BERLIN 2025 ESMO congress

2391P

LuPARP: Phase I trial of [177Lu]Lu-PSMA-617 (LuPSMA) and olaparib in patients (pts) with metastatic castration resistant prostate cancer (mCRPC)

S.K. Sandhu[1], A.M. Joshua[2], L. Emmett[3], M. Crumbaker[2], M. Bressel[4], R. Huynh[5], J. Chan[1], P.D. Banks[1], R. Wallace[1], A. Hamid[1], A.J. Inderjeeth[1], R. Alipour[6], G. Kong[6], A.S. Ravi Kumar[6], B. Tran[1], S.H. Tolmeijer[7], J.P. Buteau[6], S. Williams[8], R.J. Hicks[9], M.S. Hofman[6]

[1] Department of Medical Oncology, Peter MacCallum Cancer Centre and Sir Peter MacCallum Department of Oncology, The University of Melbourne, Melbourne, Australia, [2] Medical Oncology, The Kinghorn Cancer Centre, Sydney, Australia, [3] Department of Molecular Imaging, St. Vincent's Hospital, Sydney, Australia, [4] Centre for Biostatistics and Clinical Trials, Peter MacCallum Cancer Centre, Melbourne, Australia, [5] Parkville Cancer Clinical Trials Unit, Peter MacCallum Cancer Centre, Melbourne, Australia, [6] Molecular Imaging and Therapeutic Nuclear Medicine, Peter MacCallum Cancer Centre and Sir Peter MacCallum Department of Oncology, The University of Melbourne, Melbourne, Australia, [7] Department of Urologic Sciences, Vancouver Prostate Centre The University of British Columbia, Vancouver, Canada, [8] Department of Radiation Oncology, Peter MacCallum Cancer Centre and Sir Peter MacCallum Department of Oncology, The University of Melbourne, Melbourne, Australia[9] St Vincent's Medical School, The University of Melbourne, Melbourne, Australia

Background

LuPSMA, a radioligand (RLT) therapy improved radiological progression-free survival (rPFS) (median 8.7 months) and overall survival (OS) (median 15.3 months) for mCRPC in the VISION trial. Preclinical studies support using potent PARP inhibitors such as olaparib as a radiosensitizer to enhance RLT activity. LuPARP evaluates the safety and preliminary efficacy of LuPSMA with olaparib.

Methods

LuPARP is a phase 1 trial utilizing a 3+3 design for dose escalation followed by dose expansion. Pts with mCRPC with high PSMA expression (SUVmax ≥15) without discordant FDG+ /PSMA- sites were enrolled. All pts received LuPSMA 7.4 GBq every 6 weeks for up to 6 cycles. Olaparib was dosed across 10 dose levels (DL) (DL1-6: 50mg - 300mg BD days 2 to 15, DL7: 200mg BD days -4 to 14; DL8: 300mg BD days -4 to 14; DL9: 300mg BD days -4 to 18; DL10: 300mg BD, days -4 to day 42). Primary endpoints were safety and dose limiting toxicity (DLT). Key secondary endpoints were rPFS, PSA response rate (PSA50-RR), PSA-PFS, objective response rate and OS.

Results

Between Sept 2019 to Nov 2023, 48 pts were enrolled; median age 70 years, all received prior ARPI, 98% received prior docetaxel. There were no DLTs. DL9 (n=22) was determined to be the recommended phase II dose (RP2D) based on combined safety and efficacy. At DL9, treatment related adverse events (TRAE) (≥10%) included grade (G) 1-2 xerostomia (77%), nausea (64%), neutropenia (59%), fatigue (55%), anemia (41%), constipation (23%) and vomiting (14%). Four pts had G3-4 hematological TRAE: two G3 thrombocytopenia, one G3 anemia + thrombocytopenia and one G4 thrombocytopenia. At DL9, PSA50-RR was 68% (15/22) and PSA90-RR was 55% (12/22). With a median follow-up of 17 months in DL9, the median rPFS was 13.3 months (95% CI: 5.7, 14.8) and the median OS was not reached. With a median follow-up of 19 months in the day -4 cohorts (DL7-9, n=29) the median OS was 33.5 months (95% CI: 33.5, NE). At DL9, the 12-month PSA-PFS, rPFS and OS rates were 50% (95% CI: 30-67), 52% (95% CI: 32-69) and 93% (95% CI: 74-98), respectively. Of the 8 pts with RECIST measurable disease in DL9, 7 (88%) had a partial response.

