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Abiraterone acetate plus prednisolone (AAP) with or without enzalutamide (ENZ) added to androgen deprivation therapy (ADT) compared to ADT alone for men with high-risk non-metastatic (M0) prostate cancer (PCa): Combined analysis from two comparisons in the STAMPEDE platform protocol

G. Attard[1], L.C. Brown[2], N. Clarke[3], L. Murphy[2], W. Cross[4], R. Jones[5], S. Gillessen[6], J.M. Russell[7], A. Cook[8], J. Bowen[9], A. Lydon[10], I.D. Pedley[11], O. Parikh[12], S. Chowdhury[13], Z. Malik[14], D. Matheson[15], C. Parker[16], M.R. Sydes[17], M.K. Parmar[18], N.D. James[19]

[1] Research Department of Oncology, University College London Cancer Institute, London, UK, [2] MRC Clinical Trials Unit, University College London, London, UK, [3] Surgery, Manchester University, Manchester, UK, [4] Department of Urology, St James University Hospital, Leeds, UK, [5] Institute of cancer sciences, BWSCC - Beatson West of Scotland Cancer Centre - NHS Greater Glasgow and Clyde, Glasgow, UK, [6] Medical Oncology Department, EOC - Ospedale Regionale Bellinzona e Valli - Istituto Oncologico della Svizzera Italiana (IOSI), Bellinzona, Switzerland, [7] Institute of Cancer Sciences, University of Glasgow, Glasgow, UK, [8] Clinical Trials Unit, Institute of Clinical Trials and Methodology-UCL, London, UK, [9] Oncology, Gloucester NHS Foundation Trust, Gl El, UK, [10] Oncology, Torbay and South Devon NHS Foundation Trust, Tqaa, UK, [11] Oncology, The Freeman Hospital (NHS Foundation Trust) Northern Centre for Cancer Care, Newcastle-upon-Tyne, UK, [12] Oncology, Royal Preston Hospital-Lancashire Teaching Hospitals NHS Foundation Trust, Preston, UK, [13] Medical Oncology Dept., Guy's and St. Thomas' Hospital NHS Trust, London, UK, [14] Oncology, The Clatterbridge Cancer Centre NHS Foundation Trust, L Ya, UK, [15] Faculty of Education, Health and Wellbeing, University of Wolverhampton, Wv Ly, UK, [16] Department of Urology, The Royal Marsden Hospital NHS Foundation Trust, Sutton, UK, [17] MRC Clinical Trials Unit at UCL, Medical Research Council Clinical Trials Unit, London, UK, UK, [18] MRC Clinical Trials Unit, Institute of Clinical Trials and Methodology-UCL, London, UK[19] Prostate and Bladder Cancer Research Department, ICR - Institute of Cancer Research, London, UK

Background

Patients (pts) with high-risk M0 PCa are treated with ADT and when indicated, local radiotherapy (RT). Intensifying hormone treatment with AAP, ENZ or apalutamide continuous to progression improves outcomes of metastatic PCa but its efficacy in M0 PCa starting ADT is unknown.

Methods

STAMPEDE is a multi-arm, multi-stage trial that, as part of 2 separate comparisons randomised PCa pts with M0 node positive or high-risk node negative (>1 T3/4, PSA ≥40ng/ml, Gleason 8-10 or relapsing) 1:1 to ADT (control) vs ADT with AAP (1000mg AA + 5mg P od) or ADT vs ADT with AAP + ENZ (160mg od) for 2 years (y), unless RT was omitted when treatment could be to progression. The primary end-point was metastasis-free survival (MFS, time to death or distant metastases). The sub-group of pts who received ADT +/- AAP was partially reported with metastatic pts in 2017 so one-sided type 1 error rate was set to 1.25%. All analyses were pre-specified, pooled using meta-analyses methods and stratified as described previously. Data frozen 3rd August 2021.

