

1398P

Overall survival (OS) in patients (pts) with metastatic hormone-sensitive prostate cancer (mHSPC) who received prior androgen deprivation therapy (ADT) and reached low prostate-specific antigen (PSA) levels treated further with enzalutamide (ENZA): Post hoc analyses of ARCHES

D.P. Petrylak¹, A.A. Azad², R.Z. Szmulewitz³, T. Iguchi⁴, N.D. Shore⁵, J. Holzbeierlein⁶, B. Alekseev⁷, N.N. El-Chaar⁸, B. Rosbrook⁹, J. Ma⁸, F. Zohren⁹, G.P. Haas⁸, A. Stenzl¹⁰, A.J. Armstrong¹¹

¹ Medical Oncology Department, Yale Cancer Center, New Haven, CT, USA, ² Department of Medicine, Peter MacCallum Cancer Centre, Melbourne, VIC, Australia, ³ Department of Medicine, The University of Chicago, Chicago, IL, USA, ⁴ Department of Urology, Kanazawa Medical University, Ishikawa, Japan, ⁵ Department of Urology, Carolina Urologic Research Center, Myrtle Beach, SC, USA, ⁶ Urologic Oncology Department, The University of Kansas Medical Center, Kansas City, KS, USA, ⁷ Department of Oncology, Herten Moscow Cancer Research Institute, Moscow, Russian Federation, ⁸ Oncology Department, Astellas Pharma Inc., Northbrook, IL, USA, ⁹ Clinical Statistics, Pfizer Inc., San Diego, CA, USA, ¹⁰ Department of Urology, University Hospital, Eberhard Karls University of Tübingen, Tübingen, Germany, ¹¹ Divisions of Medical Oncology and Urology, Duke Cancer Institute Center for Prostate & Urologic Cancers, Durham, NC, USA

Background

In the phase 3 ARCHES trial, >90% of men with mHSPC received prior ADT and achieved a range of PSA values (≤ 0.2 , $>0.2-4$, and >4 $\mu\text{g/L}$) before randomization. This *post hoc* analysis examined the effect of treatment intensification with ENZA + ADT versus continuing ADT alone on OS and other efficacy outcomes by baseline PSA categories.

Methods

Pts with mHSPC were randomized 1:1 to ENZA (160 mg/day) + ADT or placebo (PBO) + ADT. Prior ADT (≤ 3 months [mo]/ ≤ 6 mo + docetaxel) and up to 6 cycles of prior docetaxel were permitted before baseline assessment of PSA levels and study treatment initiation. After unblinding, 31.3% of PBO + ADT-treated pts crossed over to open-label ENZA + ADT (median time to crossover, 21.5 mo). *Post hoc* analyses of the primary endpoint radiographic progression-free survival (rPFS) and secondary endpoints such as OS were conducted to assess the efficacy of ENZA + ADT in pts achieving different baseline PSA categories after prior treatment with ADT.

Results

In the overall population (n=1150), >90% received prior ADT and 18% had prior docetaxel treatment. Median duration (range) of prior ADT was 1.6 mo (0.03–55.3) for ENZA + ADT pts versus 1.6 mo (0.03–198.8) for PBO + ADT pts. Of the overall population with available baseline PSA values who received prior ADT (n=1045), 133 pts had ≤ 0.2 $\mu\text{g/L}$, 372 had $>0.2-4$ $\mu\text{g/L}$, and 540 had >4 $\mu\text{g/L}$ PSA at baseline (Table). A beneficial effect of ENZA + ADT was observed across all baseline PSA categories, including OS (adjusted for crossover) in pts with baseline PSA ≤ 0.2 $\mu\text{g/L}$, with no evidence of heterogeneity (Table).

Conclusions

These *post hoc* analyses in pts with mHSPC who received prior ADT and achieved baseline PSA values even to ≤ 0.2 $\mu\text{g/L}$ support the additional durable clinical benefits of treatment intensification with ENZA + ADT for rPFS and OS and other secondary endpoints. Table: 1398P

	Baseline PSA, $\mu\text{g/L}$		
Endpoint, HR (95% CI) ^a	≤ 0.2 (n=62; ^b n=71 ^c)	$>0.2-4$ (n=191; ^b n=181 ^c)	>4 (n=278; ^b n=262 ^c)
rPFS ^d	0.60 (0.27, 1.33)	0.32 (0.20, 0.50)	0.45 (0.32, 0.63)
OS	0.58 (0.27, 1.24)	0.56 (0.38, 0.82)	0.75 (0.56, 1.00)
Crossover-adjusted OS	0.48 (0.17, 0.96)	0.54 (0.33, 0.80)	0.65 (0.47, 0.88)
Time to PSA progression ^e	0.25 (0.09, 0.69)	0.28 (0.19, 0.42)	0.27 (0.21, 0.37)
Time to castration resistance	0.44 (0.24, 0.81)	0.40 (0.29, 0.55)	0.36 (0.28, 0.46)

^aHR<1 favors ENZA + ADT; ^bENZA + ADT; ^cPBO + ADT; ^dIndependent central review or death within 24 weeks of stopping treatment; ^e $\geq 25\%$

increase and absolute increase ≥ 2 ng/mL above nadir.CI=confidence interval; HR=hazard ratio.

Clinical trial identification

NCT02677896.

Editorial acknowledgement

Medical writing and editorial assistance were provided by Laura Gibbons, PhD, Lauren Smith, BA (Hons), and Jane Beck, MA, from Complete HealthVizion, funded by the study sponsors.

Legal entity responsible for the study

Astellas Pharma Inc.; Pfizer Inc.

Funding

This study was funded by Astellas Pharma Inc. and Pfizer Inc., the co-developers of enzalutamide.

Disclosure

D.P. Petrylak: Financial Interests, Institutional, Research Grant: Ada Cap (Advanced Accelerator Applications), Agensys Inc., Astellas Pharma Inc., AstraZeneca, Bayer, BioXcel Therapeutics, Bristol Myers Squibb, Clovis Oncology, Eisai, Lilly, Endocyte, Genentech, Gilead Sciences, Innocrin, MedImmune, Medivation, Merck, Mirati, Novartis, Pfizer, Progenics, Replimune, Roche, Sanofi Aventis, Seattle Genetics; Financial Interests, Personal, Other, Consultant fees: Astellas Pharma Inc., Pfizer; Financial Interests, Personal, Advisory Board: AstraZeneca, Bayer, Exelixis, Johnson&Johnson/Janssen, Lilly, Clovis Oncology, Roche, Seattle Genetics, Ada Cap (Advanced Accelerator Applications), Amgen, Bicycle Therapeutics, Boehringer Ingelheim, Bristol Myers Squibb, Incyte, Mirati, Monopteros, Pharmacyclics, Gilead Sciences, Ipsen, Regeneron, UroGen; Financial Interests, Personal, Expert Testimony: Sanofi, Celgene; Financial Interests, Personal, Stocks/Shares, sold 10/2019: Tyme; Financial Interests, Personal, Stocks/Shares, sold 7/2020: Bellicum Pharmaceuticals. A.A. Azad: Financial Interests, Personal, Research Grant: Astellas, AstraZeneca, Merck-Serono, Bayer; Financial Interests, Institutional, Principal Investigator: Bristol Myers Squibb, AstraZeneca, Aptevo Therapeutics, Glaxo Smith Kline, MedImmune, Astellas, SYNthorx, Bionomics, Sanofi Aventis, Novartis, Ipsen, Exelixis, Merck Sharpe Dome, Janssen; Financial Interests, Personal, Advisory Role: Astellas, Novartis, Pfizer, Janssen, Sanofi, AstraZeneca, Bristol Myers Squibb, Tolmar, Bayer, Telix Pharmaceuticals, MSD, Aculeus Therapeutics, Amgen, Merck Serono, Ipsen, Noxopharm; Financial Interests, Personal, Speaker’s Bureau: Astellas, Janssen, Ipsen, Bristol Myers Squibb, Merck Serono, Novartis, Amgen, Bayer; Financial Interests, Personal, Other, Travel/accommodations/expenses: Astellas, Pfizer, Novartis, Janssen, Tolmar, Amgen, Merck-Serono; Financial Interests, Personal, Advisory Board: Astellas, Novartis, Sanofi, AstraZeneca, Tolmar, Pfizer, Telix, Merck Serono, Janssen, Bristol Myers Squibb, Ipsen, Bayer, MSD, Amgen, Noxopharm; Financial Interests, Personal, Other, Data Safety Monitoring Board: Oncosec; Non-Financial Interests, Personal, Leadership Role: ANZUP Cancer Trials Group, COSA. R.Z. Szmulewitz: Financial Interests, Personal, Advisory Role: AstraZeneca, AbbVie, Exelixis, Merck, Amgen, Sanofi, Astellas Pharma Inc., Pfizer, Janssen Oncology; Financial Interests, Personal, Other, Honoraria: Astellas Pharma Inc.; Financial Interests, Personal, Other, Travel/Accommodations/Expences: Corcept Therapeutics; Financial Interests, Institutional, Other, Patent Co Inventor: Corcept Therapeutics; Financial Interests, Personal and Institutional, Funding: AbbVie, Astellas Pharma Inc., Incyte, MacroGenics, Janssen Oncology. T. Iguchi: Financial Interests, Personal, Advisory Role: Astellas Pharma Inc., Bayer, Janssen; Financial Interests, Personal, Speaker’s Bureau: Astellas Pharma Inc., Bayer, Janssen, Sanofi, AstraZeneca, Takeda; Financial Interests, Institutional, Funding: Astellas Pharma Inc., Bayer. N.D. Shore: Financial Interests, Personal, Advisory Role: Bayer, Janssen Scientific Affairs, Dendreon, Tolmar, Ferring, Medivation, Amgen, Pfizer, AstraZeneca, Genentech/Roche, Myovant Sciences, Astellas Pharma; Financial Interests, Personal, Speaker’s Bureau: Janssen, Bayer, Dendreon. J. Holzbeierlein: Financial Interests, Institutional, Funding: Astellas Pharma Inc.; Financial Interests, Institutional, Principal Investigator: MDxHealth. B. Alekseev: Financial Interests, Personal, Advisory Role: Astellas Pharma Inc., Pfizer, AstraZeneca, Bayer, BMS, Ferring, Janssen, MSD, Sanofi, Eisai, Roche; Financial Interests, Personal, Speaker’s Bureau: Astellas Pharma Inc., Pfizer, AstraZeneca, Bayer, BMS, Ferring, Janssen, MSD, Sanofi, Eisai; Financial Interests, Personal, Other, Travel/accommodation/expenses: Astellas Pharma Inc., Pfizer, AstraZeneca, Bayer, BMS, Ferring, Janssen, MSD, Sanofi, Eisai; Financial Interests, Institutional, Funding: Astellas Pharma Inc., Pfizer, AstraZeneca, Bayer, BMS, Janssen, MSD. N.N. El-Chaar: Financial Interests, Personal, Other, Travel, accomodations, expenses: Astellas Pharma Inc.; Financial Interests, Personal, Stocks/Shares: TNXP, SNGX, BNGO, SESN, RXRX; Financial Interests, Personal, Full or part-time Employment: Astellas Pharma Inc. B. Rosbrook: Financial Interests, Personal, Full or part-time Employment: Pfizer; Financial Interests, Personal, Stocks/Shares: Pfizer. J. Ma: Financial Interests, Personal, Full or part-time Employment: Astellas Pharma Inc. F. Zohren: Financial Interests, Personal, Full or part-time Employment: Pfizer; Financial Interests, Personal, Stocks/Shares: AlloVir, Inc., Pfizer. G.P. Haas: Financial Interests, Personal, Full or part-time Employment: Astellas Pharma Inc. A. Stenzl: Financial Interests, Personal, Advisory Role: Astellas Pharma Inc., Ipsen Pharma, Roche, Janssen, Ferring, Synergo, Molecular Health, miRScientific, AstraZeneca; Financial Interests, Personal, Invited Speaker: Ipsen Pharma, Astellas Pharma Inc., Janssen, Ferring, AstraZeneca; Financial Interests, Personal, Expert Testimony, photodynamic therapy of prostrate cancer: GBA; Financial Interests, Personal, Other, Travel/accommodations/expenses: Ipsen Pharma, Janssen, Ferring, CureVac, Sanofi Aventis; Financial Interests, Personal, Other, Patents (A290/99, AT00/0001:C-Trap, 2018/6579): N/A; Financial Interests, Personal, Principal Investigator: Astellas Pharma Inc., Medivation, Roche, Janssen, Karl Storz AG, AstraZeneca, Johnson&Johnson, Cepheid, Amgen, CureVac, Immatics, GemeDX Bioscience,

Novartis. A.J. Armstrong: Financial Interests, Personal, Advisory Role: Astellas Pharma Inc., Pfizer, Medivation, Bayer, Forma, Novartis, Dendreon, Janssen, Merck, AstraZeneca, BMS, Exelixis, Epic Sciences, Myovant; Financial Interests, Personal, Other, Travel/accommodations/expenses: Astellas Pharma Inc.; Financial Interests, Institutional, Funding: Astellas Pharma Inc., Pfizer, Medivation, Bayer, Forma, Novartis, Dendreon, Janssen, Merck, AstraZeneca, Roche/Genentech, Bristol Myers Squibb, Amgen.

© *European Society for Medical Oncology*