BERLIN 2025 ESMO congress

LBA93

First results from RAMPART: An international phase III randomised-controlled trial of adjuvant durvalumab monotherapy or combined with tremelimumab for resected primary renal cell carcinoma (RCC) led by MRC CTU at UCL

J. Larkin[1], T.B. Powles[2], E. Frangou[3], G.D. Stewart[4], L. Albiges[5], I.D. Davis[6], M.R. Stockler[7], C. Suarez Rodriguez[8], B. Venugopal[9], P. Nathan[10], A. Bex[11], C. Gedye[12], D.J. Harrison[13], T.Q.G. Eisen[14], G. Patel[15], H. Plant[16], H.L. Rush[16], B. Choodari-Oskooei[17], M.K. Parmar[18], A.M. Meade[17]

[1] Medicine Department, The Royal Marsden Hospital - Chelsea, London, United Kingdom, [2] Oncology Department, St. Bartholomew's Hospital - Barts Health NHS Trust, London, United Kingdom, [3] Cancer Group, MRC Clinical Trials Unit at University College London (UCL), London, United Kingdom, [4] Clinical Oncology - R block (R4), University of Cambridge - Clinical Oncology - R block (R4), Cambridge, United Kingdom, [5] Medical Oncology, Institut Gustave Roussy, Université Paris Saclay, Villejuif, France, [6] Eastern Health Clinical School, Eastern Health Clinical School - Monash University, Box Hill, Australia, [7] NHMRC Clinical Trials Centre, NHMRC Clinical Trials Centre, Camperdown, Australia, [8] Department of Oncology, Vall d'Hebron University Hospital, Barcelona, Spain, [9] Medical Oncology Department, BWSCC - Beatson West of Scotland Cancer Centre - NHS Greater Glasgow and Clyde, Glasgow, United Kingdom, [10] Medical Oncology Department, Mount Vernon Cancer Centre, Northwood, United Kingdom, [11] Surgical Oncology/ Urology Dept, Royal Free London NHS Foundation Trust, London, United Kingdom, [12] ICON Cancer Centre Adelaide (Kurralta Park), ICON Cancer Centre Adelaide (Kurralta Park), Adelaide, Australia, [13] School of Medicine, University of St Andrews - School of Medicine, St Andrews, United Kingdom, [14] Department of Oncology, University of Cambridge, Cambridge, United Kingdom, [15] Cancer Group, MRC Clinical Trials Unit at UCL, Institute of Clinical Trials and Methodology, UCL, London, United Kingdom, [16] Cancer Division, MRC Clinical Trials Unit at University College London (UCL), London, United Kingdom, [17] Cancer Group, MRC Clinical Trials Unit-University College London, London, United Kingdom[18] Institute of Clinical Trials and Methodology, MRC Clinical Trials Unit at UCL, Institute of Clinical Trials and Methodology, UCL, London, United Kingdom

Background

RAMPART is a randomised trial of immune checkpoint inhibitor therapy for 1 year versus active monitoring after resection of primary renal cell carcinoma.

Methods

We recruited participants (pts) from 80 sites and randomised them in a 3:2:2 ratio between: Arm A, active monitoring; Arm B, 1 year (13 cycles) of durvalumab; or Arm C, 1 year (13 cycles) of durvalumab plus tremelimumab (cycles 1 and 2 only). Recruitment was stopped early for reasons other than efficacy or safety, and the statistical analysis plan was adjusted before any unblinded analyses. The modified plan gives 80% power to detect a true hazard ratio (HR) for disease free survival (DFS) of 0.55 for Arms C vs. A, and 0.60 for Arms B vs. A, with an overall, familywise, 1-sided type I error rate strongly controlled at 2.5% across all primary analyses. Here we present results of Arms C vs A. All p-values are 1-sided; 95% confidence intervals are 2-sided.

