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OCTOPUS - ovarian cancer trials of weekly paclitaxel

Submission date 20/10/2015	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 21/10/2015	**Overall study status** Completed	
Last Edited 20/03/2023	**Condition category** Cancer	

Plain English summary of protocol
http://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-of-azd2014-and-paclitaxel-for-women-with-ovarian-cancer-that-has-come-back-octopus

Contact information

Type(s)
Public

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Additional identifiers

Clinical Trials Information System (CTIS)
2014-005221-12

Protocol serial number
OCTOPUS-2014

Study information

Scientific Title

A randomised phase II umbrella trial of weekly paclitaxel +/- novel agents in platinum-resistant ovarian cancer

Acronym
OCTOPUS

Study objectives
Addition of novel agents to weekly paclitaxel will improve clinical efficacy compared to paclitaxel alone in patients with platinum-resistant/refractory, high grade serous ovarian (fallopian tube, primary peritoneal) carcinoma.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Brighton and Sussex NRES Committee, 09/10/2015, ref:15/LO/1302

Study design
Randomised, placebo-controlled, double blind multi centre trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Ovarian cancer

Interventions
1. Control arm: Paclitaxel 80mg/m2 IV D1, 8, 15 of a 28 day cycle (3 weeks on, 1 week off) + placebo
2. Experimental arm: Paclitaxel 80mg/m2 IV D1, 8, 15 of a 28 day cycle (3 weeks on, 1 week off) + AZD2014

Patients who need to stop weekly paclitaxel prior to completing four cycles will require to come off study drug, but continue to be followed up as per protocol (i.e. cannot continue on continuous novel study drug/placebo). Patients going beyond 6 cycles can continue with weekly paclitaxel at the discretion of the Investigator however confirmation is required by the chief investigator.

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
Paclitaxel, vistusertib (AZD2014)

Primary outcome(s)

Progression-free survival (PFS) based on combined RECIST v1.1/GCIG CA125 criteria is measured using Radiological/CA125 Disease Assessment every 8 weeks for the 1st year and then every 12 weeks therefore (or until evidence of progression).

Key secondary outcome(s))

1. Response (based on RECIST 1.1 and GCIG CA125 criteria) is measured using Radiological /CA125 Disease Assessment every 8 weeks for the 1st year and then every 12 weeks therefore (or until evidence of progression)
2. Overall survival is measured documenting patient status every 8 weeks for the first year and every 12 weeks thereafter
3. Safety and tolerability are measured using Blood parameters, toxicity assessment every 4 weeks during treatment
4. Quality of life (QoL) is measured using EQ-5D assessment every 4 weeks while on treatment then every 8 weeks in the 1st year following completion of treatment and then every 12 weeks (or until evidence of progression)
5. Resource use for health economic assessment is measured using EQ-5D assessment every 4 weeks while on treatment then every 8 weeks in the 1st year following completion of treatment and then every 12 weeks (or until evidence of progression)

Completion date

08/12/2019

Eligibility

Key inclusion criteria

1. Age ≥ 18 years
2. Histologically confirmed high grade serous ovarian, fallopian tube or primary peritoneal cancer (please note that patients who have an original diagnosis based on cytology only will not be eligible for entry into the study unless a biopsy confirming high grade serous histology is performed). Please note that Grade 3 serous on pathology reports are accepted as high grade serous. Any patient originally diagnosed with a ‘grade 2 serous’ pathology must undergo pathology review to confirm high grade pathology
3. Platinum-resistant disease defined as progression within 6 months of completing prior platinum therapy. This includes platinum-refractory disease. Progression is defined by RECIST criteria v1.1 (radiologically with measurable disease), but patients with CA125 progression (GCIG CA125 Criteria (see Appendix 3 for full definition)) plus symptoms indicative of progression will also be allowed to enter.
4. Measurable or evaluable disease (if not measurable by RECIST criteria v1.1, must be evaluable by GCIG CA125 criteria – see Appendix 3 for full definition). Patients with CA125 progression in the absence of symptoms will NOT be eligible
5. Histological tissue specimen available (tissue block or 8-10 unstained slides) must be available (specimen can be the sample at diagnosis or taken at relapse). Otherwise, a biopsy must be carried out to obtain sufficient tissue for histological assessment
6. Willingness to undergo mandatory biopsy pre cycle 1 day 1. Target lesions (RECIST criteria v1. 1) should be avoided if possible
7. Prior taxane use: Patients whom have received prior 3 weekly paclitaxel (or other 3 weekly taxane) are permitted. Patients whom received weekly paclitaxel as part of first line treatment in combination with platinum are eligible if the interval since the last dose of weekly paclitaxel is > 6months at the time of randomisation. Patients whom received prior weekly paclitaxel (alone or in combination) for platinum-resistant disease are excluded. If patients have received prior taxane, the interval since the last taxane treatment must be known. The treatment immediately

