

LBA89

A randomized phase II study of ¹⁷⁷Lu-PSMA-617 vs docetaxel in patients with metastatic castration-resistant prostate cancer (mCRPC) and PSMA-positive disease: Canadian Cancer Trials Group (CCTG) study PR.21

K.N. Chi¹, F. Saad², K. Ding³, G. Bauman⁴, U. Emmenegger⁵, S.J. Hotte⁶, F. Pouliot⁷, J. Lee⁸, J-M. Beauregard⁹, L. Nappi¹⁰, C.K. Kollmannsberger¹¹, Z. Hamilou², G. Abikhzer¹², M. Pavic¹³, S. North¹⁴, D.M. Jiang¹⁵, S.M. Yip¹⁶, C. Dellar¹⁷, W.R. Parulekar¹⁷, F. Benard¹⁸

¹ Medical Oncology, BC Cancer - Vancouver Centre, Vancouver, Canada, ² Urology Department, Centre Hospitalier de Université de Montréal (CHUM), Montreal, Canada, ³ Canadian Cancer Trials Group, Kingston, Canada, ⁴ Radiation Oncology, London Health Sciences Centre and Western University, London, Canada, ⁵ Medical Oncology Department, Sunnybrook Health Sciences Centre - Odette Cancer Centre, Toronto, Canada, ⁶ Oncology Department, JCC - Juravinski Cancer Centre - Hamilton Health Sciences, Hamilton, Canada, ⁷ Surgery Department ni, Université Laval, CHU de Québec, Québec City, Canada, ⁸ Dept of Urologic Sciences, UBC - The University of British Columbia, Vancouver, Canada, ⁹ Dept of Medical Imaging, CHU de Québec - Université Laval, Québec City, Canada, ¹⁰ Medical Oncology, BC Cancer Vancouver and Vancouver Prostate Centre, Vancouver, Canada, ¹¹ Medical Oncology Department, BC Cancer Agency - Vancouver, Vancouver, Canada, ¹² Dept of Radiology, Jewish General Hospital McGill University, Montreal, Canada, ¹³ Dept of Medical Oncology, Centre Hospitalier Universitaire de Sherbrooke, Québec, Canada, ¹⁴ Medical Oncology Department, University of Alberta Cross Cancer Institute, Edmonton, Canada, ¹⁵ Medical Oncology Dept., University Health Network - Princess Margaret Cancer Center, Toronto, Canada, ¹⁶ Oncology Department, Arthur J.E. Child Comprehensive Cancer Centre and Cumming School of Medicine, Calgary, Canada, ¹⁷ Queen's University - Sinclair Cancer Research Institute, Canadian Cancer Trials Group, Kingston, Canada ¹⁸ Molecular Imaging and Therapeutics, BC Cancer - Vancouver, Vancouver, Canada

Background

Compared to a change in androgen receptor pathway inhibitor (ARPI), ¹⁷⁷Lu-PSMA-617 (LU-P) prolongs radiographic progression free survival (rPFS) in patients with mCRPC. We sought to compare treatment with LU-P vs. docetaxel (DOC) in patients with mCRPC progressing after ARPI therapy.

Methods

CCTG PR.21 is a multi-centre open-label randomized phase II trial. Patients with chemotherapy-naïve, PSMA-PET positive mCRPC progressing after ARPI therapy were randomized 1:1 to receive LU-P 7.4 GBq IV q6 weeks max 6 cycles or DOC 75 mg/m² IV q3 weeks max 12 cycles with cross-over at progression. The primary endpoint is rPFS; secondary endpoints include: overall survival (OS), PSA response rate (RR), objective response rate (ORR) and patient reported outcomes (PROs). Correlative studies include baseline PSMA PET SUV and serial ctDNA sampling.

Results

199 patients were enrolled from 08/21-01/24;189 treated. Study arms were balanced: median age 70 years, 53% ECOG PS 0, 21% visceral metastases, 14% received prior DOC in the mCSPC setting (≥1 year prior to enrollment was permitted). At the protocol prespecified minimum 152 rPFS events for the primary analysis, the median follow-up was 9.7 months (mo) and 54% had crossed-over to per protocol therapy: 40 from LU-P to DOC; 62 from DOC to LU-P. PSA decline of ≥50% (PSA RR) occurred in 53% and 32% in the LU-P and DOC arms respectively. In patients with measurable disease, ORR was 16% (LU-P) vs 8% (DOC). Grade 3/4 treatment related adverse events were higher in the DOC arm: 34% vs 13%. There were 2 DOC treatment related deaths. Table: LBA89

Outcome	LU-P (n=100) Median	DOC (n=99) Median	HR (LU-P/DOC)	p-value
rPFS(mo)	8.6 (90%CI 7.13 -10.60)	10.7 (90%CI 7.82-11.10)	1.02 (90%CI 0.77-1.35)	0.54 (1 sided)
OS(mo)	14.3 (90%CI 10.8-16.6)	18.2 (90%CI 16.1-23.0)	1.64 (90%CI 1.14-2.35)	0.02 (2 sided)

Conclusions

In the PR21 study population of patients with chemo-naïve mCRPC, there was no significant rPFS difference between LU-P and DOC. PSA RR, ORR and frequency of treatment related grade 3/4 AEs favoured LU-P; OS favoured the arm assigned to DOC at randomization.

Clinical trial identification

NCT04663997.

Legal entity responsible for the study

Canadian Cancer Trials Group.

Funding

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Disclosure

K.N. Chi: Financial Interests, Personal, Invited Speaker: Astellas, AstraZeneca, Janssen, Novartis; Financial Interests, Personal, Advisory Board: Astellas, AstraZeneca, AstraZeneca, BMS, Janssen, Merck, Novartis, Pfizer, Roche, Amgen; Financial Interests, Institutional, Steering Committee Member: AstraZeneca, Janssen, Novartis, Roche; Financial Interests, Institutional, Trial Chair: AstraZeneca, Janssen, Novartis, BMS. F. Saad: Financial Interests, Personal, Advisory Board: Astellas, Bayer, BMS, Janssen, Pfizer, Novartis, AstraZeneca, Merck, Sumitomo; Financial Interests, Institutional, Local PI: Novartis, Astellas, bayer, Janssen, Sanofi, Bms, Pfizer, Merck; Financial Interests, Institutional, Coordinating PI: AstraZeneca; Non-Financial Interests, Principal Investigator: Bayer, AstraZeneca. G. Bauman: Financial Interests, Personal, Speaker’s Bureau: Novartis, Ter Sera, AbbVie; Non-Financial Interests, Personal, Advisory Role: Probe Development and Commercialization; Financial Interests, Personal, Leadership Role: Ontario Institute for Cancer Research. U. Emmenegger: Financial Interests, Personal, Advisory Board, and CME activities: Amgen, AstraZeneca, Bayer, Ferring, Janssen, Merck, Novartis (Endocyte/AAA), Pfizer; Financial Interests, Personal, Other, CME activities: Ipsen; Financial Interests, Personal, Advisory Board: Knight; Financial Interests, Personal, Research Funding, Investigator Initiated Study: Astellas, Bayer, Janssen; Financial Interests, Institutional, Funding, Financial support to Sunnybrook Research Institute for the conduct of clinical studies: Amgen, Arvinas, Astellas, AstraZeneca, Bayer, Clovis/Pharma, Janssen, Merck, Novartis (Endocyte/AAA), Pfizer, Eli Lilly (Point Biopharma), Roche Genetech, Telix. S.J. Hotte: Financial Interests, Personal, Advisory Board, Consultancy: Novartis, Astellas, Bayer, J&J; Financial Interests, Personal, Advisory Role, Consultancy: Pfizer; Financial Interests, Institutional, Other, Clinical Trials, Contracted Research: Astellas, Bayer, Janssen, Novartis; Financial Interests, Institutional, Other, Clinical Trials: AstraZeneca, Ayala, BMS, Eisai, Ipsen, Merck, Roche, Lilly, Sanofi, SeaGen/Pfizer, SignalChem; Non-Financial Interests, Personal, Leadership Role, GU DSG Chair: Canadian Cancer Trials Group; Non-Financial Interests, Personal, Leadership Role, GU Drug Advisory Committee; Program for Evidence Based Care; RLT Working Group: OntarioHealth/CancerCare Ontario; Non-Financial Interests, Personal, Leadership Role, Director, Board of Directors: Hamilton Health Sciences Foundation. F. Pouliot: Financial Interests, Personal, Advisory Role, Grant, Honoraria & Advisor: Ter Sera, Tolmar, Janssen, Astellas, Bayer, Pfizer, Novartis, Merck, Roche. J. Lee: Financial Interests, Personal, Advisory Role: Ter Sera. J. Beauregard: Financial Interests, Personal, Advisory Role: Novartis; Financial Interests, Personal, Other, Conference Honoraria: Novartis. L. Nappi: Financial Interests, Personal, Advisory Board, Speaker at educational events, Advisory Board: Ipsen, Bayer, Pfizer, AstraZeneca; Financial Interests, Personal, Speaker’s Bureau, Speaker at educational events: Merck, Janssen, EMD Serono; Financial Interests, Personal, Advisory Board: Eisai, Novartis; Financial Interests, Personal, Funding, Educational Grant: Ipsen, Bayer, EMD Serono; Non-Financial Interests, Personal, Leadership Role, Adolescent and Young Adults Committee Vice-Chair: SWOG. C.K. Kollmannsberger: Financial Interests, Personal, Advisory Board, ad-hoc advisory board: Pfizer, Ipsen, BMS, Eisai, Merck, Bayer, Astellas; Financial Interests, Personal, Invited Speaker, honoraria for educational presentation: Pfizer; Financial Interests, Personal, Invited Speaker, honoraria for educational lectures: Ipsen; Financial Interests, Personal, Invited Speaker, honoraria for presentations: BMS, Eisai, Merck, Seagen, Bayer, Astellas, Janssen; Financial Interests, Personal, Advisory Board, Ad-hoc advisory board: Seagen, Janssen, AstraZeneca; Financial Interests, Personal, Advisory Board, ad hoc advisory board: BionTech, Novartis; Financial Interests, Personal, Invited Speaker: Novartis. G. Abikhzer: Financial Interests, Personal, Speaker’s Bureau, Consultancy and Speaker Honoraria: Novartis; Financial Interests, Personal, Speaker’s Bureau, Speaker Honoraria: Cyclomedica; Non-Financial Interests, Personal, Member of Board of Directors, General Clinical Nuclear Medicine Board of Directors: SNMMI. M. Pavic: Financial Interests, Personal, Advisory Role, Consultancy; Advisory Role; Teaching Program: Janssen, Sanofi, AbbVie, Pfizer, Novartis, Bayer, Merck; Financial Interests, Institutional, Research Funding, Research: Sanofi, Merck, AstraZeneca, BMS, Novartis, Janssen, Pfizer, Takeda. S. North: Financial Interests, Personal, Advisory Board, honoraria: Astellas, BMS, Merck, roche, Bayer, AstraZeneca, Novartis; Financial Interests, Institutional, Local PI, per case funding: AstraZeneca, Ipsen, Astellas, Roche. D.M. Jiang: Financial Interests, Personal, Advisory Board, Advisory Board; Speaker Fees: Novartis, Bayer, Pfizer, EMD Serono, AstraZeneca, Merck, Janssen, Astellas, Amgen; Financial Interests, Personal, Advisory Board: McKesson; Financial Interests, Institutional, Principal Investigator, Site PI for Clinical Trial: Point Biopharma, Eli Lilly, AstraZeneca, Pfizer, Merck; Non-Financial Interests, Personal, Leadership Role, PMH Site Representative: Canadian Cancer Trials Group; Non-Financial Interests, Personal, Leadership Role, Co-Lead, Theranostic Centre, UHN: UHN; Other, Personal, Other, Travel: Janssen, Pfizer, EMD, Serono, Novartis. S.M. Yip: Financial Interests, Personal, Advisory Board, Consultancy, advisory board, honoraria, speaking engagement, speaker’s bureau: Amgen, Astellas, AstraZeneca, Bayer, BMS, Hoffman La Roche, Ipsen, Janssen, Merck, Novartis, Oncohelix, Pfizer. F. Benard: Financial Interests, Personal, Other, Consultant: Alpha-9 Oncology; Financial Interests, Personal, Stocks or ownership, Founder and Shareholder: Alpha-9 Oncology; Financial Interests, Personal, Licencing Fees or royalty for IP, IP Licensing: Alpha-9 Oncology, Telix; Financial Interests, Personal, Research Funding, Collaborative Research Agreement: Alpha-9 Oncology; Financial Interests, Institutional, Licencing Fees or royalty for IP, IP Licensing: Alpha-9 Oncology, Telix. All other authors have declared no conflicts of interest.