838P TRIOC-A randomised phase II trial to examine MVA-5T4 vaccine in patients with relapsed asymptomatic epithelial ovarian, fallopian tube or primary peritoneal cancer

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Background: Continued surveillance is often used in patients with ovarian cancer who have asymptomatic relapse. Immunotherapy directed at 5T4, an onco-foetal tumour antigen (TAA) may contain the relapse and delay the need for further chemotherapy. MVA-5T4 (TroVax®) consists of an attenuated Vaccinia Virus (Modified Vaccinia Ankara, MVA) containing the gene encoding for the human TAA, 5T4. We examined whether MVA-5T4 vaccination can delay tumour progression of relapsed ovarian cancer.

Methods: The trial started as a double-blind randomised phase II trial with placebo, but an unforeseen interim trial suspension led to limited drug supply, so it later changed to a single arm study. Eligible patients had asymptomatic (CA-125 rise only- or low volume disease) relapsed ovarian cancer; $\geq$6 months since prior chemotherapy and ECOG 0-1. Primary endpoint was progression rate at 25 weeks (PR-25): confirmed progression using RECIST and immune-related response criteria, clinical intervention for symptoms of progression or death. We aimed to detect an improvement in PR from 70% (placebo) to 50% (MVA-5T4).

Results: 94 eligible patients were recruited from 12 centres (11/13 to 11/17). There were 69 randomised patients, 25 were added in a single arm study. Median age was 65 years (range 42 to 82), and median time since prior chemotherapy 18 months (7 to 86); median follow up 34 months (2 to 46). 22 patients were withdrawn from trial treatments during the suspension. The PR-25 was similar: 80.0% (MVA-5T4) vs 82.9% (placebo) p-0.74. In the pre-specified per protocol analysis (patients who had $\geq$5 treatment injections and were unaffected by trial suspension), the corresponding rates were 78.8% and 90.9%. Median PFS was the same in both arms (3.0 months). Median time to clinical intervention appeared to be improved with MVA-5T4 9.7 (6.7-14.3) vs 6.1 (5.1-8.6), p-0.14. 27.6% (MVA-5T4) vs 22.9% (placebo) had a grade 3-4 adverse event. QoL was also similar in both arms.

Conclusions: MVA-5T4 vaccination in patients with asymptomatic relapse was well-tolerated but did not improve the progression rate at 25 weeks. Further immunological analysis to identify subsets of patients who might benefit from MVA-5T4 is ongoing.

Clinical trial identification: EudraCT: 2011-001836-44.

Legal entity responsible for the study: Cancer Research UK & UCL Cancer Trials Centre.

Funding: Oxford Biomedica.

Disclosure: A. Michael: Advisory/Consultancy, Travel/Accommodation/Expenses: Clovis; Advisory/Consultancy, Travel/Accommodation/Expenses: Ipsen; Advisory/Consultancy, Travel/Accommodation/Expenses: Tesaro; Advisory/Consultancy, Travel/Accommodation/Expenses: Eisai; Honoraria (self), Travel/Accommodation/Expenses: BMS; Honoraria (self), Advisory/Consultancy: GSK; Honoraria (self): Novartis; Honoraria (self): Pfizer. R. Harrop: Full/Part-time employment: Oxford Biomedica. I. McNeish: Advisory/Consultancy: AstraZeneca; Advisory/Consultancy: Tesaro; Advisory/Consultancy: GSK; Advisory/Consultancy: Carrick Therapeutics; Advisory/Consultancy: Roche; Research grant/Funding (institution): AstraZeneca. R. Lord: Advisory/Consultancy, Travel/Accommodation/Expenses: Tesaro; Advisory/Consultancy, Travel/Accommodation/Expenses: AstraZeneca. D. Blount: Full/Part-time employment: Oxford Biomedica. A.R. Clamp: Advisory/Consultancy, Research grant/Funding (self): AstraZeneca; Advisory/Consultancy, Travel/Accommodation/Expenses: GSK; Honoraria (self), Travel/Accommodation/Expenses: Clovis. R. Kristeleit: Advisory/Consultancy, Travel/Accommodation/Expenses: GSK; Advisory/Consultancy: AstraZeneca; Advisory/Consultancy, Travel/Accommodation/Expenses: Clovis; Advisory/Consultancy: Basilea; Advisory/Consultancy: InCyte; Advisory/Consultancy: Merck; Advisory/Consultancy: IGEM Therapeutics; Advisory/Consultancy: Sierra Oncology; Advisory/Consultancy, Travel/Accommodation/Expenses: Roche. S. Nicum: Advisory/Consultancy, Travel/Accommodation/Expenses: Roche; Advisory/Consultancy, Travel/Accommodation/Expenses: Tesaro; Advisory/Consultancy: GSK; Advisory/Consultancy, Travel/Accommodation/Expenses: AstraZeneca. A. Walther: Advisory/Consultancy, Travel/Accommodation/Expenses: Tesaro; Advisory/Consultancy: Roche; Advisory/Consultancy: AstraZeneca. A. Hackshaw: Honoraria (self), Advisory/Consultancy, Non-remunerated activity/ies: Roche; Shareholder/Stockholder/Stock options: Thermo Fisher; Shareholder/Stockholder/Stock options: Illumina; Honoraria (self): Boehringer; Honoraria (self): AbbVie; Honoraria (self): Merck /Serono; Honoraria (self): Merck /MSD; Honoraria (self): Daiichi Sankyo; Advisory/Consultancy: GRAIL Inc; Advisory/Consultancy: Abbvie; Honoraria (self): Takeda. J.A. Ledermann: Honoraria (self), Speaker Bureau/Expert testimony, Research grant/Funding (self): MSD/Merck; Honoraria (self), Speaker Bureau/Expert testimony, Research grant/Funding (self): AstraZeneca; Honoraria (self), Speaker Bureau/Expert testimony: Clovis; Honoraria (self): Pfizer; Honoraria (self): Tesaro; Honoraria (self): GSK; Honoraria (self): Seattle Genetics; Honoraria (self): Artios; Honoraria (self): Eisai; Honoraria (self): Amgen. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2020.08.977

839P A phase Ib/II study of rebastinib and paclitaxel in advanced or metastatic platinum-resistant ovarian cancer

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Background: Rebastinib is a switch control inhibitor of TIE2 kinase. TIE2 is expressed in endothelial cells and in some macrophages with pro-angiogenic, pro-metastatic and immunosuppressive properties associated with chemotherapy resistance. This is a 2-part open-label, phase Ib/II study with orally administered rebastinib in combination with weekly paclitaxel 80 mg/m^2. In part 1, we observed antitumor activity across multiple tumor types (5 PRs in 24 pts at 50 mg BID and 3 PRs in 19 pts at 100 mg BID), including 3 PRs in platinum-resistant ovarian cancer (PROC). Part 2 has 5 cohorts: TNBC, inflammatory breast cancer, PROC, endometrial cancer and carcinosarcoma. Here, we present preliminary results from the PROC cohort.

Methods: Part 2 is a Simon 2-stage design enrolling 18 pts into the first stage, and if $\geq$5 responses, an additional 15 pts in the second stage. Pts were treated with rebastinib in combination with paclitaxel 80 mg/m^2 intravenous weekly (D1, D8, D15 of repeated 28-day cycles) and evaluated for safety (CTCAE v5.0) and efficacy (RECIST v1.1).

Results: As of March 20, 2020, 20 pts were enrolled; the median age was 58 years. All received $\geq$ 1 prior regimen with paclitaxel/carboplatin; the median number of prior therapies was 5 (2, 7). Ten pts were initially treated with 100 mg BID rebastinib (reduced to 50 mg BID due to muscular weakness [4 pts in this cohort]) and 10 pts with 50 mg BID with a treatment median duration of 16 weeks (0.7, 31.9). In 17 evaluable pts, there were 5 PRs and 9 SDs (at 8 weeks) for an ORR of 29% and CBR of 82%. In addition, 8/13 (62%) pts had a CA-125 response. TEAEs ($\geq$n=5) were mostly $\leq$ grade 2, including fatigue (n=8), nausea (n=8), diarrhea, dry mouth, peripheral sensory neuropathy, vomiting (n=6 each); abdominal pain, alopecia, constipation, peripheral edema and stomatitis (n=5 each). Serious AEs possibly related to rebastinib included grade 2, reversible muscular weakness (at 100 mg BID with no additional occurrences at rebastinib 50 mg BID), fatigue and constipation (n=1 each).