prior to study entry need not be platinum-based. Entry into the trial is not limited to first line treatment for platinum-resistant ovarian cancer i.e. patients can have prior lines of therapy for platinum-resistant disease.
8. Ability to provide written informed consent prior to participating in the trial and any trial related procedures being performed
9. Adequate haematological and biochemical function as indicated below. These measurements must be performed within 7 days prior to randomisation:
9.1.Absolute neutrophil count >1.5 x 109/L
9.2. Platelet count >100 x 109/L
9.3. Haemoglobin >90 g/L
9.4. Serum creatinine <1.5 times ULN or creatinine clearance ≥50 mL/min (measured or calculated by Cockcroft and Gault equation/Wright formula – see Appendix 4); confirmation of creatinine clearance is only required when serum creatinine is >1.5 times the ULN
9.5. Total bilirubin <1.5 times ULN. In cases of Gilbert's syndrome, bilirubin < 2 x ULN is allowed
9.6. Alanine aminotransferase (ALT) or aspartate aminotransferase (AST) <2.5 times the upper limit of normal (ULN) if no demonstrable liver metastases or <5 times ULN in the presence of liver metastases
9.7. Alkaline phosphatase <5 x ULN
10. Willingness to comply with scheduled visits, treatment plans and laboratory tests and other study procedures
11. Evidence of non-childbearing status for women of childbearing potential: negative urine or serum pregnancy test within 7 days of trial treatment
11.1. Post-menopausal defined as aged more than 50 years and amenorrhoeic for at least 12 months following cessation of all exogenous hormonal treatments, or, women under 50 years old who have been amenorrhoeic for at least 12 months following cessation of all exogenous hormonal treatments, and have serum follicle-stimulating hormone (FSH) and luteinizing hormone (LH) levels in the post-menopausal range for the institution
OR
11.2. Documentation of irreversible surgical sterilisation by hysterectomy, bilateral oophorectomy or bilateral salpingectomy but not tubal ligation
12. Patients with synchronous tumours e.g. ovarian and endometrial or history of prior malignancy are eligible provided that there is biopsy evidence that the disease measurable on CT and/or MRI is ovarian in origin
13. Life expectancy of at least 12 weeks
14. ECOG Performance Status of 0,1

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
Female

Key exclusion criteria
1. Non high grade serous histologies including carcinosarcoma.
2. Prior chemotherapy, biological therapy, radiation therapy, hormonal anti-cancer therapy, immunotherapy, other anticancer agents within 14 days of starting study treatment (not including palliative radiotherapy at focal sites). Treatment with any investigational agent within the preceding 4 weeks or within 5 half-lives of the investigational agent, whichever is longer.
3. Pregnant or lactating women
4. Women of childbearing age and potential who are not willing to use two highly effective forms of contraception as detailed in Section 8.2 (Pregnancy). In addition, patients will be excluded if they are not willing to use contraception for the duration as documented in Section 8.2 (Pregnancy) and Appendix I, Section 6.1 (Pregnancy – Duration of Contraception and Follow-up for Pregnancy).
5. With the exception of alopecia, any unresolved toxicities from prior chemotherapy should be no greater than CTCAE (Version 4.03) Grade 1 at the time of starting study treatment.
6. Major surgery within 4 weeks prior to entry to the study or minor surgery within 2 weeks of entry into the study (excluding placement of vascular access)
7. Spinal cord compression, known leptomeningeal involvement or brain metastases, unless treated and stable off steroids for at least 4 weeks prior to randomisation
8. Oral anticoagulants such as warfarin are not permitted, with the exception of 1mg daily warfarin dose for the prevention of Hickman line clotting. Anticoagulation with low molecular weight heparin is allowed.
9. Any haemopoietic growth factors (e.g., G-CSF, GM-CSF) and blood transfusions within 2 weeks prior to randomisation
10. As judged by the Investigator, any evidence of severe or uncontrolled systemic diseases e.g., severe hepatic impairment, interstitial lung disease [bilateral, diffuse, parenchymal lung disease], uncontrolled chronic renal diseases (glomerulonephritis, nephritic syndrome, Fanconi Syndrome or Renal tubular acidosis), current unstable or uncompensated respiratory or cardiac conditions, uncontrolled hypertension, active bleeding diatheses or active infection including hepatitis B, hepatitis C, and human immunodeficiency virus. Screening for chronic conditions is not required
11. Torsades de Pointes within 12 months of study entry
12. Judgment by the Investigator that the patient is unsuitable to participate in the study and the patient is unlikely to comply with study procedures, restrictions and requirements
13. Patients with a history of grade 3 or 4 allergic reaction (CTCAEv4.03) to paclitaxel are not permitted. Patients who have had prior grade 1 or 2 hypersensitivity reactions are permitted providing the weekly paclitaxel is administered using the desensitisation schedule (section 5.7.2)
14. Patients who have a new diagnosis of deep vein thrombosis or pulmonary embolism within 2 weeks of randomisation are permitted if clinically stable on a therapeutic dose of LMWH