Conclusions

The combination of LuPSMA with intermittent olaparib dosing is safe and has promising activity.

Clinical trial identification

NCT03874884.

Legal entity responsible for the study

Peter MacCallum Cancer Centre, Australia.

Funding

Prostate Cancer Foundation, USA; AstraZeneca; Endocyte (A Novartis company).

Disclosure

S.K. Sandhu: Financial Interests, Institutional, Advisory Board, I have served on advisory boards for MSD. The e contracts for my role are set up with the institution and the funds go to a research fund at Peter MacCallum Cancer Centre.: Merck Sharp and Dohme; Financial Interests, Institutional, Advisory Board, I have served on advisory boards for AstraZeneca. The contracts for my role as an advisor are set up with the institution and the funds go to a research fund at Peter MacCallum Cancer Centre.: AstraZeneca; Financial Interests, Institutional, Advisory Board, I have served on advisory boards for Novartis. The contracts for my role as an advisor are set up with the institution and the funds go to a research fund at Peter MacCallum Cancer Centre.: Novartis; Financial Interests, Institutional, Advisory Board, I have served on an advisory board for Merck Serono. The contracts for my service are set up with the institution and funds go into a research fund at the Peter MacCallum Cancer Centre.: Merck Serono; Financial Interests, Institutional, Advisory Board, I have served on an advisory board for SkylineDx. The contracts for my service are set up with the institution and funds go into a research fund at the Peter MacCallum Cancer Centre.: SkylineDx; Financial Interests, Institutional, Advisory Board, I have served on an advisory board for AbbVie. The contracts for my role are with the institution and funds go into a research fund at the Peter MacCallum Cancer Centre.: AbbVie; Financial Interests, Institutional, Invited Speaker, I have received honoraria for invited speaker role only which is paid to my institution. Funds go into a research fund at the Peter MacCallum Cancer Centre.: Janssen; Financial Interests, Personal, Other, Equity (stock): AdvanCell; Financial Interests, Personal, Stocks/Shares: AdvanCell; Financial Interests, Institutional, Research Grant, My institution receives grant funding to run an investigator initiated trial that I lead.: Novartis, Genentech, Amgen, AstraZeneca, Merck Serono, Merck Sharp and Dohme; Financial Interests, Institutional, Research Grant, Pfizer are providing funding to my institution for the conduct of an investigator initiated clinical trial.: Pfizer; Financial Interests, Institutional, Research Grant, Senwha are providing funding to my institution for the conduct of an investigator initiated clinical trial.: Senwha; Non-Financial Interests, Other, I serve on the Independent Safety and Data Monitoring committee for 2 of Novartis sponsored studies and don't receive any compensation for this.: Novartis; Non-Financial Interests, Other, I serve on the steering committee for several Janssen sponsored trials and i do not receive compensation for this.: Janssen; Non-Financial Interests, Other, I serve on the steering committee for one AstraZeneca sponsored trial and I do not receive compensation for this.: AstraZeneca; Non-Financial Interests, Other, I serve on the steering committee for one Genentech sponsored trials and I do not receive compensation for this.: Genentech; Non-Financial Interests, Other, I serve on the steering committee for a Bristol Myer Squibb sponsored trial and I do not receive renumeration for this.: Bristol Myer Squibb; Non-Financial Interests, Principal Investigator, I am a principal investigator on several of Janssen sponsored studies and don't receive any renumeration for this.: Janssen; Non-Financial Interests, Principal Investigator, I am a principal investigator on several Novartis sponsored studies and don't receive any renumeration for this.: Novartis; Non-Financial Interests, Principal Investigator, I