Patient (pt) Population and Radiation Therapy (RT) Type in the Long-Term Phase 3 Double-Blind, Placebo (PBO)-Controlled ATLAS Study of Apalutamide (APA) Added to Androgen Deprivation Therapy (ADT) in High-Risk Localized or Locally Advanced Prostate Cancer (HRLPC)

Howard M. Sandler (howard.sandler@cshs.org),[1] Stephen J. Freedland,[1,2] Neal D. Shore,[3] Matthew R. Smith,[4] Rosamerlinda Rosales,[5] Sabine D. Brookman-May,[5,6] David P. Dearnaley,[7] Adam P. Dicker,[8] Michael R. McKenzie,[9] Alberto Bossi,[10] Anders Widmark,[11] Thomas Wiegel,[12] Jason L. Martin,[13] Branko Miladinovic,[14] Jennifer Whalen,[15] Marika Ciprotti,[16] Sharon A. McCarthy,[15] Suneel Mundle,[15] Bertrand F. Tombal,[17] Felix Feng,[18]

[1]Cedars-Sinai Medical Center, Los Angeles, CA; [2]Durham VA Medical Center, Durham, NC; [3]Carolina Urologic Research Center, Myrtle Beach, SC; [4]Massachusetts General Hospital Cancer Center, Boston, MA; [5]Janssen Research & Development, Los Angeles, CA; [6]Ludwig-Maximilians-University, Munich, Germany; [7]The Royal Marsden Hospital and The Institute of Cancer Research, London, UK; [8]Sidney Kimmel Cancer Center, Thomas Jefferson University, Philadelphia, PA; [9]British Columbia Cancer Agency, Vancouver, BC, Canada; [10]Institute Gustave Roussy, Villejuif, France; [11]Umeå University, Umeå, Sweden; [12]University Hospital Ulm, Ulm, Germany; [13]Janssen Research & Development, High Wycombe, UK; [14]Janssen Research & Development, San Diego, CA; [15]Janssen Research & Development, Raritan, NJ; [16]Janssen Research & Development, Beerse, Belgium; [17]Cliniques Universitaires Saint-Luc, Brussels, Belgium; [18]Helen Diller Family Comprehensive Cancer Center, University of California San Francisco, San Francisco, CA

INTRODUCTION

- Current management of HRLPC includes long-term ADT with primary RT[1,2] (Table 1)
- Despite definitive primary treatment, these patients have a high risk of metastasis and death
- The phase 3 ATLAS study (NCT02531516) is investigating the benefit of adding APA to gonadotropin-releasing hormone agonist (GnRHa) and external beam radiation therapy (EBRT) in high-risk patients (Figure 1)
- The study is fully enrolled and ongoing at 255 sites in 24 countries

TABLE 1: Treatment outcomes from current management of HRLPC

	Patients
Patients treated with RT alone	
Clinical disease-free survival[a]	23%[3]
Patients treated with RT and ADT	
Clinical disease-free survival[a]	48%[3]
Biochemical-free survival[b]	74%[4]

PSA, prostate-specific antigen. [a]Time to first clinical progression (local, local and regional, distant, local and distant, or local, regional, and distant) and/or death from any cause. [b]No PSA recurrence (PSA ≥2 ng/mL above nadir) or death from prostate cancer.
Values are cumulative 10-year data.

OBJECTIVES

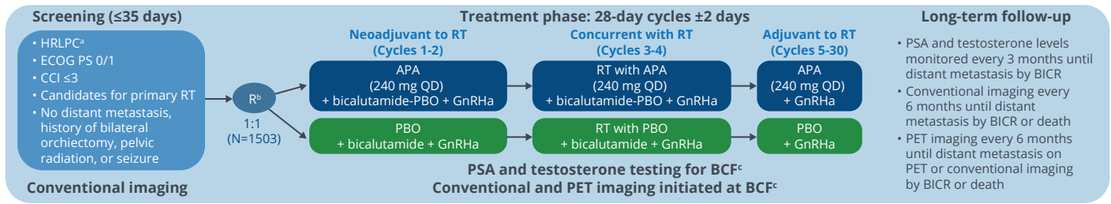
- To describe the distribution of baseline characteristics in this high-risk patient population enrolled in ATLAS
- To describe the application of different RT regimens reflecting recent international guidelines and clinical practice changes for patients with HRLPC

