

10640**ICON8B: GCIG phase III randomised trial comparing first-line weekly dose-dense chemotherapy + bevacizumab to three-weekly chemotherapy + bevacizumab in high-risk stage III-IV epithelial ovarian cancer (EOC): Final overall survival (OS) analysis**

A.R. Clamp¹, I. McNeish², D. Radice³, R. Lord⁴, A. Michael⁵, A. Cook⁶, R. Agarwal⁷, A. Walther⁸, S.P. Blagden⁹, D. O'Donnell¹⁰, J.D. Brenton¹¹, S. Sundar¹², C. Sessa¹³, L.R. Murphy³, F. Schiavone³, A. Gentry-Maharaj³, R.S. Kaplan³, M.K. Parmar³, J.A. Ledermann¹⁴

¹ Department of Medical Oncology, The Christie NHS Foundation Trust and University of Manchester, Manchester, United Kingdom, ² Surgery & Cancer Dept., Imperial College London - Hammersmith Hospital, London, United Kingdom, ³ MRC Clinical Trials Unit at UCL, Institute of Clinical Trials and Methodology-UCL, London, United Kingdom, ⁴ Medical Oncology, The Clatterbridge Cancer Centre, Liverpool, United Kingdom, ⁵ Department of Oncology, University of Surrey - Faculty of Health and Medical Sciences, Guildford, United Kingdom, ⁶ Clinical Oncology, Gloucestershire Oncology Centre - Cheltenham General Hospital, Cheltenham, United Kingdom, ⁷ Oncology Dept., Northampton General Hospital, Northampton, United Kingdom, ⁸ Oncology Department, University Hospitals Bristol NHS Foundation Trust, Bristol, United Kingdom, ⁹ Oncology Dept., Churchill Hospital - Oxford University Hospitals NHS Foundation Trust, Oxford, United Kingdom, ¹⁰ Department of Haematology Oncology, St James's Hospital, Dublin, Ireland, ¹¹ Department of Oncology, CRUK - Cancer Research UK Cambridge Institute - University of Cambridge, Cambridge, United Kingdom, ¹² Institute of Cancer and Genomic Sciences - University of Birmingham, Birmingham, United Kingdom, ¹³ Oncology Dept., EOC - Ospedale Regionale Bellinzona e Valli - Istituto Oncologico della Svizzera Italiana (IOSI), Bellinzona, Switzerland ¹⁴ Cancer Research UK & UCL Cancer Trials Centre, UCL Cancer Institute, University College London, London, United Kingdom

Background

In ICON8B the use of dose-dense weekly paclitaxel (ddwT) with 3-weekly (q3w) carboplatin (C) and bevacizumab (BEV) as first-line treatment improved median progression-free survival (PFS) by 5.5 months (m) compared to standard q3w paclitaxel (T) dosing with C+BEV (22.2m vs 16.7m; Hazard Ratio (HR) 0.75, 95% CI 0.62-0.90 p=0.002). We now report the final OS analysis conducted at trial closure.

Methods

Eligible participants (pts) with high-risk stage III (residual disease >1 cm diameter after immediate primary surgery (IPS) or requirement for primary chemotherapy) or stage IV EOC were randomised 1:1:1 to Arm B1 (standard- q3w C AUC5/6+q3w T 175mg/m²+ q3w BEV 7.5mg/kg); Arm B2- (q3w C AUC5/6+ddwT 80mg/m²); Arm B3- (q3w C AUC5/6+ddwT 80mg/m²+ q3w BEV 7.5mg/kg). Up to six cycles chemotherapy and 18 BEV cycles were administered. Arm B2 recruitment discontinued after ICON8 saw no evidence of PFS improvement with q3wCddwT vs q3wCT. OS was a key secondary outcome and pts were followed for survival endpoints until trial closure on 18th Dec 2024 at end of academic funding.