Conclusions: The preliminary activity and safety of rebastinib at 50 mg BID in combination with weekly paclitaxel for heavily pretreated pts with PROC, all of whom received prior carboplatin/paclitaxel, is encouraging. Simon stage 2 enrollment is ongoing.

Clinical trial identification: NCT03601897.

Legal entity responsible for the study: Deciphera Pharmaceuticals, LLC.

Funding: Deciphera Pharmaceuticals, LLC.

Disclosure: E.P. Hamilton: Advisory/Consultancy, Research grant/Funding (institution), Travel/Accommodation/Expenses: AstraZeneca; Advisory/Consultancy, Research grant/Funding (institution): Black Diamond; Advisory/Consultancy, Research grant/Funding (institution): Boehringer Ingelheim; Advisory/Consultancy: Daiichi Sankyo; Research grant/Funding (institution): AbbVie; Research grant/Funding (institution): Acerta Pharma; Research grant/Funding (institution): Aravive; Research grant/Funding (institution): ArQule; Research grant/Funding (institution): Arvinas; Research grant/Funding (institution): BerGenBio; Research grant/Funding (institution), Travel/Accommodation/Expenses: Clovis Oncology; Research grant/Funding (institution): Compugen; Research grant/Funding (institution): Curis; Research grant/Funding (institution): CytomX Therapeutics; Research grant/Funding (institution): Daiichi Sankyo; Research grant/Funding (institution): Deciphera; Research grant/Funding (institution): eFFECTOR Therapeutics; Research grant/Funding (institution), Travel/Accommodation/Expenses: Eisai; Research grant/Funding (institution), Travel/Accommodation/Expenses: EMD Serono; Research grant/Funding (institution): Fochon; Research grant/Funding (institution): Fujifilm; Research grant/Funding (institution): G1 Therapeutics; Advisory/Consultancy, Research grant/Funding (institution), Travel/Accommodation/Expenses: Genentech/Roche; Research grant/Funding (institution): H3 Biomedicine; Research grant/Funding (institution): Harpoon; Research grant/Funding (institution): Hutchison MediPharma; Research grant/Funding (institution): Immunomedics; Research grant/Funding (institution): InventisBio; Research grant/Funding (institution): Karyopharm Therapeutics; Research grant/Funding (institution): Leap Therapeutics; Advisory/Consultancy, Research grant/Funding (institution), Travel/Accommodation/Expenses: Lilly; Research grant/Funding (institution): Lycera; Research grant/Funding (institution): Macrogenics; Research grant/Funding (institution): MedImmune; Research grant/Funding (institution): Medivation; Advisory/Consultancy, Research grant/Funding (institution): Mersana; Research grant/Funding (institution): Merus; Research grant/Funding (institution): Millennium; Research grant/Funding (institution): Molecular Templates; Advisory/Consultancy, Research grant/Funding (institution), Travel/Accommodation/Expenses: Novartis; Research grant/Funding (institution): Nucana; Research grant/Funding (institution): OncoMed; Research grant/Funding (institution): Orinove; Advisory/Consultancy, Research grant/Funding (institution), Travel/Accommodation/Expenses: Pfizer; Advisory/Consultancy, Research grant/Funding (institution): Puma Biotechnology; Research grant/Funding (institution): Radius Health; Research grant/Funding (institution): Regeneron; Research grant/Funding (institution): Rgenix; Research grant/Funding (institution): Seattle Genetics; Research grant/Funding (institution): Sermonix Pharmaceuticals; Advisory/Consultancy, Research grant/Funding (institution): Silverback; Research grant/Funding (institution): Stem CentRx; Research grant/Funding (institution):