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Randomised phase II trial of olaparib compared to weekly paclitaxel or olaparib plus cediranib in patients with platinum-resistant ovarian cancer (OCTOVA)

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Background

The main aims of the OCTOVA trial were to compare the efficacy and toxicity of olaparib (O) with weekly paclitaxel (wP) and also the oral combination of olaparib plus cediranib (O+C) in recurrent ovarian cancer (OC).

Methods

Participants with high grade ovarian, fallopian tube, primary peritoneal cancer who relapsed within 12 months of previous platinum-based therapy were randomised, with stratification for germline *BRCA1/2* mutation status, prior PARP inhibitor (PARPi) or anti-angiogenic therapy, to receive O (300mg daily) or either wP (80mg/m² d1,8,15, q28) or O+C (300mg/20mg daily respectively). Treatment continued until disease progression or unacceptable toxicity. Primary endpoint was Progression Free Survival (PFS). Secondary endpoints were safety and tolerability of the combination of O+C, overall survival, objective response rate, and quality of life. A sample size of 138 (46 per arm) was sufficient to observe HR 0.64 in favour of O+C compared to O alone and 1.44 for wP compared to O (20% one-sided type I error, 80% power, 15% dropout, one-sided p-value <0.2).

Results

OCTOVA recruited 139 participants, median 65 years (IQR:38-84), from 15 UK centres over 34 months. 31 (22%) had had prior PARPi therapy, 47 (34%) prior anti-angiogenic therapy. 41 (29%) had known germline *BRCA1/2* mutations. 125 (90%) had relapsed <6 months after prior platinum. Median 2 prior lines of chemotherapy (range 1-7). There was no difference in PFS between wP and O (HR=0.97, 60%CI: 0.79, 1.19; p=0.55). PFS was increased for O+C compared to O (HR=0.70; 60%CI: 0.57, 0.86; p=0.08). There were 239, 176, and 137 treatment related adverse events (all grades) in the O+C, wP and O arms respectively.

Conclusions

The OCTOVA trial demonstrated that the combination of O+C showed greater efficacy than O alone, but we did not find evidence that wP was inferior to O in women with multiply relapsed OC.

Clinical trial identification

ISRCTN14784018, NCT03117933.

Legal entity responsible for the study

University of Oxford.

Funding

AstraZeneca.

Disclosure

S. Nicum: Financial Interests, Other, Advisory and speaker honoraria, travel expenses: GSK; Financial Interests, Other, Advisory and speaker honoraria, travel expenses: Tesaro; Financial Interests, Other, Advisory and speaker honoraria, travel expenses: Roche; Financial Interests, Other, Advisory and speaker honoraria: Abbvie; Financial Interests, Other, Advisory and speaker honoraria: Clovis; Financial Interests, Other, Advisory and speaker honoraria, travel expenses and peer-reviewed research funding: AstraZeneca. I. McNeish: Financial Interests, Advisory Board, Advisory Board and institutional funding: AstraZeneca; Financial Interests, Advisory Board: GSK; Financial Interests, Advisory Board: Clovis Oncology; Financial Interests, Advisory Board: Roche; Financial Interests, Advisory Board: Scancell. R.M. Glasspool: Financial Interests, Advisory Board, Advisory boards speaker fees: AstraZeneca; Financial Interests, Advisory Board: MSD; Financial Interests, Advisory Board, Advisory boards speaker fees: Clovis; Financial Interests, Advisory Board, Advisory boards speaker fees: GSK/Tesaro; Financial Interests, Other, Consultancy fees: Sotio; Financial Interests, Advisory Board: Immunogen; Financial Interests, Research Grant, Investigator Initiated Trial Grant: Clovis; Financial Interests, Principal Investigator, Site PI for commercially sponsored trials: Clovis; Financial Interests, Principal Investigator, Site PI for commercially sponsored trials: AstraZeneca; Financial Interests, Principal Investigator, Site PI for commercially sponsored trials: GSK; Financial Interests, Principal Investigator, Site PI for commercially sponsored trials: Immunogen; Financial Interests, Research Grant, Investigator Initiated Trial Grant: Boehringer Ingelheim; Financial Interests, Research Grant, Investigator Initiated Trial Grant: Lilly/Ignyta; Financial Interests, Principal Investigator, Site PI for commercially sponsored trials: Lilly/Ignyta; Financial Interests, Other, Consultancy fees for trial steering committee: Novartis; Financial Interests, Leadership Role: NCR1 Ovarian Group Chair; Financial Interests, Leadership Role: SGCTG Ovarian lead; Financial Interests, Leadership Role: IGCS council member; Financial Interests, Leadership Role: ESMO Gyn Cancer Faculty; Financial Interests, Leadership Role: GCIG Meta-Analysis Group Chair; Financial Interests, Leadership Role: ENGOT early phase Co-Chair; Financial Interests, Leadership Role: Horizons Study Expert Panel member; Financial Interests, Leadership Role: Target Ovarian Cancer Scientific Advisory Board. M. Hall: Financial Interests, Research Grant, Clinical Trial grants: BMS; Financial Interests, Research Grant, Clinical Trial grants: Merck; Financial Interests, Invited Speaker, grants and personal fees: Clovis Oncology; Financial Interests, Invited Speaker, personal fees for Advisory Boards and educational roles: GSK; Financial Interests, Invited Speaker, personal fees for Advisory Boards and educational roles: Amgen; Financial Interests, Invited Speaker, personal fees for Advisory Boards and educational roles: Roche; Financial Interests, Invited Speaker, personal fees for Advisory Boards and educational roles: AstraZeneca. A. Michael: Financial Interests, Advisory Board: Clovis; Financial Interests, Advisory Board: ESAI; Financial Interests, Advisory Board: Ipsen; Financial Interests, Advisory Board: Roche; Financial Interests, Advisory Board: Tesaro; Financial Interests, Advisory Board: GSK. S. Banerjee: Financial Interests, Institutional, Research Grant: AstraZeneca; Financial Interests, Institutional, Research Grant: Tesaro; Financial Interests, Institutional, Research Grant: GSK; Financial Interests, Personal, Advisory Board: Amgen; Financial Interests, Personal, Advisory Board: AstraZeneca; Financial Interests, Personal, Advisory Board: Genmab; Financial Interests, Personal, Advisory Board: Immunogen; Financial Interests, Personal, Advisory Board: Mersana; Financial Interests, Personal, Advisory Board: MSD; Financial Interests, Personal, Advisory Board: Merck Serono; Financial Interests, Personal, Advisory Board: Oncxerna; Financial Interests, Personal, Advisory Board: Pfizer; Financial Interests, Personal, Advisory Board: Roche; Financial Interests, Personal, Invited Speaker: Amgen; Financial Interests, Personal, Invited Speaker: AstraZeneca; Financial Interests, Personal, Invited Speaker: Pfizer; Financial Interests, Personal, Invited Speaker: Clovis; Financial Interests, Personal, Invited Speaker: GSK; Financial Interests, Invited Speaker: Takeda. G. Jayson: Financial Interests, Institutional, Research Grant: AstraZeneca. A. Clamp: Financial Interests, Institutional, Research Grant: AstraZeneca; Financial Interests, Personal, Advisory Board: AstraZeneca. All other authors have declared no conflicts of interest.