Results

1974 M0 pts at 113 sites in UK & Switzerland were randomised, 914 (Nov 2011 to Jan 2014) to ADT +/- AAP & 1060 (Mar 2016 to Jul 2014) to ADT +/- AAP + ENZ. Groups were well balanced: median age 68 y, range 43-86; median PSA 34 ng/ml, range 0.4-2773; Gleason 8-10, 79%; node positive 39%; planned for RT 85%. Median months to stopping AAP, 23.7 (IQR: 17.6-24.1); AAP when given with ENZ, 20.7 (IQR: 4.4-24); ENZ, 23.2 (IQR: 6.3-24). 180 MFS events occurred in the research group and 306 in the control group. AAP-based therapy improved MFS (HR 0.53, 95% CI 0.44-0.64, $P=2.9\times10^{-11}$) & survival (HR 0.60, 95% CI 0.48-0.73, $P=9.3\times10^{-7}$): 6-y MFS from 69% to 82%, 6-y survival from 77% to 86%. Treatment effect was consistent in major subgroups and between AAP & AAP + ENZ randomisation periods (MFS HR=0.54, 95% CI 0.43-0.68; HR=0.53, 95% CI 0.39-0.71 respectively; interaction HR = 1.02, 95% CI: 0.70-1.50, p=0.908).

Conclusions

2 y of AAP-based therapy significantly improves MFS & survival of high-risk M0 PCa starting ADT and should be considered a new standard of care.

Clinical trial identification

NCT00268476.

Legal entity responsible for the study

Medical Research Council Clinical Trials Unit at University College London.

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Disclosure

G. Attard: Financial Interests, Personal, Invited Speaker: Janssen; Financial Interests, Personal, Advisory Board: Janssen; Financial Interests, Personal, Invited Speaker: Astellas; Financial Interests, Personal, Advisory Board: Astellas; Financial Interests, Personal, Advisory Board: Novartis; Financial Interests, Personal, Advisory Board: Bayer; Financial Interests, Personal, Invited Speaker: AstraZeneca; Financial Interests, Personal, Advisory Board: AstraZeneca; Financial Interests, Personal, Advisory Board: Pfizer; Financial Interests, Personal, Advisory Board: Sanofi; Financial Interests, Personal, Advisory Board: Sapience; Financial Interests, Personal, Advisory Board: Orion; Financial Interests, Personal, Royalties: Janssen; Financial Interests, Institutional, Research Grant: Janssen; Financial Interests, Institutional, Research Grant: Astellas; Non-Financial Interests, Principal Investigator: Janssen; Non-Financial Interests, Advisory Role: Janssen; Non-Financial Interests, Advisory Role: AstraZeneca; Non-Financial Interests, Principal Investigator: Astellas. L.C. Brown: Financial Interests, Institutional, Research Grant, FOCUS4-C Trial from June 2017 to Dec 2021: AstraZeneca. N. Clarke: Financial Interests, Personal, Invited Speaker: Astellas; Financial Interests, Personal, Invited Speaker: AstraZeneca; Financial Interests, Personal, Invited Speaker: Ferring; Financial Interests, Personal, Invited Speaker: Janssen; Financial Interests, Personal, Advisory Board: Astellas; Financial Interests, Personal, Advisory Board: AstraZeneca; Financial Interests, Personal, Advisory Board: Ferring; Financial Interests, Personal, Advisory Board: Janssen; Financial Interests, Institutional, Research Grant: AstraZeneca . W. Cross: Financial Interests, Personal, Invited Speaker, Speaker fee: Myriad Genetics; Financial Interests, Personal, Invited Speaker, Speaker fee: Janssen; Financial Interests, Personal, Advisory Board, Advisory Board fee: Bayer; Financial Interests, Personal, Invited Speaker, Speaker fee: Astellas; Financial Interests, Institutional, Research Grant, Research grant: Myriad Genetics. R. Jones: Financial Interests, Personal, Advisory Board, advisory board attendance: AstraZeneca; Financial Interests, Personal, Advisory Board, advisory board attendance: Astellas; Financial Interests, Personal, Invited Speaker, Honoraria for speaking: Astellas; Financial Interests, Personal, Advisory Board: Bayer; Financial Interests, Personal, Invited Speaker: Bayer; Financial Interests, Personal, Advisory Board: Clovis; Financial Interests, Personal, Advisory Board: Exelixis; Financial Interests, Personal, Advisory Board: Ipsen; Financial Interests, Personal, Invited Speaker: Ipsen; Financial Interests, Personal, Advisory Board: Bristol Myers Squipp; Financial Interests, Personal, Invited Speaker: Bristol Myers Squibb; Financial Interests, Personal, Advisory Board: Merck Serono; Financial Interests, Personal, Invited Speaker: Merck Serono; Financial Interests, Personal, Advisory Board: Merck Sharpe Dome; Financial Interests, Personal, Invited Speaker: Merck Sharpe Dome; Financial Interests, Personal, Invited Speaker: Pfizer; Financial Interests, Personal, Advisory Board: Roche; Financial Interests, Institutional, Other, IDMC membership: Roche; Financial Interests, Personal, Invited Speaker: Roche; Financial Interests, Personal, Advisory Board: Janssen; Financial Interests, Personal, Invited Speaker: Janssen; Financial Interests, Institutional, Other, IDMC member: Stab; Financial Interests, Personal, Advisory Board: Novartis / AAA; Financial Interests, Institutional, Invited Speaker: Janssen; Financial Interests, Institutional, Invited Speaker: Pfizer; Financial Interests, Institutional, Invited Speaker: Tail; Financial Interests, Institutional, Invited Speaker: AstraZeneca; Financial Interests, Institutional, Invited Speaker: BioXcel; Financial Interests, Institutional, Invited Speaker: Bristol Myers Squibb; Financial Interests, Institutional, Invited Speaker: Novartis / AAA; Financial Interests, Institutional, Invited Speaker: Roche; Financial Interests, Institutional, Invited Speaker: MSK. S. Gillessen: Financial Interests, Personal, Advisory Board, 2018: Sanofi; Financial Interests, Personal, Advisory Board, 2018, 2019: Orion; Financial Interests, Personal, Advisory Board, 2018: Roche; Financial Interests, Personal, Invited Speaker, 2019 Speaker's Bureau: Janssen Cilag; Financial Interests, Personal, Advisory Board, 2020: Amgen; Financial Interests, Personal, Invited Speaker, 2020: ESMO; Financial Interests, Personal, Other, Travel Grant 2020: ProteoMEdiX; Financial Interests, Institutional, Advisory Board, 2018, 2019: Bayer; Financial Interests, Institutional, Advisory Board, 2020: Janssen Cilag; Financial Interests, Institutional, Advisory Board, 2020: Roche; Financial Interests, Institutional, Advisory Board, 2018: AAA International; Financial Interests, Institutional, Advisory Board, 2018: Menarini Silicon Biosystems; Financial Interests, Institutional, Advisory Board, 2019, 2020: Astellas Pharma; Financial Interests, Institutional, Advisory Board, 2019: Tolero Pharmaceuticals; Financial Interests, Institutional, Advisory Board, 2020: MSD Merck Sharp & Dohme; Financial Interests, Institutional, Advisory Board, 2020: Pfizer; Financial Interests, Personal, Invited Speaker, 2021: SAKK; Financial Interests, Institutional, Advisory Board, 2021: Telixpharma; Financial Interests, Institutional, Other, Steering Committee 2021: Amgen; Financial Interests, Institutional, Invited Speaker, 2021: DESO; Financial Interests, Institutional, Advisory Board, 2021: BMS; Financial Interests, Institutional, Advisory Board, 2021: AAA International; Financial Interests, Institutional, Advisory Board, 2021: Orion; Financial Interests, Personal, Invited Speaker, 2021: SAKK; Financial Interests, Personal, Invited Speaker, 2021: SAKK; Financial Interests, Institutional, Advisory Board, 2021: Bayer; Financial Interests, Personal, Advisory Board, 2021: MSD Merck Sharp & Dhome; Financial Interests, Personal, Other, 2021: RSI (Televisione Svizzera Italiana); Financial Interests, Personal, Invited Speaker, 2021: SAMO - IBCSG; Financial Interests, Institutional, Funding, 2021, Unrestricted grant for a Covid related study as co-investigator: Astellas; Non-Financial Interests, Advisory Role, 2019: Menarini Silicon Biosystems; Non-Financial Interests, Advisory Role, 2019: Aranda; Non-Financial Interests, Advisory Role, Continuing: ProteoMediX. S. Chowdhury: Financial Interests, Personal, Advisory Board: Astellas; Financial Interests, Personal, Advisory Board: Janssen; Financial Interests, Personal, Invited Speaker: Janssen; Financial Interests, Personal, Advisory Board: Huma; Financial Interests, Personal, Invited Speaker: AstraZeneca; Financial Interests, Personal, Advisory Board: Bayer; Financial Interests, Personal, Invited Speaker: Bayer; Financial Interests, Personal, Advisory Board: Novartis/AAA; Financial Interests, Personal,

Advisory Board: Beigene; Financial Interests, Personal, Advisory Board: Remedy Bio; Financial Interests, Personal, Advisory Board: Athenex; Financial Interests, Personal, Advisory Board: Telix; Financial Interests, Personal, Advisory Board: Clovis Oncology; Financial Interests, Personal, Stocks/Shares: Curve Life; Financial Interests, Institutional, Research Grant: Clovis Oncology; Non-Financial Interests, Advisory Role, Non-compensated advice: NHS England; Non-Financial Interests, Advisory Role: NICE NHS England. Z. Malik: Financial Interests, Personal, Advisory Board, advisry board for new hormonal therapy for breast cancer: Sanofi; Other, support to attend meetings or advisory boards in the past: Astellas, Jaansen, Bayer. C. Parker: Financial Interests, Personal, Advisory Board, Education Steering Committee: Bayer; Financial Interests, Personal, Invited Speaker, Speaker at prostate cancer educational events: Janssen; Financial Interests, Personal, Advisory Board, Advisory board on apalutamide: Janssen; Financial Interests, Personal, Advisory Board, Advisory board: Clarity Pharmaceuticals; Financial Interests, Personal, Advisory Board, Advisory board on relugolix: Myovant; Financial Interests, Personal, Advisory Board, Advisory board: ITM Oncologics. M.R. Sydes: Financial Interests, Personal, Invited Speaker, Speaker fees at clinical trial statistics training sessions for clinicians (no discussion of particular drugs): Janssen; Financial Interests, Personal, Invited Speaker, Speaker fees at clinical trial statistics training session for clinicians (no discussion of particular drugs): Eli Lilly; Financial Interests, Institutional, Research Grant, Educational grant and drug for STAMPEDE trial: Astellas; Financial Interests, Institutional, Research Grant, Educational grant and biomarker costs for STAMPEDE trial: Clovis Oncology; Financial Interests, Institutional, Research Grant, Educational grant and drug for STAMPEDE trial: Janssen; Financial Interests, Institutional, Research Grant, Educational grant and drug for STAMPEDE trial: Novartis; Financial Interests, Institutional, Research Grant, Educational grant and drug for STAMPEDE trial: Pfizer; Financial Interests, Institutional, Research Grant, Educational grant and drug for STAMPEDE trial: Sanofi. M.K. Parmar: Financial Interests, Institutional, Research Grant: AstraZeneca, Astellas, Janssen, Clovis. N.D. James: Financial Interests, Personal, Advisory Board, Advice around PARP inhibitors: AstraZeneca; Financial Interests, Personal, Advisory Board, Prostate cancer therapies: Janssen; Financial Interests, Institutional, Expert Testimony, Assisted with submissions regarding licencing for abiraterone: Janssen; Financial Interests, Personal, Advisory Board, Docetaxel: Sanofi; Financial Interests, Institutional, Expert Testimony, Providing STAMPEDE trial data to facilitate licence extensions internationally for docetaxel: Sanofi; Financial Interests, Personal, Advisory Board, Prostate cancer therapies: Clovis; Financial Interests, Personal, Advisory Board, Prostate cancer therapies: Novartis; Financial Interests, Personal, Advisory Board, Bladder cancer therapy: Merck; Financial Interests, Institutional, Invited Speaker, Funding for STAMPEDE trial: Janssen; Financial Interests, Institutional, Invited Speaker, Funding for STAMPEDE trial: Astellas; Financial Interests, Institutional, Invited Speaker, Funding for RADIO trial bladder cancer: AstraZeneca. All other authors have declared no conflicts of interest.

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