ICON8 Trials Programme

Submission date	Recruitment status No longer recruiting	Prospectively registered			
27/05/2011		☐ Protocol			
Registration date	Overall study status	Statistical analysis plan			
27/05/2011	Completed	[X] Results			
Last Edited	Condition category	[] Individual participant data			
20/01/2025	Cancer				

Plain English summary of protocol

http://cancerhelp.cancerresearchuk.org/trials/a-trial-looking-at-weekly-chemotherapy-for-ovarian-cancer-icon8

https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-looking-at-chemotherapy-with-or-without-bevacizumab-for-advanced-ovarian-cancer-icon8b http://www.icon8trial.org/patients/icon8-trial-summary/

Contact information

Type(s)

Scientific

Contact name

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Additional identifiers

Clinical Trials Information System (CTIS)

2010-022209-16

Integrated Research Application System (IRAS)

64812

ClinicalTrials.gov (NCT)

Protocol serial number 9812

Study information

Scientific Title

ICON8: An international phase III randomised trial of dose fractionated chemotherapy compared to standard three weekly chemotherapy, following immediate primary surgery or as part of delayed primary surgery, for women with newly diagnosed epithelial ovarian, fallopian tube or primary peritoneal cancer

and

ICON8B: A phase III randomised trial investigating the combination of dose-fractionated chemotherapy and bevacizumab compared to standard three weekly chemotherapy and bevacizumab for the first-line treatment of women with newly diagnosed high-risk stage III-IV epithelial ovarian, fallopian tube or primary peritoneal cancer

Acronym

ICON8 and ICON8B

Study objectives

Ovarian cancer is the most lethal gynaecological malignancy in the UK. Most patients respond well to firstline treatment, surgery and chemotherapy, but the majority go on to develop relapsed disease and the 5-year survival rate for patients with advanced disease is only 30%. There is a significant need to develop more effective first-line treatments.

ICON8:

Standard firstline chemotherapy is a combination of two drugs: carboplatin and paclitaxel, given once every 3 weeks for 6 cycles. However, giving these agents weekly may be more effective; this is called dose-fractionated chemotherapy. In ICON8 two dose-fractionated chemotherapy regimens are compared with standard carboplatin-paclitaxel.

The main outcome measures are whether dose-fractionated chemotherapy extends the time until ovarian cancer relapses (improved progression-free survival) and whether women who receive it live longer (improved overall survival). Secondary outcome measures are comparative toxicity, impact on quality of life and costeffectiveness. Two interim-analyses are planned: the first looking at feasibility and safety of the dose-fractionated regimens; and the second at their activity.

Women with newly diagnosed epithelial ovarian, fallopian tube or primary peritoneal cancers are eligible; including those with highrisk early stage (FIGO IC/IIA) or advanced (FIGO IIBIV) cancers. They can enter the trial either following primary surgery or with a plan to undergo delayed primary surgery between the 3rd and 4th cycles of chemotherapy. Women will be randomised to receive either: standard chemotherapy; or carboplatin given 3-weekly with weekly paclitaxel; or both carboplatin and paclitaxel weekly. Treatment duration in all three arms is 18 weeks.

ICON8B (added 12/08/2015):

As of 2014, the incorporation of bevacizumab and weekly dose dense paclitaxel respectively into the first-line management of ovarian cancer have shown improved survival in phase III clinical trials, hence both of these approaches can be considered new standards of care. They do

however have markedly different economic implications for healthcare providers, and also place distinct burdens on patients with respect to treatment-related toxicity and duration of therapy. Hence there is an urgent need to compare these treatment approaches in a randomised trial. In ICON8B standard 3-weekly carboplatin-paclitaxel and bevacizumab will be compared to dose fractionated chemotherapy with or without bevacizumab in a randomised controlled trial.

The main outcome measures are to determine whether dose-fractionated chemotherapy with bevacizumab extends the time until ovarian cancer relapses (improved progression-free survival) and whether women who receive it live longer (improved overall survival). Secondary outcome measures are comparative toxicity, impact on quality of life and cost effectiveness. One interim analysis is planned after 50 delayed primary surgery patients have been randomised to each trial arm to establish the safety of bevacizumab in the neo-adjuvant treatment of patients undergoing delayed primary ovarian cancer surgery.

Ethics approval required

Old ethics approval format

Ethics approval(s)

1. Approved 06/06/2011, London- Chelsea (Research Ethics Committee (REC) London Centre, 2 Redman Place, London, E20 1JQ, United Kingdom; +44 (0)207 104 8150; chelsea.rec@hra.nhs. uk), ref: 11/LO/0043

2. NRES Committee London - Chelsea, 08/04/2011, ref: 11/LO/0043

Study design

Randomized; Interventional; Design type: Treatment

Primary study design

Interventional

Study type(s)

Treatment

Health condition(s) or problem(s) studied

Ovarian/gynaecological cancer

Interventions

Current interventions as of 01/10/2021:

ICON8.

- 1. Dose-fractionated carb-pacl (carboplatin and paclitaxel given by intravenous infusion once every week)
- 2. The treatment course is 6 cycles with each cycle lasting 3 weeks
- 3. Dose-fractionated paclitaxel, carboplatin given by intravenous infusion once every 3 weeks at standard dose
- 4. Dose-fractionated paclitaxel given by intravenous infusion once every week
- 5. The treatment course is 6 cycles with each cycle lasting 3 weeks.
- 6. Standard treatment, carboplatin and paclitaxel given by intravenous infusion once every 3 weeks for 6 cycles.
- 7. Study entry: single randomisation only

ICON8B:

1. Arm B1: (Control arm): Carboplatin (AUC5 by intravenous infusion over 30-60 minutes) and

paclitaxel (175mg/m2 by intravenous infusion over 3 hours) plus bevacizumab (7.5mg/kg by intravenous infusion over 30-90 minutes) on day 1 of a 21-day cycle for 6 cycles followed by bevacizumab (7.5mg/kg by intravenous infusion over 30-90 minutes) as maintenance therapy to complete 18 cycles in total

- 2. Arm B2 (Control arm): Carboplatin (AUC55 by intravenous infusion over 30-60 minutes) on day 1 and dose-fractionated weekly paclitaxel (80mg/m2 by intravenous infusion over 1 hour) on day 1, 8 and 15 of a 21-day cycle for 6 cycles (Closed 05/05/2017)
- 3. Arm B3 (Research arm): Carboplatin (AUC55 by intravenous infusion over 30-60 minutes) on day 1 and dose-fractionated weekly paclitaxel (80mg/m2 by intravenous infusion over 1 hour) on day 1, 8 and 15 of a 21-day cycle plus bevacizumab (7.5mg/kg by intravenous infusion over 30-90 minutes) on day 1 of a 21-day cycle for 6 cycles followed by bevacizumab (7.5mg/kg by intravenous infusion over 30-90 minutes) as maintenance therapy to complete 18 cycles in total. 4. Study entry: Single randomisation only

Previous interventions:

ICON8:

- 1. Dose-fractionated carb-pacl (carboplatin and paclitaxel given by intravenous infusion once every week)
- 2. The treatment course is 6 cycles with each cycle lasting 3 weeks
- 3. Dose-fractionated paclitaxel, carboplatin given by intravenous infusion once every 3 weeks at standard dose
- 4. Dose-fractionated paclitaxel given by intravenous infusion once every week
- 5. The treatment course is 6 cycles with each cycle lasting 3 weeks.
- 6. Standard treatment, carboplatin and paclitaxel given by intravenous infusion once every 3 weeks for 6 cycles.
- 7. Study entry: single randomisation only

ICON8B (added 12/08/2015):

- 1. Arm B1: (Control arm): Carboplatin (AUC5 by intravenous infusion over 30-60 minutes) and paclitaxel (175mg/m2 by intravenous infusion over 3 hours) plus bevacizumab (7.5mg/kg by intravenous infusion over 30-90 minutes) on day 1 of a 21-day cycle for 6 cycles followed by bevacizumab (7.5mg/kg by intravenous infusion over 30-90 minutes) as maintenance therapy to complete 18 cycles in total
- 2. Arm B2 (Control arm): Carboplatin (AUC55 by intravenous infusion over 30-60 minutes) on day 1 and dose-fractionated weekly paclitaxel (80mg/m2 by intravenous infusion over 1 hour) on day 1, 8 and 15 of a 21-day cycle for 6 cycles
- 3. Arm B3 (Research arm): Carboplatin (AUC55 by intravenous infusion over 30-60 minutes) on day 1 and dose-fractionated weekly paclitaxel (80mg/m2 by intravenous infusion over 1 hour) on day 1, 8 and 15 of a 21-day cycle plus bevacizumab (7.5mg/kg by intravenous infusion over 30-90 minutes) on day 1 of a 21-day cycle for 6 cycles followed by bevacizumab (7.5mg/kg by intravenous infusion over 30-90 minutes) as maintenance therapy to complete 18 cycles in total. 4. Study entry: Single randomisation only

Intervention Type

Drug

Phase

Phase III

Drug/device/biological/vaccine name(s)

Carboplatin, paclitaxel, bevacizumab

Primary outcome(s)

Current primary outcome measure as of 01/10/2021:

ICON8:

Progression-free survival and overall survival in dose-fractionated arms. Timepoint(s): analyses will take place when the required number of events have occurred

ICON8B:

Progression-free survival. Timepoint(s): analyses will take place when the required number of events have occurred

Previous primary outcome measure:

ICON8:

Progression-free survival and overall survival in dose-fractionated arms. Timepoint(s): analyses will take place when the required number of events have occurred

ICON8B (added 12/08/2015):

Progression-free survival and overall survival in the experimental arm. Timepoint(s): analyses will take place when the required number of events have occurred

Key secondary outcome(s))

Current secondary outcome measures as of 01/10/2021:

ICON8:

- 1. Activity of dose-fractionated arms; timepoint(s): after first 186 (approx) pts enter the trial and 9 months after randomisation
- 2. Feasibility and safety of dose-fractionated arms
- 3. Timepoint(s): when first 50 pts randomised to each arm could have completed 6 cycles of chemotherapy
- 4. Feasibility and safety of DPS dose-fractionated patients

Timepoint(s): when 1st 50 pts randomised each arm (with planned DPS) could have completed 6 cycles of chemotherapy

ICON8B:

- 1. Safety of neo-adjuvant bevacizumab in patients undergoing DPS. Timepoint(s): when first 50 DPS pts randomised to each arm could have completed 6 cycles of chemotherapy
- 2. Overall Survival. Timepoints(s): analyses will take place only if a positive PFS result is observed.

Previous secondary outcome measures:

ICON8:

- 1. Activity of dose-fractionated arms; timepoint(s): after first 186 (approx) pts enter the trial and 9 months after randomisation
- 2. Feasibility and safety of dose-fractionated arms
- 3. Timepoint(s): when first 50 pts randomised to each arm could have completed 6 cycles of chemotherapy
- 4. Feasibility and safety of DPS dose-fractionated patients

Timepoint(s): when 1st 50 pts randomised each arm (with planned DPS) could have completed 6 cycles of chemotherapy

ICON8B (added 12/08/2015):

Safety of neo-adjuvant bevacizumab in patients undergoing DPS. Timepoint(s): when first 50 DPS pts randomised to each arm could have completed 6 cycles of chemotherapy

24/12/2024

Eligibility

Key inclusion criteria

Current ICON8 inclusion criteria as of 12/09/2018:

- 1. Females aged ≥18 years
- 2. Signed informed consent and ability to comply with the protocol
- 3. Histologically confirmed, with core biopsy from a disease site as minimum requirement (cytology alone is insufficient for diagnosis):
- 3.1. Epithelial ovarian carcinoma
- 3.2. Primary peritoneal carcinoma of Müllerian histological type
- 3.3. Fallopian tube carcinoma
- 3.4. Ovarian carcinosarcoma (malignant mixed Müllerian tumour (MMMT) of the ovary).
- 4. FIGO (1988) stage IC or above, which may be based on clinical and radiological assessment in patients who have not undergone immediate primary surgery
- 5. Confirmed high-risk histological subtype for patients with FIGO (1988) stage IC/IIA disease, namely:
- 5.1. High grade serous carcinoma
- 5.2. Clear cell carcinoma
- 5.3. Other histological subtype considered poorly differentiated/grade 3
- 6. ECOG Performance Status (PS) 0-2
- 7. Life expectancy >12 weeks
- 8. Adequate bone marrow function:
- 8.1. Absolute Neutrophil Count (ANC) ≥1.5 x 10(9)/l
- 8.2. Platelets (Plt) \geq 100 x 10(9)/l
- 8.3. Haemoglobin (Hb) \geq 9 g/dl (can be post transfusion)
- 9. Adequate liver function:
- 9.1. Serum bilirubin (BR) ≤1.5 x ULN
- 9.2. Serum transaminases ≤ 3 x ULN in the absence of parenchymal liver metastases or ≤ 5 x ULN in the presence of parenchymal liver metastases
- 10. Adequate renal function as defined by:
- 10.1. Directly measured GFR (Glomerular Filtration Rate) ≥ 30 ml/min, or
- 10.2. Calculated creatinine clearance ≥60 ml/min
- 11. Able to start chemotherapy within 8 weeks after immediate primary surgery (where applicable)

Previous ICON8 inclusion criteria:

- 1. Females aged 18 years and above
- 2. Signed informed consent and ability to comply with the protocol
- 3. Histologically confirmed, with core biopsy from a disease site as minimum requirement (cytology alone is insufficient for diagnosis):
- 3.1. Epithelial ovarian carcinoma
- 3.2. Primary peritoneal carcinoma of Müllerian histological type
- 3.3. Fallopian tube carcinoma
- 4. FIGO stage IC or above, which may be based on clinical and radiological assessment in patients who have not undergone immediate primary surgery
- 5. Confirmed high-risk histological subtype for patients with FIGO stage IC/IIA disease, namely:
- 5.1. High grade serous carcinoma
- 5.2. Clear cell carcinoma

- 5.3. Other histological subtype considered poorly differentiated/grade 3
- 6. ECOG Performance Status (PS) 02
- 7. Life expectancy >12 weeks
- 8. Adequate bone marrow function:
- 8.1. Absolute Neutrophil Count > $1.5 \times 10^9/l$
- 8.2. Platelets (Plt) > $100 \times 10^9/l$
- 8.3. Haemoglobin (Hb) > 9g/dl (can be post transfusion)
- 9. Adequate liver function (within 28 days prior to randomisation)
- 9.1. Serum bilirubin = 1.5 x ULN
- 9.2. Serum transaminases = $3 \times 100 \times 10^{-5} = 3 \times 100 \times 100$
- 10. Adequate renal function as defined by GFR (Glomerular Filtration Rate) = 30ml/min
- 11. Target gender: female
- 12. Lower age limit 18 years

Current ICON8B inclusion criteria as of 12/09/2018:

- 1. Females aged ≥18 years
- 2. Signed informed consent and ability to comply with the protocol
- 3. Histologically confirmed, with core biopsy from a disease site as minimum requirement (cytology alone is insufficient for diagnosis):
- 3.1. Epithelial ovarian carcinoma
- 3.2. Primary peritoneal carcinoma of Müllerian histological type
- 3.3. Fallopian tube carcinoma
- 3.4. Ovarian carcinosarcoma (malignant mixed Müllerian tumour (MMMT) of the ovary)
- 4. High-risk disease defined as:
- 4.1. FIGO (2013) Stage IIIA1(ii), IIIA2 with positive retroperitoneal lymph nodes >10mm in diameter, IIIB or IIIC disease
- 4.1.1. With >1 cm residual disease following IPS or
- 4.1.2. Planned to undergo primary chemotherapy with or without DPS
- 4.2. FIGO Stage IV disease
- 4.2.1. With any volume of residual disease following IPS or
- 4.2.2. Planned to undergo primary chemotherapy with or without DPS
- 5. ECOG Performance Status (PS) 0-2
- 6. No clinical symptoms or radiological evidence of bowel obstruction (including sub-acute obstruction), abdominal fistulae or extensive recto-sigmoid involvement on imaging related to ovarian cancer
- 7. No recent history of proven active peptic ulcer disease, diverticulitis or inflammatory bowel disease (Crohn's Disease and ulcerative colitis) or any prior episode of gastrointestinal perforation.
- 8. Life expectancy >12 weeks
- 9. Adequate bone marrow function:
- 9.1. Absolute Neutrophil Count (ANC) ≥1.5 x 10(9)/l
- 9.2. Platelets (Plt) \geq 100 x 10(9)/l
- 9.3. Haemoglobin (Hb) \geq 9 g/dl (can be post transfusion)
- 10. Adequate liver function:
- 10.1. Serum bilirubin (BR) ≤1.5 x ULN
- 10.2. Serum transaminases ≤ 3 x ULN in the absence of parenchymal liver metastases or ≤ 5 x ULN in the presence of parenchymal liver metastases.
- 11 Adequate renal function as defined by:
- 11.1. Directly measured GFR (Glomerular Filtration Rate) ≥30 ml/min, or
- 11.2. Calculated creatinine clearance ≥60 ml/min.
- 12. Adequate coagulation profile:

- 12.1. International normalised ratio (INR) \leq 1.5
- 12.2. Activated prothrombin time (APTT) ≤1.5xULN
- 13. Able to start chemotherapy within 8 weeks after IPS (where applicable)

Previous ICON8B inclusion criteria (added 12/08/2015):