am a principal investigator on several of Genentech sponsored studies and don't receive any renumeration for this.: Genentech; Non-Financial Interests, Principal Investigator, I am a principal investigator on several of Bristol Myer Squibb sponsored studies and don't receive any renumeration for this.: Bristol Myer Squibb; Non-Financial Interests, Principal Investigator, I am the Principal Investigator for several AstraZeneca sponsored studies and am not remunerated for this.: AstraZeneca; Non-Financial Interests, Principal Investigator, I am a principal investigator on a MacroGenics sponsored study and don't receive any renumeration for this.: MacroGenics; Non-Financial Interests, Principal Investigator, I am a principal investigator on a Regeneron sponsored study and do not receive any renumeration for this.: Regeneron; Non-Financial Interests, Principal Investigator, I am the Principal Investigator on several Merck Sharp and Dohme studies and I do not receive any renumeration for this.: Merck Sharp and Dohme; Non-Financial Interests, Principal Investigator, I am a principal investigator on an IO Biotech study and I do not receive any renumeration for this.: IO Biotech; Non-Financial Interests, Principal Investigator, I am principal investigator on an Evaxion sponsored study and I do not receive any renumeration for this: Evaxion. A.M. Joshua: Financial Interests, Institutional, Local PI: Janssen, Ipsen, AstraZeneca, Sanofi, Pfizer, Novartis, Bristol-Myers Squibb, Merck Serono; Financial Interests, Institutional, Steering Committee Member: Iqvia; Financial Interests, Institutional, Coordinating PI: ideaya, essa; Non-Financial Interests, Advisory Role: Bristol-Myers Squibb, Janssen, Merck, Mayne, Roche, Bayer, Pfizer, Eli-Lilly, Eisai, Medison, Grey Wolf Therapeutics; Non-Financial Interests, Principal Investigator: Ideaya, essa. L. Emmett: Non-Financial Interests, Institutional, Research Grant: Novartis, Clarity Pharma; Non-Financial Interests, Institutional, Advisory Role: Astellas; Other, Institutional, Speaker, Consultant, Advisor: Janssen, AstraZeneca, Clarity, Advancell, Telix. M. Crumbaker: Financial Interests, Personal, Advisory Board, Advisory board member periodically - Most recently Feb 2025, previously Mar 2023.: Astellas; Financial Interests, Personal, Full or part-time Employment, Associate medical director part-time for Advancell: Advancell. A. Hamid: Financial Interests, Personal, Advisory Board, Advisory Board: MSD; Financial Interests, Personal, Advisory Board: AstraZeneca, Astellas; Financial Interests, Personal, Invited Speaker: Bayer; Financial Interests, Institutional, Local PI: Astellas. G. Kong: Financial Interests, Personal, Advisory Board: ITM; Financial Interests, Personal, Invited Speaker: IPSEN; Financial Interests, Institutional, Invited Speaker: SAM NORDIC; Financial Interests, Institutional, Local PI: Clarity; Financial Interests, Institutional, Coordinating PI: Cyclotek; Non-Financial Interests, Other, Committee member: Neuroendocrine Cancer Australia. B. Tran: Financial Interests, Personal, Advisory Board: Amgen, AstraZeneca, Astellas, Bayer, BMS, Ipsen, IQVIA, Janssen, Merck, MSD, Novartis, Pfizer, Roche, Sanofi, Tolmar, Sanofi Ammunix; Financial Interests, Personal, Invited Speaker: Amgen, Astellas, AstraZeneca, Bayer, BMS, Merck, Pfizer; Financial Interests, Institutional, Research Grant: Amgen, Astellas, AstraZeneca, Bayer, BMS, Genentech, Ipsen, Janssen, Pfizer, MSD; Financial Interests, Personal, Steering Committee Member: CG Oncology, Janssen, MSD. M.S. Hofman: Financial Interests, Institutional, Advisory Board: Novartis; Financial Interests, Personal, Invited Speaker, PROSPECT23: Janssen; Financial Interests, Personal, Advisory Board: MSD; Financial Interests, Institutional, Research Grant: Novartis, Isotopia Molecular Imaging, Bayer; Other, Other, Research Support: Prostate Cancer Foundation (PCF). All other authors have declared no conflicts of interest.