Date of first enrolment
08/12/2015

Date of final enrolment
30/04/2018

Locations

Countries of recruitment
United Kingdom

England

Northern Ireland

Scotland

Study participating centre
The Beatson West of Scotland Cancer Centre
Glasgow
United Kingdom
G12 0YN

Study participating centre
Belfast City Hospital
Belfast
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BT9 7AB

Study participating centre
Dorset Cancer Centre
Poole
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BH15 2JB

Study participating centre
Briston Oncology & Haematology Centre
Bristol
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BS2 8ED

Study participating centre
Royal Preston Hospital
Preston
United Kingdom
PR2 9HT

Study participating centre
Royal Sussex County Hospital
Sussex
United Kingdom
BN2 1ES

Study participating centre
Birmingham City Hospital
Birmingham
United Kingdom
B18 7QH

Study participating centre
Musgrove Park Hospital
Taunton
United Kingdom
TA1 5DA

Study participating centre
Nottingham City Hospital
Nottingham
United Kingdom
NG5 1PB

Study participating centre
St James University Hospital
Leeds
United Kingdom
LS7 9TF

Study participating centre
Hammersmith Hospital
London
United Kingdom
W12 0HS

Study participating centre
Weston Park Hospital
Sheffield
United Kingdom
S10 2SJ

Study participating centre
Ninewells Hospital
Dundee
United Kingdom
DD1 9SY

Study participating centre
Northampton General Hospital
Northampton
United Kingdom
NN1 5BD

Study participating centre
Mount Vernon Hospital
Middlesex
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HA6 2RN

Study participating centre
United College London Hospital
London
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NW1 2BU

Study participating centre
The Royal Marsden Hospital
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SM2 5PT

Study participating centre
The Royal Marsden Hospital
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SW3 6JJ

Study participating centre
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CT9 4AN

Study participating centre
Royal United Hospitals Bath NHS Foundation Trust
Bath
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BA1 3NG

Study participating centre
Western General Hospital
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EH4 2XU

Study participating centre
Addenbrookes Hospital
Cambridge
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CB2 0QQ

Study participating centre
Clatterbridge Centre for Oncology
Bebington
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Study participating centre
Guys and St Thomas's NHS Foundation Trust
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SE1 9RT

Study participating centre
Churchill Hospital
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OX3 7LE

Sponsor information

Organisation
NHS Greater Glasgow and Clyde

ROR
https://ror.org/05kdz4d87

Organisation
The University of Glasgow

Funder(s)

Funder type
Industry

Funder Name
Astra Zeneca

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated and/or analysed during the current study during this study will be included in the subsequent results publication.

IPD sharing plan summary
Other

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		16/03/2023	20/03/2023	Yes	No
Abstract results		20/05/2017	12/05/2021	No	No
Abstract results		01/10/2019	12/05/2021	No	No
HRA research summary			28/06/2023	No	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes