiore della Carità" University Hospital, Novara, Italy; [5]Hospital Universitario de la Princesa, Madrid, Spain; [6]Hospital Universitario de Salamanca, Salamanca, Spain; [7]Janssen Inc., Issy Les Moulineaux, France 8Janssen-Cilag B.V., Beerse, Belgium; [9]Janssen Pharmaceuticals, Zug, Switzerland; [10]Janssen Pharmaceutica NV, Beerse, Belgium; [11]Janssen, Neuss, Germany

Background: Understanding of the association between HRR mutations and outcomes in mCRPC pts is limited. This analysis investigated the prevalence and outcomes of pts with/out HRR mutations (somatic and/or germline), stratified as BRCA, non-BRCA, or HRR non-BRCA, who initiated 1L mCRPC treatment with novel hormonal therapy (NHT) or taxane.

Methods: Eligible pts from PROREPAIR-B (NCT03075735), PROSENZA (NCT02922218), PROSTAC (NCT02362620), and PROSABI (NCT02787837) studies underwent paired somatic/germline DNA analyses using a custom NGS panel that included *ATM, BRCA1, BRCA2, BRIP1, CDK12, CHEK2, FANCA, HDAC2, PALB2, RAD51B, and RAD54L*. Those with pathogenic (likely) mutations in ≥1 allele of ≥1 gene were considered deficient (HRR).
rPFS, PFS2, and OS were reported for BRCA, non-BRCA, and HRR non-BRCA subgroups; associations between mutations and outcomes were assessed using inverse probability weighted Cox models, which balanced the baseline (BL) characteristics between subgroups. Hazard ratios (HRs) with 95% confidence intervals (CIs) and p values are presented.

Results: Of 729 pts, 223 (30.6%) were HRR, including 96 (13.2%) BRCA. 60.4% of pts were treated with NHT and 39.6% with taxane in 1L; 80.7% received at least second-line treatment. Median age at BL was 72.2 years, 63.5% had Gleason >7, 53.1% had ECOG ≥1, and 13.3% presented with visceral metastases. BL characteristics after adjustment were similar (standard mean difference: <0.1 in HRR and maximum 0.11 for all pts).
BRCA pts had significantly worse rPFS, PFS2, and OS than non-BRCA pts; BRCA pts also had significantly worse PFS2 and OS than HRR non-BRCA pts (Table 1). There were no significant differences between the outcomes of somatic and germline BRCA pts.

Conclusions: BRCA pts, regardless of somatic/germline origin, had significantly worse rPFS, PFS2, and OS than the total non-BRCA population and significantly worse PFS2 and OS than non-BRCA pts in the HRR subgroup. It is crucial to screen early for HRR mutations, particularly in BRCA1/2, to begin timely, targeted mCRPC treatment and improve prognosis.

Source of Funding: Janssen Research & Development

Table 1: Median rPFS, PFS2, and OS (months) comparison of BRCA, non-BRCA, and HRR non-BRCA subgroups

		BRCA (n=96) vs. Non-BRCA (n=633)	BRCA (n=96) vs. HRR non-BRCA (n=127)
rPFS	Median (95% CI)¥	BRCA: 7.0 (6.1–8.4) Non-BRCA: 10.6 (9.7–11.5)	BRCA: 7.0 (6.1–8.4) HRR non-BRCA: 8.9 (7.0–9.9)
	HR (95% CI)	**1.7 (1.3–2.2)***	**1.3 (1.0–1.9)**
PFS2	Median (95% CI)¥	BRCA: 12.7 (11.4–14.7) Non-BRCA: 17.9 (16.8–18.7)	BRCA: 12.7 (11.4–14.7) HRR non-BRCA: 14.6 (12.4–16.7)
	HR (95% CI)	**1.9 (1.6–2.4)#**	**1.5 (1.1–1.9)***
OS	Median (95% CI)¥	BRCA: 18.1 (16.5–19.9) Non-BRCA: 27.7 (25.7–29.5)	BRCA: 18.1 (16.5–19.9) HRR non-BRCA: 21.6 (18.0–24.1)
	HR (95% CI)	**2.0 (1.6–2.5)#**	**1.4 (1.1–1.9)***

*p<0.05; #p<0.0001; ¥observed

Abstract 014

Phase 3 Trial of [^{177}Lu]Lu-PSMA-617 in Taxane-Naive Patients with Metastatic Castration-Resistant Prostate Cancer (PSMAfore)

Oliver Sartor[1], Daniel Castellano Gauna[2], Ken Herrmann[3], Johann de Bono[4], Neal Shore[5], Kim Nguyen Chi[6], Michael Crosby[7], Josep Maria Piulats Rodríguez[8], Aude Flechon[9], Xiao Xiao Wei[10], Hakim Mahammedi[11], Guilham Roubaud[12], Hana Studentova[13], Samson Ghebremariam[14], Euloge Kpamegan[14], Teri Kreisl[14], Neda Delgoshaie[15], Katja Lehnhoff[15], Michael J. Morris[16], Karim Fizazi[17]

[1]Hematology/Oncology Department, Mayo Clinic - Rochester, Rochester, MN, United States of America; [2]Department of Medical Oncology, Hospital Universitario 12 de Octubre, Madrid, Spain; [3]Department of Nuclear Medicine, University of Duisburg-Essen and German Cancer Consortium (DKTK), partner site University Hospital Essen, Essen, Germany; [4]Prostate Cancer Targeted Therapies Group, The Institute of Cancer Research and Royal Marsden Hospital, Sutton, United Kingdom; [5]Uro-Oncology Department, Carolina Urologic Research Center, Myrtle Beach, SC, United States of America; [6]Department of Medicine, BC Cancer and Vancouver Prostate Centre, Vancouver, British Columbia, Canada; [7]Veterans Prostate Cancer Awareness Inc, Veterans Prostate Cancer Awareness Inc, Washington DC, United States of America; [8]Medical Oncology Department, ICO -Institut Català d'Oncologia l'Hospitalet (Hospital Duran i Reynals), Hospitalet De Llobregat, Spain; [9]Medical Oncology Department, Centre Leon Berard, Lyon, France; [10]Medical Oncology, Dana-Farber Cancer Institute, Boston, United States of America; [11]Medical Oncology Department, Centre Jean PERRIN, Clermont-Ferrand, Cedex, France; [12]Medical Oncology, Institute Bergonié, Bordeaux, France; [13]Oncology Department, FN Olomouc/University Hospital Olomouc, Olomouc, Czech Republic; [14]Global Drug Development Analytics, Novartis Pharmaceuticals Corporation, East Hanover, NJ, United States of America; [15]Global Drug Development, Novartis International AG - Basel, Basel, Switzerland; [16]Genitourinary Oncology Service, Memorial Sloan Kettering Cancer Center, New York, NY, United States of America; [17]Department of Cancer Medicine, Gustave Roussy, University of Paris-Saclay, Villejuif, France.