Results

From 07/2015 to 03/2020 579 pts were randomised to arms B1 + B3. Median age was 64 years; 91% had High Grade Serous Carcinoma; 93% Stage IIIc/IV; 84% primary chemotherapy with planned delayed primary surgery, 14% IPS, 2% inoperable; 50.2% cases sequenced for germline BRCA1/2 mutations. After a median follow-up of 72.0m, 411 deaths were reported (197 in B3; 214 in B1). Median OS was 49.8m (95% CI 43.7-54.5m) in B3 and 39.6m (95% CI 34.7-45.0m) in B1 (HR 0.79, 95% CI 0.65-0.95, p=0.010). In pts receiving primary chemotherapy, median OS was 47.3m (95% CI 42.0-52.6m) in B3 and 37.1m (95% CI 32.3-42.1m) in B1.

Conclusions

In pts with high-risk stage III-IV EOC, the use of ddwT in combination with q3w C + BEV as first-line systemic therapy improves median OS by 10.2m compared to q3w T dosing. ddwT with q3wC+BEV should now be considered a standard-of-care first-line treatment option in this group. Further research is required to determine whether efficacy of this regimen is impacted by tumour homologous recombination deficiency and intrinsic chemosensitivity.

Clinical trial identification

ISRCTN10356387.

Legal entity responsible for the study

University College London.

Funding

Cancer Research UK and Medical Research Council.