METHODS

- Patients were randomized to receive APA or PBO throughout a 30-cycle treatment phase. All patients received concurrent GnRHa and primary RT as standard of care. The control PBO group also received bicalutamide neoadjuvant and concurrent with RT (Figure 1)
- Collection of positron emission tomography (PET) imaging (prostate-specific membrane antigen, fluciclovine, or choline) was added to the protocol to guide treatment of patients with biochemical failure (BCF) or progressive disease after definitive RT and hormonal therapy
- Patient-reported outcomes are being collected to evaluate the effect of adding APA to GnRHa on symptoms, function, and health-related quality of life

PROSTATE CANCER

FIGURE 1: ATLAS study design



BICR, blinded independent central review; CCI, Charlson comorbidity index; CRPC, castration-resistant prostate cancer; ECOG PS, Eastern Cooperative Oncology Group performance status; PFS, progression-free survival; QD, daily; R, randomization; SRE, skeletal–related event.
[a]High-risk localized or locally advanced prostate cancer (with or without N1 disease) defined by 1 of the following at diagnosis: 1) Gleason score of ≥8 and ≥cT2c, or 2) Gleason score of 7 and PSA ≥20 ng/mL and ≥cT2. [b]Patients were stratified by Gleason score, pelvic nodal status, use of brachytherapy boost, and region. [c]Defined by 2 ng/mL increase in PSA over the nadir achieved after completion of RT treatment.

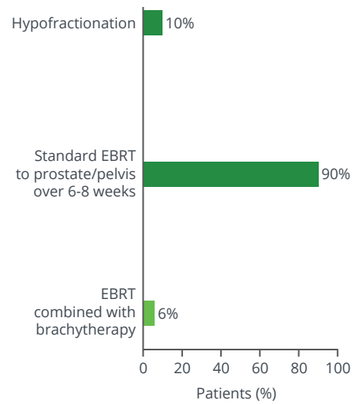
ATLAS PATIENT DEMOGRAPHICS AND CHARACTERISTICS

Patient baseline characteristics

	N=1503		N=1503
Age, mean (SD), yrs	66.8 (6.7)	Gleason score, n (%)	
Race, n (%)		≥8	1065 (71)
White	1130 (75)	7	438 (29)
Asian	137 (9)	ECOG PS, n (%)	
Black or African American	86 (6)	0	1337 (89)
Other	150 (10)	1	166 (11)
Region, n (%)		CCI, n (%)	
North America	195 (13)	0-1	169 (11)
Europe	571 (38)	2	583 (39)
Other	737 (49)	3	747 (50)
Tumor stage at diagnosis, n (%)		PSA, mean (SD), ng/mL	20.6 (43)
T2c	662 (44)	Used systemic therapy prior to randomization, n (%)[a]	692 (46)
T3	757 (50)	Time from diagnosis to randomization, mean (SD), mos	3.6 (3)
T4	83 (6)		
Regional lymph node stage N1 at diagnosis, n (%)	193 (13)		

[a]GnRHa could be started up to 3 months prior to treatment Cycle 1.

Radiation therapy schedules during ATLAS



REFERENCES:

1. McKay RR, et al. *Am Soc Clin Oncol Educ Book*. 2020;40:1-12. 2. Payne HA, Hughes S. *Oncologist*. 2012;17(suppl 1):9-15. 3. Bolla M, et al. *Lancet*. 2010;11:1066-1073. 4. Widmark A, et al. *Lancet*. 2009;373:301-308.