Background: [^{177}Lu]Lu-PSMA-617 (^{177}Lu-PSMA-617) prolonged radiographic progression-free survival (rPFS) and overall survival (OS) in patients with metastatic castration-resistant prostate cancer (mCRPC) who received prior androgen receptor pathway inhibition (ARPI) and taxane therapy. PSMAfore (NCT04689828) examined ^{177}Lu-PSMA-617 in taxane-naive patients (except [neo]adjuvant >12 months prior).

Methods: Eligible adults had mCRPC, were candidates for ARPI change after one progression on prior ARPI, and had ≥1 PSMA-positive and no exclusionary PSMA-negative lesions by [^{68}Ga]Ga-PSMA-11 positron emission tomography / computed tomography. Candidates for poly-ADP ribose polymerase inhibition and patients with prior systemic radiotherapy (<6 months prior), immunotherapy (except sipuleucel-T), or chemotherapy (except [neo] adjuvant >12 months prior) were ineligible. Randomization was 1:1 to open-label ^{177}Lu-PSMA-617 (7.4 GBq every 6 weeks; 6 cycles) or change of ARPI (abiraterone/enzalutamide). Patients randomized to ARPI could cross over treatment with ^{177}Lu-PSMA-617 following centrally confirmed radiographic progression (rPD). Endpoints included: rPFS (Prostate Cancer Working Group 3 [PCWG3]-modified Response Evaluation Criteria in Solid Tumors [RECIST] v1.1; primary), OS (key secondary) (both overall α=0.025, one-sided), Functional Assessment of Cancer Therapy–Prostate (FACT–P; secondary) and objective response rate (ORR) / duration of response (DOR) (both exploratory). Primary analysis was to occur at ~156 rPFS events and second OS interim analysis (IA) at ~125 deaths. Crossover-adjusted analysis was the prespecified method for OS by rank-preserving structural failure time (RPSFT).

Results: 468 patients were randomized. At primary analysis (median follow-up, 7.3 months; N=467), the primary endpoint of rPFS was met (hazard ratio [HR]: 0.41; 95% confidence interval [CI]: 0.29–0.56; p<0.0001); this was similar at second IA (HR: 0.43; 95% CI: 0.33–0.54; p<0.0001). At second IA (45.1% of target deaths; median follow-up, 15.9 months; N=468), patients in the ^{177}Lu-PSMA-617 arm received a median (range) of 6.0 (1–6) cycles. A total of 123/146 (84.2%) patients in the change of ARPI arm with rPD who discontinued ARPI crossed over; there was a positive OS trend in favor of ^{177}Lu-PSMA-617 per RPFST but not per unadjusted OS analysis. For ^{177}Lu-PSMA-617 vs ARPI change, median time to worsening in FACT–P total score (7.46 vs 4.27 months, respectively; HR: 0.59; 95% CI, 0.47–0.72), ORR (50.7% [N=71] vs 14.9% [N=74], respectively), and DOR (13.6 [N=36] vs 10.1 [N=11] months, respectively) favored the ^{177}Lu-PSMA-617 arm. For ^{177}Lu-PSMA-617 vs ARPI change, incidence of grade ≥3 adverse events (AEs) was 34% (most common: anemia, dry mouth) vs 44%, serious AEs 20% vs 28%, and AEs leading to discontinuation 5.7% vs 5.2%.

Conclusions: ^{177}Lu-PSMA-617 prolonged rPFS vs ARPI change in taxane-naive patients with PSMA-positive mCRPC, with a favorable safety profile.

Abstract 015

Use of the Prostatype® Test, a genomic classifier (GC), to Predict Adverse Pathology (AP) at Radical Prostatectomy (RP)

Gerald Andriole[1], Emelie Berglund[1], Steven Gaal[1]; Vladimir Bykov[2]

[1]Prostatype Genomics, Castle Rock, CO and Solna, Sweden;
[2]Karolinska Institutet, Solna, Sweden

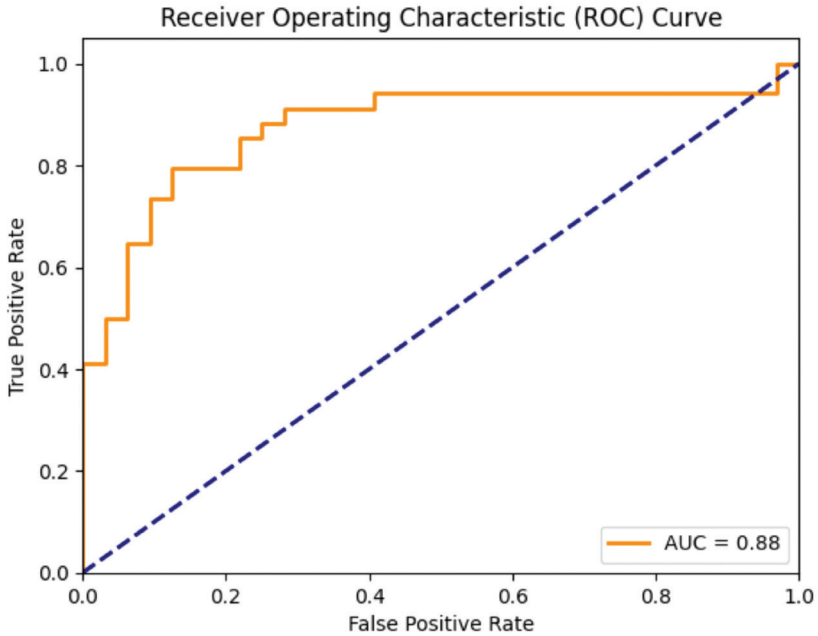
Background: Men with prostate cancer (PCa) may undergo Active Surveillance (AS) or curative treatment. Among the factors patients and clinicians use to determine which approach to take is the likelihood of AP at RP.

The Prostatype® test has been developed from prostate biopsy specimens of men with localized PCa. It has been validated in 2 large studies and accurately predicts 10-year PCa Specific Mortality and 10-year PCa Metastasis. The Prostatype® test is generated from the signature of 3 embryonic stem cell genes (IGFBP3, F3, and VGLL3) measured from the biopsy along with PSA, Gleason Score, and Tstage. Its intended use is to guide treatment decisions in men currently on or considering AS. The Prostatype® test is CE marked and is available for clinical use in Europe.

Methods: This study validated the ability of the Prostatype® test performed on prostate biopsy tissue to predict AP (Gleason score 4+3 or higher and/or non-organ confined disease (pT3)) at RP. 214 patients (median age 65 (59,68); median PSA 7.6 (5.3, 11.1); 20% Gleason 6; 64% Gleason 7; 16% Gleason >8) underwent RP , of which 117 (55%) had AP. The model to predict AP at RP is an Artificial Neural Network (ANN) algorithm.

Results: This ANN showed excellent performance, e.g., great balance between precision and sensitivity and had a high overall accuracy (AUC of 0.88) at predicting AP at RP (Figure 1). This 5-layer ANN model includes IGFBP3, F3, % positive biopsies and biopsy primary Gleason score (Figure 2). Confusion matrix provides a more detailed measurement of the performance of the model, minimizing misclassification of patients with AP. The confusion matrix and Matthews Correlation coefficient, (0.639) provides evidence that the ANN model manages false positives and false negatives correctly.

Conclusion: This study shows that the Prostatype® test is a strong predictor of AP at RP and may be used to guide decision making of clinicians and patients who are currently on or considering AS.



Abstract 016

Initial Experience with Low Field MR-guided Prostate Cryoablation: Treatment Planning and Clinical Workflow

John T. Price[1], Haydar Celik[2], Camille Turner[1], Ram Narayanan[2], Srirama S. Venkataraman[2], James Bennett[1]

[1]Midtown Urology, Atlanta, GA; [2]Promaxo, Inc., Oakland, CA

Background: Prostate cancer is one of the most common cancers in men, and its treatment can be challenging. Cryotherapy is a minimally invasive treatment option that has been used to treat prostate cancer for many years. However, traditional cryotherapy methods require an endorectal probe, which can be uncomfortable for patients. Additionally, the use of multiple needles can lead to complications such as bleeding and infection.

Methods: We present a novel prostate cryoablation treatment procedure that addresses these issues using the FDA cleared low-field Promaxo MR guidance system operating between 55mT and 74 mT. This report is the first to present a treatment guidance study using the low field MRI system, which does not require an endorectal probe.

Results: Our approaches are very localized and targeted, treating the index lesions that increase risks for the patients while preserving healthy tissue and other structures of importance for maintaining quality of life after treatment. We were able to target the cancerous tissue while sparing healthy tissue with a minimum number of needles targeting the cancers, resulting in fewer needles used compared with traditional methods that reduces the risk of complications (See Table). Six-weeks post PSA results show the significant reduction for 2 patients (Patient 1: from 7.0 ng/ml to 2.0 ng/ml, and patient 2: from 13.6 ng/ml to 5.6 ng/ml). Remaining 3 patients treated with local cryoablation and their PSA tests are yet to be done.

A major advantage of the low-field MRI is that a longitudinal follow-up of the patients can be performed as there was no endorectal coil used in target planning.

Conclusions: This novel prostate cryoablation treatment planning with the low field MRI is a promising option for patients with prostate cancer. Due to its ability to support longitudinal follow-up, the lesions to be treated can be targeted more precisely. This helps reduce the overall treatment time, reduces the number of needles required, and spares healthy tissues and structures. The longitudinal capability of the low-field system plays a crucial role in effective monitoring of patient outcomes. We believe that our method has the potential to improve the quality of life for patients with prostate cancer and should be considered as a viable alternative to radical treatments.

Table 1. Patient demographics and the treatment parameters: age, biopsy results, genetic test results, treatment type, pre-post treatment PSA, and number of needles used.

Patient Number	Age	Biopsy Results	Genetic Test Reults	Treatment Type	Pre-Post Treatment PSA	Number of Needles
1	66	4+3	BRCA and GPS -42	Right hemi-cryo	7.0 - 2.0	4
2	79	4+3	BRCA	Right hemi-cryo	13.6 - 5.6	4
3	66	3+4	MyRisk - negative and GPS 19	Cryoablation	6.13 - N/A	2
4	69	3+4	BRCA and GPS 20	Cryoablation	7.3 - N/A	1
5	76	3+4	GPS 28	Cryoablation	10.31 - N/A	2

Abstract 017

Accurate Prostate Biopsies Using Low-Field Portable Interventional MRI In an Ambulatory Surgical Center

John H. Price[1], Jae Eun Song[2], Dinesh Kumar[2], Srirama S. Venkataraman[2], Jame K. Bennett[1]

[1]Midtown Urology, Atlanta, GA, USA
[2]Promaxo Inc., Oakland, California, USA

Introduction and Background: The Promaxo system is a portable, open, and low field Magnetic Resonance Imaging (MRI) system for transperineally (TP) guided prostate biopsy (Promaxo Inc., Oakland, California, United States). It operates at 65 mTesla so does not require additional shielding or other facility upgrades usually needed for high field MRI. To accurately guide and target lesions of the prostate tissue, low-field MRI is co-registered with the T2-weighted (T2W) high-field (3 Tesla) images of the patients.

Methods and Materials: Thirty (30) male patients of age between 48 and 78 years old (67.47.6). The patients' blood prostate-specific antigen (PSA) score were from 1.4 to 16.3 (5.54.0). Prior to the TP procedure under low-field MRI guidance, the lesions (PI-RADS> 3) were annotated by radiologists on T2W high-field (3 Tesla) MRI. The low-field MRI protocol includes a 1 min of scout and 7 min of 3D-T2W images obtained with a surface coil were used for both high and low-field images. The T2W low-field image, that includes MR visible markers, is used to accurately register with the corresponding T2W images from 3T MRI. Targets for biopsy are assigned with the brachy grade biopsy template that is attached to the patient's perineum. Biopsy was done with patients under general anesthesia.

Results: The cancer detection rate from this limited study at an ambulatory surgical setting is 77% with a Gleason group (GG) of 1 and 2, implying 23 patients were positive among 30 patients. Especially, the PSA of four patients were below 3 but with improved targeting with Promaxo low-field MRI cancers with Gleason score 3+3 was detected enabling the patient to be under active surveillance protocol.

Conclusions: The Promaxo MRI is able to provide biopsy targets accurately, benefitting the patients by mitigating the false negative.

Abstract 018

IL-15 Treatment Enhances The In Vivo Anti-Tumor Efficacy of Sipuleucel-T By Activating CD8+ T And NKT Effector Cells, Augmenting Tumor Infiltration, and Reversing Immunoresistance Pathways

Russell Pachynski, Muhammad Saeed, Bo Peng, Kevin Kim, Ariel Borkowski, Brian Van Tine, Nadeem Sheikh, Vu Tuyen, Daniel LJ Thorek, Todd Fehniger

Division of Oncology, Department of Medicine, Washington University School of Medicine

Background: Metastatic castration-resistant prostate cancer (mCRPC) represents the most lethal form of prostate cancer. Sipuleucel-T (sip-T) is an autologous therapeutic produced using a tumor antigen-cytokine fusion protein, and the only FDA approved cellular immunotherapy for mCRPC patients. Sip-T significantly improves overall survival (OS), but has limited impact on PSA and radiographic responses. Here, we present the first high dimensional analysis of sip-T in detail using a mass cytometric approach, and highlight immune subsets and inhibitory/stimulatory receptors expression. Furthermore, we show the effects of IL-15 on the anti-tumor efficacy of sip-T using in vitro and in vivo and studies.

Methods: We performed a comprehensive assessment of the sip-T product (n=13 samples) collected from prostate cancer patients using mass cytometry (CyTOF). Control and IL-15 stimulated sip-T were evaluated, and changes in leukocyte subsets as well as markers of activation and exhaustion were identified. Finally, we examined the effects of IL-15 on cytotoxicity of sip-T against human prostate cancer lines using in vitro cytotoxicity assays and in vivo studies in NSG mice.

Results: CyTOF analysis revealed that CD3+ T cells constituted the highest proportion of sip-T, followed by B-cells, natural killer (NK) cells, NKT, and monocytes, with only a small percentage of dendritic cells. Following sip-T stimulation with IL-15, a significant expansion and activation of CD8+ T-cell and NK cell populations was seen. Co-culture of sip-T with IL-15 and control or prostate-relevant antigens showed significant activation and expansion of CD8 T and NKT cells in an antigen-specific manner. Furthermore, IL-15 stimulated sip-T showed significantly higher in vitro tumor cytotoxicity compared to control or other cytokines tested. Adoptive transfer of IL-15 treated sip-T into NSG mice resulted in potent prostate tumor growth inhibition compared to control. Evaluation of tumor-infiltrating lymphocytes revealed a 2 to 14-fold higher influx of sip-T and a significant increase in interferon (IFN)-γ producing CD8+ T and NKT cells within the tumor microenvironment in the IL-15 group. Tumor transcriptomic analyses revealed IL-15 treatment was able to reverse immunoresistance induced by sip-T alone. Evaluation of IL15 superagonist reveals similar finding and supports the development of a clinical trial of IL15 directed agents in combination with sip-T.

Conclusion: This is the first comprehensive study to evaluate sip-T from prostate cancer patients using high dimensional CyTOF analysis, and reveals potential targets for improvement of sip-T efficacy. Furthermore, this is the first pre-clinical in vivo prostate tumor model of sip-T adoptive transfer, showing that IL-15 treatment can significantly enhance anti-tumor efficacy, effector immune cell activation and tumor infiltration, and reverse mediators of immune suppression. .

Abstract 019

Scoping Review of RCTs on Exercise, Nutrition, and Psychologic Support for Prostate Cancer

Briggs, Logan G, M.D.[1,2,3], Psutka, Sarah P, M.D.[4] , Debarshi, Neil, B.S.[2], Gill, Vikram, B.S[2]., Van Ligten, Matthew J, B.S.[2], Beck, Kelsey L, B.S.[2], Quillen, Jaxon K,[5] , Dodoo, Christopher A, M.S.[5], Abdul-Muhsin, Haider, M.D., Ch.B.[1,2] , Humphreys, Mitchell R, M.D.[1,2], Morgans, Alicia K, M.D., M.P.H.[6], Branstiter, Keith A., M.S., P.T. [8] , De Luigi, Arthur J, D.O., M.H.A.[8] , Trinh, Quoc-Dien, M.D., M.B.A.[3,7] , Parke, Sara C, M.D.[8]

[1]Department of Urology, Mayo Clinic Az, Phoenix, AZ; [2]Mayo Clinic Alix School of Medicine, Scottsdale, AZ; [3]Center for Surgery and Public Health, Brigham and Women's Hospital, Harvard Medical School, Boston, MA;[4]Department of Urology, University of Washington Medical Center, Seattle, WA;[5]Department of Statistics, Mayo Clinic, Phoenix, AZ ; [6]Department of Medical Oncology, Dana-Farber Cancer Institute, Boston, MA; [7]Division of Urology, Brigham and Women's Hospital, Harvard Medical School, Boston, MA; [8]Department of Physical Medicine and Rehab, Mayo Clinic, Phoenix, AZ

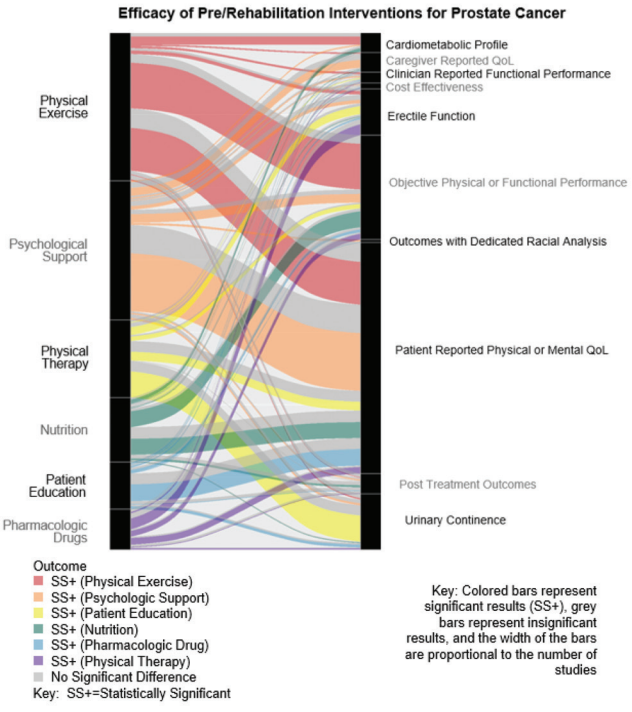
Objectives: As one of the most prevalent cancers causing significant morbidity and mortality, prostate cancer (PCa) has been the focus of extensive rehabilitative efforts, however comprehensive evaluation has not been performed. Thus, we aim to summarize efforts to date and identify promising areas for future work.

Methods: A scoping review including randomized controlled trials (RCTs) from Jan 2004 to Sept 2021 was performed per PRISMA Extension for Scoping Reviews Guidelines across six databases. This included patients with PCa or their caregivers enrolled in outpatient exercise, nutrition, psychologic support, or pre/rehabilitative programs characterizing outcomes within nine prespecified categories: 1) post-treatment outcomes, 2) erectile function, 3) urinary continence, 4) patient-reported physical or mental quality of life (QoL), 5) caregiver-reported QoL, 6) physical or functional performance, 7) cost effectiveness, 8) cardiometabolic profile and 9) differential efficacy by race. For each study, we tabulated whether ≥1 outcome within each category was reported, and if so, whether it reported ≥1 statistically significant positive association.

Results: The search retrieved 10,968 unique records, 407 of which met inclusion criteria and described 372 unique RCTs. A total of ≥52,173 unique subjects were included, ≥40,065 of which were PCa patients/survivors. Of 372 interventions, 270 (73%) demonstrated at least one significant association. Included is an alluvial diagram which summarizes all 372 RCTs.

Conclusions: Nearly three quarters of RCTs involving pre/rehabilitation for PCa demonstrated statistical efficacy, though clinical relevance deserves further scrutiny. The most promising interventions for inclusion in a multimodal, personalized pre- and rehabilitation program include web-based or automated patient counseling and education, preoperative exercise, postoperative penile therapy (oral/injection/vacuum therapy), pelvic floor muscle training, biofeedback, electrostimulation, electroacupuncture, physical therapy, and psychologic support like CBT and mindfulness training. Limited research on differential efficacy by race (4 RCTs), cost-effectiveness (7 RCTs), and caregivers (20 RCTs) signal need for further exploration.

Conflicts of Interest: LGB reports consulting fees from Delfina outside of the submitted work and research funding from the Office of Scholarly Engagement at Harvard Medical School. AKM reports personal fees from Astellas, AstraZeneca, Advanced Accelerator Applications, Bayer, Clovis, Dendreon, Exelixis, Myovant, Novartis, Pfizer, Sanofi, Blue Earth, Lantheus, and Myriad. QDT reports personal fees from Astellas, Bayer and Janssen, outside the submitted work. QDT reports research funding from the American Cancer Society and Pfizer Global Medical Grants. All other authors report no conflict of interest. SPP – advisory board for Immunity Bio and Jannseen, funding from Bladder Cancer Advocacy Network at the National Institute on Aging.



Abstract 020

Efficacy and Safety of Darolutamide in Combination with Androgen-Deprivation Therapy And Docetaxel in Black Patients From the Randomized ARASENS Trial

Jay Jhaveri[1], Neal D. Shore[2], Maha Hussain[3], Fred Saad[4], Karim Fizazi[5], Cora N. Sternberg[6], David Crawford[7], Bertrand Tombal[8], Luke Nordquist[9], Michael Cookson[10], Frank Verholen[11], Shankar Srinivasan[1], Matthew R. Smith[12]

[1]Bayer Healthcare Pharmaceuticals, Inc., Whippany, NJ, USA; [2]Carolina Urologic Research Center/Genesis Care, Myrtle Beach, SC, USA; [3]Robert H. Lurie Comprehensive Cancer Center, Northwestern University, Feinberg School of Medicine, Chicago, IL, USA; [4]Centre Hospitalier de l'Université de Montréal, University of Montreal, Montreal, Quebec, Canada; [5]Institut Gustave Roussy, University of Paris-Saclay, Villejuif, France; [6]Englander Institute for Precision Medicine, Weill Cornell Department of Medicine, Meyer Cancer Center, New York-Presbyterian Hospital, New York, NY, USA; [7]University of California San Diego School of Medicine, San Diego, CA, USA; [8]Division of Urology, IREC, Cliniques Universitaires Saint Luc, UCLouvain, Brussels, Belgium; [9]GU Research Network, Omaha, NE, USA; [10]University of Oklahoma Stephenson Cancer Center, Oklahoma City, OK, USA; [11]Bayer Consumer Care, Basel, Switzerland; [12]Massachusetts General Hospital Cancer Center, Boston, MA, USA.