Disclosure

A.R. Clamp: Financial Interests, Personal, Advisory Board: GSK, Immunogen; Financial Interests, Personal, Invited Speaker: AstraZeneca; Financial Interests, Institutional, Research Grant: AstraZeneca; Financial Interests, Institutional, Local PI: Merck, Verastem, Novartis, Advenchen Laboratories, AstraZeneca, MSD, Eisai, Immunogen; Non-Financial Interests, Advisory Role: National Institute of Health and Care Excellence. I. McNeish: Financial Interests, Personal, Advisory Board, Advisory Boards and travel: AstraZeneca, GSK; Financial Interests, Personal, Advisory Board: Roche, Alkermes, OncoC4, Theolytics; Financial Interests, Personal, Advisory Board, Advisory and consultancy on development of novel therapeutics in ovarian cancer: Duke Street Bio; Financial Interests, Personal, Advisory Board, Advice ahead of NICE submission: pharma&; Financial Interests, Personal, Advisory Board, Advisory Board: BioNTech; Financial Interests, Institutional, Funding: AstraZeneca; Non-Financial Interests, Member of Board of Directors, Trustee of this charity: Worldwide Cancer Research. D. Radice: Financial Interests, Personal, Stocks/Shares: GSK, Smith & Nephew, Bunzl, RELX, Haleon; Other, I provide a monthly donation: Cancer Research UK. R. Lord: Financial Interests, Personal, Advisory Board, paid advisory work: GSK; Financial Interests, Institutional, Funding, investigator led clinical trial (COMICE) financed by AstraZeneca and run through Liverpool trials unit: AstraZeneca. A. Michael: Financial Interests, Personal, Advisory Board: EUSA Pharma, Tesaro; Financial Interests, Personal, Invited Speaker: GSK, Ipsen, Clovis, Novartis, Pfizer, MSD; Financial Interests, Personal, Other, travel, accommodation: Merck; Financial Interests, Personal, Other, conference attendance: Ipsen; Financial Interests, Local PI: CARINA Trial, Vinehealth, OVAL-1; Financial Interests, Institutional, Local PI: MODIFY. R. Agarwal: Financial Interests, Personal, Advisory Board: GSK, Amgen, AstraZeneca, MSD; Financial Interests, Personal, Other, Member of Medical Advisory Board: Sciensus; Non-Financial Interests, Personal, Training: Takeda Pharmaceuticals, AbbVie; Non-Financial Interests, Institutional, Training: Amgen. A. Walther: Financial Interests, Personal, Invited Speaker, Seminar on uterine cancer Patient/doctor session at UK meeting: GSK; Financial Interests, Personal, Advisory Board, ad board: Regeneron; Financial Interests, Personal, Full or part-time Employment, Main NHS employer: Bristol Cancer Institute. S.P. Blagden: Financial Interests, Personal, Advisory Board, Member of advisory board: Oxford Drug Design; Financial Interests, Personal, Advisory Board, Advisory board: Simbec-Orion, Theolytics; Financial Interests, Personal, Advisory Board, Study advisory committee: UCB; Financial Interests, Personal, Full or part-time Employment, Founder and CEO: RNA Guardian; Financial Interests, Personal, Other, Ad hoc advice: Oxford Hormone Clinic; Financial Interests, Personal, Ownership Interest, Early Biomarker company, development stage: RNA Guardian Ltd; Financial Interests, Institutional, Coordinating PI: NuCana PLC; Financial Interests, Institutional, Local PI: Nurix, Medannex, BioNTech, Regeneron, Theolytics; Non-Financial Interests, Officer, Treasurer: Larp Society. D. O'Donnell: Non-Financial Interests, Member, Irish Medical Oncology Society which leads nationally in advising health service and government on the needs of cancer patients from the viewpoint of medical oncologists: Irish Society of Medical Oncology; Other, Member of the above Committee which formally advises Health Service Executive when it is considering reimbursing a new technology, usually but not exclusively drug therapy, for cancer treatment. The Committee does not have the final decision as to drug reimbursement: National Cancer Control Programme Technology Review Committee. J.D. Brenton: Financial Interests, Personal, Invited Speaker: GSK, AstraZeneca, GE Healthcare; Financial Interests, Personal, Advisory Board: AstraZeneca, Clovis Oncology; Financial Interests, Personal, Member of Board of Directors: Tailor Bio; Financial Interests, Personal, Stocks/Shares: Tailor Bio; Financial Interests, Institutional, Local PI: GE Healthcare. C. Sessa: Financial Interests, Personal, Other, ESO Consultant for gynaecological cancer: ESO (European School of Oncology); Financial Interests, Personal, Other, DMC member of the MK-3475-C93 study DMC member of the MK-2870-005 study: Merck; Non-Financial Interests, Advisory Role, ESMO extended member women for oncology: ESMO; Non-Financial Interests, Advisory Role, Member of the compliance committee: ESMO. A. Gentry-Maharaj: Financial Interests, Personal, Other, Consulting fees from Mercy Bioanalytics Ltd.; Financial Interests, Personal, Full or part-time Employment, Full time employment, funded by UCL Core and Medical Research Council (MRC) Core funding: UCL; Financial Interests, Institutional, Funding, Research support grant paid to the institution: Intelligent Lab on Fiber, RNA Guardian; Financial Interests, Institutional, Funding, Research support grants paid to the institution: Mercy BioAnalytics; Non-Financial Interests, Leadership Role, UCL CRUK International Alliance for Cancer Early Detection (ACED) Deputy Director: Cancer Research UK (CRUK); Non-Financial Interests, Leadership Role, CRUK International Alliance for Cancer Early Detection (ACED) Director of Research: Cancer Research UK (CRUK). J.A. Ledermann: Financial Interests, Personal, Advisory Board, Advisory Board and Speaker Fees: AstraZeneca, GSK; Financial Interests, Personal, Advisory Board: Merck/MSD, Bristol Myers Squibb, Nuvation, Immunogen/AbbVie, Novocure, Immagine; Financial Interests, Personal, Other, Independent Data Monitoring Committee: Sutro Bio, Mersana; Financial Interests, Personal, Invited Speaker, Invited Speaker: Medison; Financial Interests, Institutional, Research Grant, Clinical Research University: AstraZeneca, MSD/Merck; Non-Financial Interests, Leadership Role, ESGO Chair of the Joint IGC/ESGO journal Committee for Int J Gyn Cancer: European Society of Gynaecological Oncology; Non-Financial Interests, Officer, Chair Gynaecological Clinical Practice Guidelines (to Dec 2023): ESMO; Non-Financial Interests, Advisory Role, Chair of the Committee: National Cancer Audit Collaborating Centre (NATCAN) (National Ovarian Cancer Audit); Other, Associate Editor: Therapeutic Advances in Medical Oncology: Sage Publishing. All other authors have declared no conflicts of interest.