Presented at the JADPRO Live 2022, October 20-23, 2022, Aurora, CO

KEY TAKEAWAYS

- ATLAS enrollment is complete. Participants are patients with high-risk and very high–risk prostate cancer planned for primary RT in clinical practice
- ATLAS is evaluating if intensifying hormonal therapy with APA improves MFS in conjunction with different types of primary RT

CONCLUSIONS

- Baseline characteristics demonstrate high- and very high–risk features of prostate cancer and pelvic nodal involvement in patients undergoing primary RT in clinical practice
- The RT schedules applied reflect recent evidence and guideline changes for the use of hypofractionation in this patient population
- ATLAS is an example of how RT can be included in phase 3 trials of HRLPC in combination with next-generation hormonal therapy

ACKNOWLEDGMENTS

This study is funded by Janssen Research & Development. Writing assistance was provided by Gwendolyn Elphick, PhD, and Emma Beddie, of Parexel, and was funded by Janssen Global Services, LLC.

DISCLOSURES

HMS reports advisory role for Janssen; stock/other ownership in Radiogel; and other for Caribou Publishing; SJF reports being an employee of Genomic Health; advisor for Astellas, AstraZeneca, Bayer, Clovis Oncology, Dendreon, Exact Sciences, Ferring, Janssen, Merck, Myovant Sciences, Pfizer, and Sanofi; speakers' bureau for AstraZeneca and Sanofi; travel expenses from Sanofi; and research funding from Bayer, Diasorin, GenomeDx, Janssen, MDxHealth, Merck, Myriad Genetics, OPKO Diagnostics, and Progenika; NDS reports advisory roles, speakers' bureau, and/or research funding for Abbvie, Amgen, Astellas, AstraZeneca, Bayer, BMS, Boston Scientific, CG Oncology, Clovis Oncology, Dendreon, Exact, FerGene, Ferring, Foundation Medicine, Guardant Health, Genesis Cancer Care, Genzyme, InVitae, Janssen, Merck, MDxHealth, Medivation, Myovant Sciences, Myriad Genetics, Nymox, Pacific Edge Biotechnology, Peerview, Pfizer, Posphorus, Propella Therapeutics, Sanofi, Sesen Bio, Speciality Networks, Tolmar, and Urogen Pharma; MRS reports advisory roles for Amgen, Astellas, Bayer, Janssen, Lilly, Novartis, and Pfizer and research funding from Bayer, ESSA, Janssen, Lilly, and ORIC Pharmaceuticals; RR, SDB-M, SAM, JLM, BM, and SM are employees of Janssen and have stock/other ownership in Johnson & Johnson; DPD reports travel expenses from Janssen and patent/royalties for abiraterone acetate; APD reports advisory roles for Accordant, Alcimed, CVS, Cybrexa Therapeutics, Deallus, EMD Serono, Genentech, IBA, Janssen, Oncohost, Orano Med, Roche, Third Bridge; travel expenses from Oncohost; expert testimony for Wilson Sonsini; patent/royalties for doped BEO compounds; stock/other ownership in Oncohost and Self Care Catalysts and other from European Commission; MRM reports honoraria from Bayer and research funding from Janssen; AB reports serving on speakers' bureau for Astellas/Agensys and Ipsen and honoraria from Astellas, Ferring, Ipsen , and Myovant Sciences; AW has nothing to disclose; TW reports advisory role for Janssen and honoraria from Janssen, Ipsen, and Recordati; JW is an employee of Janssen, has stock/other ownership in Janssen, and has received research funding from Janssen; MC is an employee of BMS and Janssen and has stock/other ownership in BMS and Janssen; BFT reports advisory role, expert testimony, speakers' bureau, travel expenses, research funding, and/or honoraria from Amgen, Astellas, Bayer, Ferring, Janssen, Myovant Sciences, Pfizer, Sanofi, Steba Biotech, and Takeda; FF reports advisory role for Astellas, Bayer, BlueStar Genomics, BMS, Exact, Foundation Medicine, Janssen, Myovant Sciences, Novartis, Roivant, Serimmune, and Varian Medical Systems; stock/other ownership in Artera; and research funding from Zenith Epigenetics.