Background: Black people have higher incidence and mortality rates with prostate cancer compared with other racial/ethnic groups. In the ARASENS trial (NCT02799602), darolutamide in addition with androgen-deprivation therapy (ADT) and docetaxel significantly reduced the risk of death by 32.5% (Hazard ratio [HR], 0.68; 95% confidence interval [CI], 0.57–0.80; P < .0001) versus ADT and docetaxel alone in patients with metastatic hormone-sensitive prostate cancer (mHSPC). However, limited data are available for Black participants from these clinical trials. In this post hoc analysis of ARASENS, we present efficacy and safety data for darolutamide versus placebo in Black patients.

Methods: ARASENS was a randomized, double-blind, placebo-controlled, phase III trial. Patients were recruited between 2016 and 2018 in 23 countries. Patients with mHSPC were randomized 1:1 to darolutamide 600 mg or placebo twice daily in combination with ADT and docetaxel. The primary endpoint was overall survival (OS). Key secondary endpoints included time to castration-resistant prostate cancer (CRPC) and safety. Kaplan-Meier estimates were used to analyze outcomes, and HRs obtained via Cox regression models were used to evaluate differences between treatment arms.

Results: Of 1305 patients in the overall ARASENS trial population, 54 were Black, of whom 26 received darolutamide and 28 received placebo. Baseline characteristics in this subgroup were generally similar compared with the overall population, except that greater proportions of Black patients were younger than 65 years of age (57.4% versus 36.6%), had an ECOG performance status of 1 (37.0% versus 28.7%), and had recurrent disease (24.1% versus 12.9%). In Black patients in ARASENS, OS favored darolutamide in combination with ADT and docetaxel versus placebo plus ADT and docetaxel (HR 0.41, 95% CI, 0.17–1.02). Median survival was not reached in the darolutamide group and was 38.7 months in the placebo group. Four-year survival rates were higher for Black patients receiving darolutamide compared with patients receiving placebo (62% versus 41%, respectively). The darolutamide group also had longer time to CRPC compared with the placebo group (HR, 0.09; 95% CI, 0.02–0.30). The median time to CRPC was not reached in the darolutamide group and was 12.6 months in the placebo group. The safety profile of darolutamide in Black patients was consistent with that observed for the overall ARASENS population. The numbers of patients with grade 3 or 4 adverse events (AEs) (16 versus 17), serious AEs (11 versus 7), and discontinuations of darolutamide or placebo due to AEs (5 versus 4) were similar between treatment groups. Incidence rates of most treatment emergent AEs (61.5% versus 66.1%) and serious treatment emergent AEs (42.3% versus 44.8%) were also similar in the darolutamide and placebo groups.

Conclusion: In this small population of Black patients with mHSPC from the ARASENS trial, darolutamide in combination with ADT and docetaxel was well tolerated and was associated with improved survival and time to CRPC compared with placebo plus ADT and docetaxel. Efficacy and safety findings in Black patients were consistent with the overall ARASENS population.

Abstract 021

Survival Outcomes in Veterans with Non-metastatic Castration-Resistant Prostate Cancer: A Retrospective Analysis by Race and Ethnicity

Kelli M. Rasmussen,[1,2]* Vikas Patil,[1,2] Chunyang Li,[1,2] Christina Yong,[1,2] Sreevalsa Appukkuttan,[3] Jamie Partridge Grossman,[3] Jay Jhaveri,[3] Ahmad S. Halwani[1,2,4]

[1]University of Utah School of Medicine, Salt Lake City, UT, USA; [2]George E. Wahlen Veterans Health Administration, Salt Lake City, UT, USA; [3]Bayer Healthcare Pharmaceuticals Inc., Whippany, NJ, USA; [4]Huntsman Cancer Institute, Salt Lake City, UT, USA.

Background: Discrimination, social determinants of health, and structural racism are major contributors to health disparities in the US. Although Black men are more likely to be diagnosed with and die of prostate cancer than men of other races and ethnicities, racial and ethnic disparities in the disease remain poorly understood. A given disparity-related factor may affect outcomes differently at each point along the highly variable trajectory of the disease. This study aimed to examine clinical outcomes by race and ethnicity in men with non-metastatic castration-resistant prostate cancer (nmCRPC) receiving care within the equal-access US Veterans Health Administration (VHA).

Methods: This was a retrospective, observational cohort study conducted using data from the electronic health care records of men diagnosed with nmCRPC in the VHA. Eligible men were US Veterans diagnosed with prostate cancer from January 1, 2006 to December 30, 2020 who had progressed to nmCRPC defined by the following criteria: (1) prostate-specific antigen (PSA) progression, (2) ongoing androgen deprivation, and (3) no evidence of metastatic disease. Men who progressed to metastatic disease and/or death within 3 months of nmCRPC diagnosis (landmark period) were excluded. The primary outcome was time to either death or metastasis. The secondary outcome was overall survival (OS). A multivariate Cox proportional hazards model, along with Kaplan–Meier estimates, and adjusted survival curves were used to evaluate differences in outcome by race and ethnicity. Statistical significance was assessed using 2-sided, unpaired testing at a significance level of P=0.01.

Results: Mean (standard deviation) follow-up time was 4.3 (3.3) years. Of 12,992 men in the cohort, 826 identified as Hispanic (6%), 3671 as Black (28%), 7323 White (56%), and 1172 of other race and ethnicity (9%; including American Indian or Alaska Native, Asian, Native Hawaiian or Other Pacific Islander, unknown, and declined to answer). Median time from nmCRPC to metastasis or death was 5.96 years (95% confidence interval [CI], 5.58–6.34; P<0.001) for Black men, 5.62 years (95% CI, 5.11–6.67; P<0.001) for Hispanic men, 4.11 years (95% CI, 3.96–4.25; P<0.001) for White men, and 3.59 years (95%CI, 3.23–3.97; P<0.001) for others. Median unadjusted OS was 6.26 years (95% CI, 6.03–6.46; P<0.001) among all men, 8.36 years (95% CI, 8.0–8.8; P<0.001) for Black men, 8.56 years (95% CI, 7.3–9.7; P<0.001) for Hispanic men, 5.48 years (95% CI, 5.2–5.7; P<0.001) for White men, and 4.48 years (95% CI, 4.1–5.0; P<0.001) for others. In the VHA, the hazard ratio (HR) for death among Black men compared with White men was 0.80 (95% CI, 0.76–0.86; P<0.001). For Hispanic patients compared with White men, the HR was 0.64 (95% CI, 0.57–0.72; P<0.001).