Results

Between October 2018 and June 2023, we randomised 790 pts: 340 Arm A, 225 Arm B, 225 Arm C. Baseline characteristics were similar in Arms C and A: median age (range) was 60 (22, 83) years, 70% were male, and 84% had clear cell histology. DFS was longer among those assigned durvalumab and tremelimumab (Arm C) than active monitoring (Arm A); DFS at 2 years 84% vs. 78%, HR 0.65, 95% CI 0.45 to 0.93, 1p=0.0094. Pre-specified and pre-powered DFS analysis in 311 higher-risk pts (Table) showed a HR= 0.52, 95% CI 0.34 to 0.80, 1p=0.0016 (2 year DFS Arm C 81% vs Arm A 67%), interaction HR 0.43, 95% CI 0.19, 0.95, 1p for testing whether the interaction equals 1=0.019; HR in intermediate risk pts was 1.19, 95% CI 0.61 to 2.32, 1p=0.309. No unexpected safety signals were observed. Results of Arms B vs A are expected in next 12 months.Table: LBA93

Risk at baseline

	A N=340	C N=225	Total N=565
Leibovich Intermediate Risk	151 (44%)	103 (46%)	254 (45%)
Leibovich High Risk	172 (51%)	111 (49%)	283 (50%)
M1NED	17 (5%)	11 (5%)	28 (5%)

Conclusions

Adjuvant therapy with durvalumab and tremelimumab after resection of RCC improved DFS, particularly among those at highest risk of relapse.

Clinical trial identification

NCT03288532; ISRCTN53348826; EudraCT: 2017-002329-39.

Legal entity responsible for the study

University College London.

Funding

AstraZeneca.

