BERLIN 2025 ESMO congress

2384MO

First interim efficacy analysis of the phase I/II PETRANHA trial of saruparib + androgen receptor pathway inhibitors (ARPI) in patients (pts) with metastatic prostate cancer (mPC)

A.A. Azad[1], A.M. Joshua[2], M. Voskoboynik[3], P. Sankey[4], S. Pacey[5], P. Pilie[6], E. Heath[7], A.J. Weickhardt[8], L. Krieger[9], C. Buttigliero[10], E. Efstathiou[11], L.G. Horvath[12], R. Jones[13], M. Maruzzo[14], B. Webb[15], N. Camacho[16], Y. Kim[17], B. De Paula[17], T. Milenkova[17], A. Hudson[18]

[1] Department of Oncology, Peter MacCallum Cancer Centre, Melbourne, Australia, [2] Medical Oncology, Kingshorn Cancer Centre, St Vincent's Hospital, Sydney, Australia, [3] Medical Oncology, Alfred Health, Monash University, Melbourne, Australia, [4] Oncology Department, University Hospitals Plymouth NHS Trust, Derriford Hospital, Plymouth, United Kingdom, [5] Oncology, Cambridge University Hospitals NHS Foundation Trust & Department of Oncology, Clinical School, University of Cambridge, Addenbrookes Hospital, Cambridge, United Kingdom, [6] Department of Genitourinary Medical Oncology, MD Anderson Cancer Center, Houston, United States of America, [7] Department of Oncology, Mayo Clinic Comprehensive Cancer Center, Rochester, United States of America, [8] Medical Oncology Dept, Olivia Newton-John Cancer and Wellness Centre, Austin Health, Heidelberg, Australia, [9] Genesis Care, North Shore and Royal North Shore Hospital, Sydney, Australia, [10] Department of Oncology, University of Turin at San Luigi Hospital, Orbassano, Italy, [11] Genitourinary Oncology, Houston Methodist Cancer Center, Houston, United States of America, [12] Medical Oncology, Chris O'Brien Lifehouse, Camperdown, Australia, [13] School of Cancer Sciences, University of Glasgow, Clinical Research Gartnavel, Glasgow, United Kingdom, [14] Oncology 1 Unit, Instituto Oncologico Veneto IOV - IRCCS, Padua, Italy, [15] Early Oncology Statistics, AstraZeneca, Cambridge, United Kingdom, [16] Oncology Data Science, Oncology R&D, AstraZeneca, Cambridge, United Kingdom, [17] Early Oncology Research and Development, AstraZeneca, Cambridge, United Kingdom[18] Department of Oncology, The Christie NHS Foundation Trust, Manchester, United Kingdom

Background

PARP inhibitor (PARPi) + ARPI combination is an established option for selected pts with castration-resistant mPC (mCRPC). Saruparib (AZD5305), a PARP1-selective inhibitor, has the potential for improved safety and efficacy compared with non-selective PARPi. We report updated safety and the first efficacy data from the PETRANHA trial in pts with castration-sensitive mPC (mCSPC) and mCRPC.

Methods

Pts, allocated by investigator choice, received saruparib 60 mg once daily (OD) + enzalutamide 160 mg OD (Arm 1), abiraterone 1000 mg OD + 5 mg prednisone OD or twice daily (BD; Arm 2), or darolutamide 600 mg BD (Arm 3) until disease progression or intolerable adverse event (AE). Primary objectives were safety and tolerability; secondary objectives included efficacy. Arm 4 (+ apalutamide 240 mg OD) is ongoing dose escalation and was not included in this analysis.

Results

As of 28 Oct 2024, 77 pts were included (Arm 1, n=18; Arm 2, n=23; Arm 3, n=36). 27 (35%) pts had mCSPC and 50 (65%) had mCRPC (prior ARPI, n=19; ARPI-naïve, n=31); 16 (20.8%) pts had a homologous recombination repair mutation (HRRm). Across all pts, median saruparib exposure duration was 12.8 months (range: 0.2–28.2) and the rate of AEs leading to saruparib discontinuation was 10.4% (8/77; other safety results per Table below). Rates of prostate specific antigen (PSA) reduction >90% compared with baseline/PSA undetectable (<0.2 ng/mL) were 100%/83.3% in mCSPC, 5.6%/5.3% in prior ARPI mCRPC, and 53.3%/29.0% in ARPI-naïve mCRPC. Objective response rates were 88.5% (23/26) in mCSPC, 25% (2/8) in prior ARPI mCRPC and 73.3% (11/15) in ARPI-naïve mCRPC. Exploratory analyses demonstrated PSA responses in pts irrespective of whether their tumour harboured an HRRm or not.

Conclusions

Saruparib + ARPI has promising safety and preliminary efficacy in pts with mCSPC and ARPI-naïve mCRPC. EvoPAR-01 is an ongoing phase 3 study evaluating this combination in mCSPC.Table: 2384MO

	mCRPC Prior ARPI N=19	mCRPC ARPI-naïve N=31	mCSPC N=27
Median duration of saruparib / ARPI exposure, months (range)	5.5 (1.2–17.7) / 5.5 (1.1–17.7)	14.7 (0.3–24.8) / 15.7 (0.4–24.8)	17.8 (0.2–28.2) / 19.7 (0.2–28.2)
Any AE, n (%)	18 (94.7)	31 (100)	26 (96.3)
Any AE causally related to saruparib, n (%)	16 (84.2)	28 (90.3)	23 (85.2)
Any AE Gr ≥3, n (%)	6 (31.6)	16 (51.6)	14 (51.9)

	mCRPC Prior ARPI N=19	mCRPC ARPI-naïve N=31	mCSPC N=27
Any serious AE, n (%)	4 (21.1)	10 (32.3)	4 (14.8)
Saruparib / ARPI discontinuation due to AE, n (%)	1 (5.3) / 1 (5.3)	4 (12.9) / 1 (3.2)	3 (11.1) / 1 (3.7)
Saruparib / ARPI dose reduction due to AE, n (%)	5 (26.3) / 4 (21.1)	11 (35.5) / 4 (12.9)	8 (29.6) / 0
Saruparib / ARPI interruption due to AE, n (%)	7 (36.8) / 6 (31.6)	21 (67.7) / 16 (51.6)	14 (51.9) / 12 (44.4)

Clinical trial identification

NCT05367440; release date: April 8, 2025.

Editorial acknowledgement

Medical writing support for the development of this abstract, under the direction of the authors, was provided by Taylor Stepien, PhD (Chicago, IL, USA) of Ashfield Medcomms, an Inizio company, and was funded by AstraZeneca.

Legal entity responsible for the study

AstraZeneca.

Funding

AstraZeneca.

Disclosure

A.A. Azad: Financial Interests, Personal, Advisory Board: Astellas, Novartis, Sanofi, AstraZeneca, Tolmar, Telix, Merck Serono, Janssen, Bristol Myers Squibb, Ipsen, Bayer, Pfizer, Amgen, Noxopharm, Merck Sharpe Dohme, Daiichi Sankyo, Arvinas; Financial Interests, Personal, Other, Consultant: Aculeus Therapeutics; Financial Interests, Personal, Invited Speaker: Astellas, Janssen, Novartis, Amgen, Ipsen, Bristol Myers Squibb, Merck Serono, Bayer; Financial Interests, Personal, Other, Travel + Accommodation: Astellas, Merck Serono, Amgen, Novartis, Janssen, Tolmar, Pfizer, Bayer; Financial Interests, Personal, Research Grant: Astellas, Merck Serono, AstraZeneca; Financial Interests, Personal, Steering Committee Member: Astellas, Pfizer, Exelixis; Financial Interests, Institutional, Local PI: Bristol Myers Squibb, Aptevo Therapeutics, AstraZeneca, Glaxo Smith Kline, Pfizer, Astellas, SYNthorx, Bionomics, Sanofi, Ipsen, Exelixis, Merck Sharpe Dohme, Janssen, Eli Lilly, Gilead Sciences, Merck Serono, Hinova; Financial Interests, Institutional, Trial Chair: Bayer; Financial Interests, Institutional, Coordinating PI: AstraZeneca, Hinova; Financial Interests, Personal, Trial Chair: Janssen, AstraZeneca; Non-Financial Interests, Leadership Role, Chair, Translational Research Committee: ANZUP Cancer Trials Group; Non-Financial Interests, Leadership Role, Member, Scientific Advisory Committee: ANZUP Cancer Trials Group; Non-Financial Interests, Leadership Role, Chair, Urologic Oncology Committee: Clinical Oncology Society of Australia; Non-Financial Interests, Other, Editorial Board Member: BMC Urology; Non-Financial Interests, Other, Associate Editor: Cancer Research Communications, Frontiers in Oncology, Clinical Genitourinary Cancer, Asia-Pacific Journal of Clinical Oncology. A.M. Joshua: Financial Interests, Institutional, Coordinating PI: AstraZeneca. M. Voskoboynik: Financial Interests, Personal, Advisory Board: AstraZeneca, MSD, Onko-innate; Financial Interests, Personal, Other, Consulting Role: PSI-CRO; Financial Interests, Institutional, Local PI: AstraZeneca, MSD, Alpine Immune Sciences, Virocure, Hinova Pharmaceuticals, Atridia, Antengene, BeiGene, Hengrui Pharmaceutical, Multitude Therapeutics, Anwita Biosciences, Pharmabcine, Immunocore. S. Pacey: Financial Interests, Personal, Advisory Board: AstraZeneca; Non-Financial Interests, Personal, Local PI: AstraZeneca; Non-Financial Interests, Personal, Principal Investigator: AstraZeneca; Financial Interests, Institutional, Research Grant: AstraZeneca. E. Heath: Financial Interests, Personal, Advisory Board: Bayer, Sanofi, AstraZeneca, Astellas, EMD Serono, Gilead Sciences, Novartis, Janssen, Seagen; Financial Interests, Personal, Invited Speaker: Sanofi. A.J. Weickhardt: Financial Interests, Personal, Advisory Board: MSD, BMS, Ipsen, Eisai, Johnson & Johnson, Bayer, Astellas; Financial Interests, Institutional, Funding: MSD; Financial Interests, Personal, Invited Speaker: MSD, Eisai, Astellas; Financial Interests, Personal, Speaker, Consultant, Advisor: MSD, Astellas; Financial Interests, Personal, Steering Committee Member: MSD. L. Krieger: Financial Interests, Personal, Advisory Board: Bayer, Pfizer, Ispen, MSD, Merck, Ferring, AstraZeneca, BMS, Astellas, Janssen-Cilag; Non-Financial Interests, Institutional, Coordinating PI: BMS, MSD, Merck, AstraZeneca, Bayer, Telix; Financial Interests, Personal, Invited Speaker: Bayer, MSD, Merck, BMS, Janssen-Cilag, Ipsen; Non-Financial Interests, Institutional, Local PI: BMS, MSD, Merck, AstraZeneca, Bayer, Telix, Ipsen, Pfizer; Financial Interests, Personal, Speaker's Bureau: Ipsen, Bayer, Merck, AstraZeneca, MSD, BMS, Astellas, Janssen-Cilag. C. Buttigliero: Financial Interests, Institutional, Invited Speaker: Janssen, Bristol Myers Squibb, Ipsen, MSD, Astellas, Bayer, Novartis, GS. E. Efstathiou: Financial Interests, Personal, Advisory Board: Johnson & Johnson, AstraZeneca, Pfizer, Astellas, Janux, Bayer, MSD, Tolmar; Financial Interests, Personal, Other, Honoraria: Johnson & Johnson, AstraZeneca, Pfizer, Astellas, Janux, Bayer, MSD, Tolmar; Financial Interests, Institutional, Research Funding: Johnson & Johnson, AstraZeneca, Pfizer, Astellas, Janux, Bayer, MSD, Tolmar. L.G. Horvath: Financial Interests, Personal, Advisory Board, Honorarium donated back to Chris O'Brien Lifehouse (My hospital): Imagion Biosystems; Financial Interests, Institutional, Invited Speaker: Astellas, Janssen, Amgen; Financial Interests, Institutional, Advisory Board: Astellas, Bayer; Financial Interests, Institutional, Invited Speaker, Bayer paid for travel to Lisbon APEX meeting and accomodation. I gave 3 talks and honorarium paid to be institution: Bayer; Financial Interests, Institutional, Advisory Board, Funding paid to my instutition: Amgen; Financial Interests, Personal, Member of Board of Directors, No payment: ANZUP (Australia and New Zealand Urogenital and Prostate) Clinical Trials Group;

Financial Interests, Personal, Full or part-time Employment, I am a medical oncologist, Director of Research and Chief Clinical Officer of this cancer centre: Chris O'Brien Lifehouse; Financial Interests, Personal, Full or part-time Employment, I am a member of the Garvan Faculty and Laboratory Head: Garvan Institute of Medical Research; Financial Interests, Institutional, Other, I am inventor of a patent lead by my institution above: International (PCT) Patent Application No. PCT/AU2023/050849Prognostic Markers (plasma lipid prognostic signature in metastatic prostate cancer).Inventors: Horvath L, Meikle P, Scheinberg S, Lin HM, Sullivan D: Chris O'Brien Lifehouse; Financial Interests, Institutional, Research Grant: Astellas; Financial Interests, Institutional, Local PI, MK7684-001MK3475-991: MSD; Financial Interests, Institutional, Local PI, AMG160 Phase 1AMG509 Phase 1AMG757 Phase 1: Amgen; Financial Interests, Institutional, Local PI, 9785-CL-0335 (ARCHES): Astellas; Financial Interests, Institutional, Local PI, SHR3680-002: Jiangsu Hengrui Medicines; Financial Interests, Institutional, Local PI, TALAPRO2, TALAPRO3: Pfizer; Financial Interests, Institutional, Local PI, CYCLONE-2, CYCLONE-3: Eli-Lilly; Financial Interests, Institutional, Steering Committee Member, ENZAMET, ENZARAD, DASL-HiCAP, GUIDE, ANZAdapt: ANZUP; Financial Interests, Institutional, Local PI, GALAHADACISPrevalence: Janssen-Cilag; Financial Interests, Institutional, Local PI, GSK204697: GSK; Financial Interests, Institutional, Local PI, XL184-021: Exelixis; Financial Interests, Institutional, Local PI, BGB-A317BGB-283BGB-A317-290: Beigene; Financial Interests, Institutional, Local PI, FPT155-001: Five Prime; Financial Interests, Institutional, Local PI, AB928CSP0003: ARCUS; Financial Interests, Institutional, Local PI, ATG-017 and ATG-019: Antagene; Financial Interests, Institutional, Local PI, JANUX007: Janux; Financial Interests, Institutional, Local PI, Petranha: AstraZeneca; Financial Interests, Institutional, Local PI, ENZAMET, ENZA-P, Upfront PSMA, ANZAdapt, GUIDE: ANZUP; Financial Interests, Institutional, Local PI, HP-518-CS-001: Hinova; Financial Interests, Institutional, Local PI, JANX007: Janux Therapeutics; Financial Interests, Institutional, Funding, Bayer is providing funding and drug for the DARO-LIPID trial run through ANZUP collaborative cancer trial group. I am chair of the trial: Bayer; Financial Interests, Institutional, Other, Redhill biopharma is providing drug for the DARO-LIPID trial run through ANZUP collaborative cancer trial group. I am chair of the trial: Redhill Biopharma; Non-Financial Interests, Leadership Role, Professor of Medical Oncology (Genitourinary cancer): University of Sydney; Non-Financial Interests, Leadership Role, Adjunct Professor: University of New South Wales. R. Jones: Financial Interests, Personal, Advisory Board: Astellas, AstraZeneca, Bayer, Johnson & Johnson, MSD, Merck, Pfizer; Financial Interests, Institutional, Funding: Exelixis, Clovis, Astellas, Roche, Bayer; Financial Interests, Personal, Invited Speaker: Astellas, AstraZeneca, Bayer, Johnson & Johnson, Merck Serono, Pfizer; Non-Financial Interests, Institutional, Local PI: Astellas, AstraZeneca, Bayer, Johnson & Johnson, MSD, Pfizer; Financial Interests, Personal, Other, IDMC member: Roche. M. Maruzzo: Financial Interests, Personal, Advisory Board: Johnson & Johnson, Astellas, Merck, AstraZeneca, Eisai, Recordati, Ipsen, MSD, Bayer, BMS. B. Webb: Financial Interests, Personal, Full or part-time Employment: AstraZeneca. N. Camacho: Financial Interests, Personal, Full or part-time Employment: AstraZeneca. Y. Kim: Financial Interests, Personal, Full or part-time Employment: AstraZeneca; Financial Interests, Personal, Stocks/Shares: AstraZeneca. B. De Paula: Financial Interests, Personal, Full or part-time Employment: AstraZeneca; Financial Interests, Personal, Stocks/Shares: AstraZeneca. T. Milenkova: Financial Interests, Personal, Full or part-time Employment: AstraZeneca; Financial Interests, Personal, Stocks/Shares: AstraZeneca. A. Hudson: Financial Interests, Personal, Advisory Board: AstraZeneca, Pfizer, Janssen; Financial Interests, Personal, Funding, Travel Support: Merck Serono, Janssen; Financial Interests, Personal, Invited Speaker: AstraZeneca, Merck Serono, Janssen, Novartis. All other authors have declared no conflicts of interest.