Conclusions: This cohort study of men with nmCRPC found that when treated in a US equal-access care setting, Black and/or Hispanic men had significantly improved OS and longer time to metastasis compared with men of other races and ethnicities. This suggests that racial and ethnic disparities in prostate cancer may arise largely from systemic socioeconomic inequity rather than molecular or genetic factors..

Abstract 022

Efficacy and Safety of Darolutamide in Combination with Androgen-Deprivation Therapy and Docetaxel by Disease Volume and Risk in the Phase 3 ARASENS Study

Jason M. Hafron, MD, CMO,[1]* Jay Jhaveri,[2] Maha Hussain, MD,[3] Bertrand Tombal, MD, PhD,[4] Fred Saad, MD,[5], Karim Fizazi, MD, PhD,[6] Cora N. Sternberg, MD,[7] E. David Crawford, MD,[8] Neal Shore, MD,[9] Evgeny Kopyltsov, MD,[10] Arash Rezazadeh Kalebasty, MD,[11] Martin Bögemann, MD,[12] Dingwei Ye, MD,[13] Felipe Cruz, MD,[14] Hiroyoshi Suzuki, MD, PhD,[15] Frank Verholen, MD,[16] Shankar Srinivasan, PhD,[2] Iris Kuss, MD,[17] Heikki Joensuu, MD,[18] Matthew R. Smith, MD, PhD[19]

[1]Michigan Institute of Urology, West Bloomfield Township, MI, USA; [2]Bayer Healthcare Pharmaceuticals Inc.,Whippany, NJ, USA; [3]Northwestern University, Feinberg School of Medicine, Chicago, IL, USA; [4]Division of Urology, IREC, Cliniques Universitaires Saint Luc, UCLouvain, Brussels, Belgium; [5]University of Montreal Hospital Center, Montreal, Quebec, Canada; [6]Institut Gustave Roussy, University of Paris-Saclay, Villejuif, France; [7] Englander Institute for Precision Medicine, Weill Cornell Department of Medicine, Meyer Cancer Center, New York-Presbyterian Hospital, New York, NY, USA; [8]UC San Diego School of Medicine, San Diego, CA, USA; [9]Carolina Urologic Research Center/Genesis Care, Myrtle Beach, SC, USA; [10]Clinical Oncological Dispensary of Omsk Region, Omsk, Russian Federation; [11]University of California Irvine, Division of Hematology/Oncology, Orange, CA, USA; [12]Department of Urology, Münster University Medical Center, Münster, Germany; [13]Fudan University Shanghai Cancer Center, Xuhui District, Shanghai, China; [14]Núcleo de Pesquisa e Ensino da Rede São Camilo, São Paulo, Brazil; [15]Toho University Sakura Medical Center, Chiba, Japan; [16]Bayer Consumer Care AG, Basel, Switzerland; [17]Bayer AG, Berlin, Germany; [18]Orion Corporation, Espoo, Finland; 19 Massachusetts General Hospital Cancer Center, Boston, MA, USA

Background: In the ARASENS trial (NCT02799602), darolutamide in combination with androgen-deprivation therapy (ADT) and docetaxel was shown to significantly reduce the risk of death by 32.5% (hazard ratio [HR] 0.68; 95% confidence interval [CI]: 0.57–0.80; P<0.0001) versus placebo + ADT + docetaxel in patients with metastatic hormone-sensitive prostate cancer (mHSPC). The incidence of treatment-emergent adverse events (TEAEs) was similar between treatment groups. The effect of darolutamide on overall survival (OS) was consistent across prespecified subgroups, including patients with de novo and recurrent disease. Outcomes based on disease volume and risk provide additional information to clinicians when making decisions about treatment intensification for patients with mHSPC. Here we report a post-hoc analysis of the efficacy and safety of darolutamide in combination with ADT and docetaxel by disease volume and risk in the ARASENS trial.

Methods: Patients with mHSPC were randomized 1:1 to darolutamide 600 mg twice daily or placebo, with ADT + docetaxel. High-volume disease was defined as patients with visceral metastases and/or ≥4 bone metastases with ≥1 beyond the vertebral column/pelvis (CHAARTED criteria). High-risk disease was defined as patients with ≥2 risk factors: Gleason score ≥8, ≥3 bone lesions, and the presence of measurable visceral metastasis (LATITUDE criteria). OS for these subgroups was assessed using an unstratified Cox regression model.

Results: Of 1305 total patients, 1005 (77%) had high-volume disease, 912 (70%) had high-risk disease, 300 (23%) had low-volume disease, and 393 (30%) had low-risk disease. Darolutamide + ADT + docetaxel prolonged OS regardless of high- or low-volume disease with HRs of 0.69 (95 CI, 0.57–0.82) and 0.68 (95% CI, 0.41–1.13) versus placebo + docetaxel + ADT, respectively. A similar OS benefit for darolutamide + ADT + docetaxel versus placebo was observed for patients with high- or low-risk disease with HRs of 0.71 (95% CI, 0.58–0.86) and 0.62 (95% CI, 0.42–0.90). Darolutamide improved clinically relevant secondary endpoints versus placebo in high-/low-volume and risk subgroups, with HRs generally in the range of those observed in the overall population. The incidence of TEAEs was consistent with the overall ARASENS population across subgroups by high/low volume and high/low risk.

Conclusions: In patients with mHSPC, early treatment intensification with darolutamide + ADT + docetaxel improved OS and clinically relevant secondary outcomes versus placebo + ADT + docetaxel in patients with high- and low-volume as well as high- and low-risk mHSPC. The favorable safety profile of darolutamide was reconfirmed in both high-/low-volume and high-/low-risk populations. Darolutamide + ADT + docetaxel sets a new standard of care for patients with mHSPC.

Abstract 023

Association Of Prostate-Specific Antigen (PSA) Response and Overall Survival in Patients With Metastatic Hormone-Sensitive Prostate Cancer (mHSPC): Results From The Phase 3 ARASENS Trial

Jason M. Hafron, MD, CMO,[1]* Jay Jhaveri,[2] Fred Saad,[3] Maha Hussain,[4] Bertrand Tombal,[5] Karim Fizazi,[6] Cora N. Sternberg,[7] Silke Thiele,[8] Rui Li,[2] Iris Kuss,[8] Heikki Joensuu,[9] Matthew R. Smith[10]

[1]Michigan Institute of Urology, West Bloomfield Township, MI, USA; [2]Bayer HealthCare Pharmaceuticals Inc., Whippany, NJ, USA; [3]University of Montreal Hospital Center, Montreal, Quebec, Canada; [4]Northwestern University, Feinberg School of Medicine, Chicago, IL, USA; [5]Division of Urology, IREC, Cliniques Universitaires Saint Luc, UCLouvain, Brussels, Belgium; [6]Institut Gustave Roussy, University of Paris-Saclay, Villejuif, France; [7]Englander Institute for Precision Medicine, Weill Cornell Department of Medicine, Meyer Cancer Center, New York-Presbyterian Hospital, New York, NY, USA; [8]Bayer AG, Berlin, Germany; [9]Orion Corporation, Espoo, Finland; [10]Massachusetts General Hospital Cancer Center, Boston, MA, USA

Introduction: In patients with metastatic hormone-sensitive prostate cancer (mHSPC), reductions in prostate-specific antigen (PSA) levels have been associated with improved overall survival. In the ARASENS trial (NCT02799602), darolutamide + androgen-deprivation therapy (ADT) + docetaxel significantly reduced the risk of death by 32.5% (hazard ratio [HR] 0.68; 95% confidence interval [CI]: 0.57–0.80; P<0.0001]) vs placebo + ADT + docetaxel in patients with mHSPC. In this study, we aim to report the association between PSA response and overall survival from ARASENS.

Methods: Patients were randomized 1:1 to darolutamide 600 mg twice daily or placebo, both with ADT plus docetaxel. Serum PSA was measured at screening and every 12 weeks. Exploratory analyses included time to PSA progression (≥25% increase from PSA nadir and PSA increase ≥2 ng/mL ≥12 weeks from nadir) and undetectable PSA (<0.2 ng/mL for 2 samples ≥3 weeks apart) at 24, 36, and 52 weeks, and any time during treatment. Between-treatment comparisons were performed using the Cochran–Mantel–Haenszel test. Post hoc landmark analyses were conducted to evaluate the association between undetectable PSA at Weeks 24 and 36 and overall survival for the overall population.

Results: The full-analysis set consisted of 1305 patients, of which 651 received darolutamide and 654 received placebo. Median (range) PSA levels at study entry were 30.3 (0.0–9219.0) and 24.2 (0.0–11,947.0) ng/mL, respectively. Darolutamide significantly prolonged time to PSA progression versus placebo (HR 0.255; P<0.0001). Undetectable PSA was achieved in more patients receiving darolutamide (48.7%) versus placebo (23.9%) at 24 weeks, increasing to 57.1% and 60.2% at 36 and 52 weeks, respectively, versus minimal change in the placebo group (25.1% and 26.1%, respectively). Undetectable PSA levels at any time were achieved in 67.3% in the darolutamide group and 28.6% in the placebo group; the treatment difference in undetectable PSA was statistically significant (P<0.0001) at all time points. For the overall population, OS was significantly improved for patients who achieved undetectable PSA levels at 24 weeks (HR 0.398; 95% CI: 0.321–0.493) and 36 weeks (HR 0.351; 95% CI: 0.284–0.434) versus those who did not.

Conclusions: The combination of darolutamide + ADT + docetaxel significantly prolonged time to PSA progression in patients with mHSPC, and significantly more patients receiving darolutamide versus placebo achieved undetectable PSA levels, reflecting a strong PSA response over time. Achievement of undetectable PSA at 24 and 36 weeks, with risk of death significantly reduced by 60% and 65%, respectively, was associated with significantly improved OS compared with those who did not.

Acknowledgment of Corporate Support

The Organizers Would Like to Thank the Following Sponsors for Their Support:

(Supporters and Exhibitors as of January 15, 2024)

GOLD LEVEL SPONSORS

Astellas US Pharma
AstraZeneca
Bayer
Johnson & Johnson
Lantheus
Pfizer Oncology
Sumitomo Pharma America
TOLMAR Pharmaceuticals

SILVER LEVEL SPONSOR

Verity Pharmaceuticals

BRONZE LEVEL SPONSORS

BioProtect
Novartis
Telix Pharmaceuticals
Promaxo

EXHIBITORS

AngioDynamics • Astellas Pharma US
AstraZeneca • Bayer
BD Bard • BioProtect
BK Medical • Blue Earth Diagnostics
Boston Scientific • CIVCO Medical Solutions
Dendreon Corporation • Exosome Diagnostics
FocalOne • Focalyx • Fujifilm
GoPath Labs • Johnson & Johnson
Lantheus • Lumea • MDxHealth
Merck • Myriad
Novartis • PathNet TruCore
Pfizer Oncology • Promaxo
Prostate Conditions Education Council • Prostatype Genomics
Sagis Diagnostics • Sumitomo Pharma America • Sun Pharma
Telix Pharmaceuticals • Theragenics
TOLMAR Pharmaceuticals • Verity Pharmaceuticals

Unrestricted educational grants have been provided by Blue Earth Diagnostics and Exelixis.

Grand Rounds in Urology
A Division of Carden Jennings Publishing Co., Ltd.

485 Hillsdale Drive, Suite 341
Charlottesville, VA 22901
www.grandroundsinurology.com