Disclosure

J. Larkin: Financial Interests, Personal, Other, Consultancy: Incyte, iOnctura, Apple Tree, Merck, BMS, Eisai, Debipharm, Pfizer, Novartis, MSD, Iovance Biotherapeutics, Boston Biomedical, YKT Global, Immunocore; Financial Interests, Personal, Other, Honorarium: touchIME, touchEXPERTS, Royal College of Physicians, Pfizer, Novartis, Incyte, Merck, Pfizer, Roche, iOnctura, Dynavax, CRUK, GSK, BMS; Financial Interests, Personal, Invited Speaker, Speaker Fee: BMS, Pfizer, Roche, Pierre Fabre, AstraZeneca, Novartis, EUSA Pharma, MSD, Merck, GSK, Ipsen, Aptitude, Eisai, Calithera, Ultimovacs, Seagen, eCancer; Financial Interests, Institutional, Funding: BMS, MSD, Novartis, Pfizer, Achilles, Roche, Nektar, Covance, Immunocore, Pharmacyclics, Aveo. T.B. Powles: Financial Interests, Personal, Advisory Board: AstraZeneca, Bristol Myers-Squibb, Exelixis, Incyte, Ipsen, Merck, Novartis, Pfizer, Seattle Genetics, Merck Serono, Astellas, Johnson & Johnson, Eisai, Roche, MSD; Financial Interests, Personal, Other, Travel/Accommodation/Expenses: Roche, Pfizer, MSD, AstraZeneca, Ipsen; Financial Interests, Personal, Other, Sponsorship for Uromigos Podcast: Mashup Ltd; Financial Interests, Institutional, Other, honoraria: Gilead; Financial Interests, Institutional, Research Grant: AstraZeneca, Roche, Bristol Myers-Squibb, Exelixis, Ipsen, Merck, MSD, Seattle Genetics, Novartis, Pfizer, Merck Serono, Astellas, Johnson & Johnson, Eisai; Financial Interests, Institutional, Other, Honoraria: Gilead. G.D. Stewart: Financial Interests, Personal, Other, Workshop on new product: Evinova; Financial Interests, Personal, Full or part-time Employment, Associate Editor - paid role: British Journal of Urology International; Financial Interests, Personal, Other, Topic Advisor of kidney cancer guideline: National Institute for Health and Care Excellence; Financial Interests, Personal, Full or part-time Employment, Clinical Director (surgery) for the National Kidney Cancer Audit: NATCAN; Financial Interests, Institutional, Funding, Funding of the WIRE clinical trial: AstraZeneca; Non-Financial Interests, Principal Investigator, Chair of the kidney cancer pathway: Getting It Right First Time; Non-Financial Interests, Member: European Association of Urology, British Association of Urological Surgeons; Other, Other, Funded attendance at ESMO 2023: MSD. L. Albiges: Financial Interests, Institutional, Other, Consulting: Astellas, BMS, Eisai, Ipsen, Janssen, MSD, Novartis, Pfizer, Roche, Merck, Amgen, Daiichi Sankyo, Xencor, Telix Pharmaceuticals; Financial Interests, Institutional, Other, Honoraria: Novartis; Non-Financial Interests, Principal Investigator, Clinical trial steering committee: Pfizer, BMS, AVEO, AstraZeneca, MSD; Non-Financial Interests, Principal Investigator: Ipsen; Non-Financial Interests, Other, Clinical trial steering committee: Roche, Exelixis, Telix Pharmaceuticals; Non-Financial Interests, Member: ASCO; Non-Financial Interests, Other, Medical Steering Committee: Kidney Cancer Association; Non-Financial Interests, Other, Member of the Renal Cell Carcinoma Guidelines Panel: European Association of Urology (EAU). I.D. Davis: Financial Interests, Personal, Full or part-time Employment, Professor of Medicine and Head of Eastern Health Clinical School: Monash University; Financial Interests, Personal, Full or part-time Employment, Professor of Medicine; Head, Eastern Health Clinical School; medical oncologist: Eastern Health; Financial Interests, Institutional, Local PI, Institutional support for clinical research: Movember Foundation, Merck/MSD, Bristol Myers Squibb, Exelixis, Astellas, Pfizer, AstraZeneca, Roche / Genentech, Eisai, Bayer, Janssen, Ipsen, Seagen; Financial Interests, Institutional, Local PI, EPI-7386-CS-010 trial: ESSA Pharma; Non-Financial Interests, Member of Board of Directors, Director and Chair; unremunerated: ANZUP Cancer Trials Group; Non-Financial Interests, Advisory Role, All honoraria and payments are made directly to ANZUP Cancer Trials Group with no pass-through payment: Roche, Eisai, Xennials Therapeutics, Telix Therapeutics, AstraZeneca, Bayer; Non-Financial Interests, Other, Member of Council: Clinical Oncology Society of Australia; Non-Financial Interests, Member: ASCO, Clinical Oncology Society of Australia, Medical Oncology Group of Australia, American Association for Cancer Research, Australian Academy of Health and Medical Sciences, Australian Society for Medical Research, American Association of Immunologists. M.R. Stockler: Financial Interests, Institutional, Research Grant, DASL: Bayer; Financial Interests, Institutional, Research Grant, ENZAMET & ENZARAD: Astellas; Financial Interests, Institutional, Research Grant, KEYPAD: Amgen, MSD; Financial Interests, Institutional, Research Grant, NIVORAD: BMS; Financial Interests, Institutional, Research Grant: Pfizer, Roche; Financial Interests, Institutional, Research Grant, ADELE: BeiGene; Financial Interests, Institutional, Research Grant, PARAGON2: Novartis; Financial Interests, Institutional, Other, Study Drug for Cannabis CINV Trial: Tilray; Financial Interests, Institutional, Research Grant, ILLUMINATE, PHAEDRA,: AstraZeneca. C. Suarez Rodriguez: Financial Interests, Personal, Advisory Board: Astellas, AstraZeneca, Bristol Myers Squibb International, Ipsen, MSD, MSD; Financial Interests, Institutional, Advisory Board: Astellas, AstraZeneca, Bristol Myers Squibb International, Ipsen, MSD, MSD; Financial Interests, Personal, Other, Travel and accommodation: Bayer; Financial Interests, Personal, Invited Speaker: Bristol Myers Squibb International, Ipsen, MSD; Financial Interests, Institutional, Invited Speaker: Bristol Myers Squibb International, Ipsen, MSD; Financial Interests, Institutional, Research Grant: Ipsen, Pfizer, Bristol Myers Squibb International, Roche, MSD. B. Venugopal: Financial Interests, Personal, Advisory Board: Bristol Myers Squibb, Merck Sharp Dohme, Eisai, Bayer; Financial Interests, Personal, Invited Speaker: Ipsen, Merck Sharp Dohme, Pfizer, Merck Sorono, Bristol Myers

Squibb; Financial Interests, Institutional, Coordinating PI: Ipsen; Non-Financial Interests, Principal Investigator: Merck Sharp and Dohme, Ipsen, Calithera, Pfizer, Exelixis. P. Nathan: Financial Interests, Personal, Invited Speaker: BMS, Novartis, Immunocore; Financial Interests, Institutional, Other, research support: Immunocore; Financial Interests, Personal, Advisory Board: Novartis, Merck, Pfizer, Ideaya, Sun Pharma; Financial Interests, Personal, Other, DMC membership: Immunocore; Financial Interests, Institutional, Coordinating PI: BMS, Novartis, Ipsen, Immunocore, Merck, Pfizer; Financial Interests, Coordinating PI: ionctura, Ideaya Biosciences. A. Bex: Financial Interests, Institutional, Advisory Board, Online advisory board: Ipsen; Financial Interests, Personal, Advisory Board: Telix; Financial Interests, Institutional, Research Grant, Restricted educational grant for an investigator initiated trial of neoadjuvant therapy in high risk renal cancer: Pfizer; Non-Financial Interests, Principal Investigator, Steering committee member and PI in an adjuvant trial: Roche/Genentech; Non-Financial Interests, Principal Investigator, Steering committee member and local investigator in an adjuvant trial: BMS; Non-Financial Interests, Advisory Role, Medical Steering committee member to advise the patient advocacy group on medical topics and strategy: International Kidney Cancer Coalition, KIdney Cancer Association; Non-Financial Interests, Leadership Role, Chair of the EAU Renal Cancer guidelines: European Association of Urology. D.J. Harrison: Financial Interests, Personal, Full or part-time Employment, Head of Translational Medicine: Nucana plc; Financial Interests, Personal, Full or part-time Employment, Non-executive director: ILC Therapeutics LTD; Financial Interests, Personal, Stocks/Shares, Shares: ILC Therapeutics LTD; Non-Financial Interests, Advisory Role, Occasional advisory role, unpaid: Panakeia. T.Q.G. Eisen: Financial Interests, Personal, Full or part-time Employment, to March 2020: AstraZeneca; Financial Interests, Personal, Full or part-time Employment, since March 2020: Roche; Financial Interests, Personal, Stocks/Shares: AstraZeneca, Roche; Non-Financial Interests, Personal, Leadership Role, Non-executive director: Cambridge University Health Partners; Non-Financial Interests, Personal, Other, Trustee for 10 years to 2021: Macmillan Cancer Support; Non-Financial Interests, Personal, Leadership Role, Director: DeviceChooser Ltd. M.K. Parmar: Financial Interests, Institutional, Full or part-time Employment, Director at MRC Clinical Trials Unit at UCL: Medical Research Council Clinical Trials Unit at UCL; Financial Interests, Personal and Institutional, Research Grant: AstraZeneca, Astellas, Janssen, Baxter, GSK; Financial Interests, Institutional, Research Grant: Clovis, Abcodia Pvt Ltd, Akagera, Amgen, Aspirin Foundation, Bayer, BMS US, Bri-BioCepheid, Cipla, CSL Behring, Eli Lilly, Emergent Biosolutions, Gilead Sciences, Grifols, Johnson & Johnson, Pfizer, Sanofi, ViiVHealthcare, Micronoma, Modus Theraputics, Mylan, Serum Institute of India, shionogi, SyntenyBiotechnology, Takeda, Tibotec, Transgene, Virco and Xenothera; Non-Financial Interests, Advisory Role, Euro Ewing Consortium: University College London; Non-Financial Interests, Advisory Role, rEECur: University of Birmingham; Non-Financial Interests, Advisory Role, CompARE Trial: University of Birmingham; Non-Financial Interests, Advisory Role, ROSSINI Trial Platform: University of Birmingham. A.M. Meade: Financial Interests, Institutional, Research Grant, Educational Grant and free IMPs for the RAMPART trial: AstraZeneca. All other authors have declared no conflicts of interest.