- 1. Females aged ≥18 years
- 2. Signed informed consent and ability to comply with the protocol
- 3. Histologically confirmed, with core biopsy from a disease site as minimum requirement (cytology alone is insufficient for diagnosis):
- 3.1. Epithelial ovarian carcinoma
- 3.2. Primary peritoneal carcinoma of Müllerian histological type
- 3.3. Fallopian tube carcinoma
- 3.4. Ovarian carcinosarcoma (malignant mixed Müllerian tumour (MMMT) of the ovary).
- 4. High-risk disease defined as
- 4.1. FIGO (2013) Stage IIIA1(ii), IIIA2 with positive retroperitoneal lymph nodes >10mm in diameter, IIIB or IIIC disease
- 4.1.1. With >1cm residual disease following IPS or
- 4.1.2. Planned to undergo primary chemotherapy with or without DPS
- 4.2. FIGO Stage IV disease
- 4.2.1. With any volume of residual disease following IPS or
- 4.2.2. Planned to undergo primary chemotherapy with or without DPS.
- 5. ECOG Performance Status (PS) 0-2
- 6. Life expectancy >12 weeks
- 7. Adequate bone marrow function:
- 7.1. Absolute Neutrophil Count (ANC) ≥1.5 x 109/l
- 7.2. Platelets (Plt) ≥100 x 109/l
- 7.3. Haemoglobin (Hb) $\geq 9g/dl$ (can be post transfusion).
- 8. Adequate liver function:
- 8.1. Serum bilirubin (BR) ≤1.5 x ULN
- 8.2. Serum transaminases ≤ 3 x ULN in the absence of parenchymal liver metastases or ≤ 5 x ULN in the presence of parenchymal liver metastases.
- 9. Adequate renal function as defined by:
- 9.1. Directly measured GFR (Glomerular Filtration Rate) ≥ 30 ml/min, or
- 9.2. Calculated creatinine clearance \geq 60 ml/min.
- 10. Adequate coagulation profile:
- 10.1. International normalised ratio (INR) \leq 1.5
- 10.2. Activated prothrombin time (APTT) \leq 1.5xULN.
- 11. Able to start chemotherapy within 8 weeks after IPS (where applicable).

Participant type(s)

Patient

Healthy volunteers allowed

No

Age group

Adult

Lower age limit

18 years

Sex

Female

Total final enrolment

2144

Key exclusion criteria

Current ICON8 exclusion criteria as of 12/09/2018:

- 1. Non-epithelial ovarian cancer
- 2. Peritoneal cancer that is not of Müllerian origin, including mucinous histology
- 3. Borderline tumours (tumours of low malignant potential)
- 4. Prior systemic anti-cancer therapy for ovarian cancer (for example chemotherapy, monoclonal antibody therapy, tyrosine kinase inhibitor therapy or hormonal therapy)
- 5. Previous malignancies within 5 years prior to randomisation apart from:
- 5.1. adequately treated carcinoma in-situ of the cervix, breast ductal carcinoma in-situ, non-melanomatous skin cancer; or
- 5.2. previous/synchronous early-stage endometrial cancer defined as stage IA (FIGO 2009) grade 1 or 2 endometrioid cancers with no lymphovascular space invasion
- 6. Pre-existing sensory or motor neuropathy grade ≥2
- 7. Evidence of any other disease/metabolic dysfunction that in the opinion of the investigator would put the subject at high-risk of treatment-related complications or prevent compliance with the trial protocol
- 8. Planned intraperitoneal cytotoxic chemotherapy
- 9. Planned maintenance treatment with systemic anti-cancer therapy following completion of protocol treatment and prior to protocol defined progression
- 10. Any previous radiotherapy to the abdomen or pelvis
- 11. Sexually active women of childbearing potential not willing to use adequate contraception (eg. oral contraceptives, intrauterine device or barrier method of contraception in conjunction with spermicidal jelly or surgically sterile) for the study duration and at least six months afterwards
- 12. Pregnant or lactating women who are currently breastfeeding
- 13. Treatment with any other investigational agent prior to protocol defined progression
- 14. Known hypersensitivity to carboplatin, paclitaxel or their excipients (including cremophor)
- 15. History or clinical suspicion of brain metastases or spinal cord compression. CT/MRI of the brain is mandatory in the case of suspected brain metastases. Spinal MRI is mandatory in the case of suspected spinal cord compression. Patients with brain or meningeal metastases are not eligible.

Previous ICON8 exclusion criteria:

- 1. Non-epithelial ovarian cancer, including malignant mixed Müllerian tumours (carcinosarcomas)
- 2. Peritoneal cancer that is not of Müllerian origin, including mucinous histology
- 3. Borderline tumours (tumours of low malignant potential)
- 4. Prior systemic anticancer therapy for ovarian cancer (for example chemotherapy, monoclonal antibody therapy, tyrosine kinase inhibitor therapy or hormonal therapy)
- 5. Previous malignancies within 5 years prior to randomisation apart from: adequately treated carcinoma insitu of the cervix, breast ductal carcinoma insitu, nonmelanomatous skin cancer; or previous/synchronous early-stage endometrial cancer defined as stage IA (FIGO 2009) grade 1 or 2 endometrioid cancers with no lymphovascular space invasion
- 6. Preexisting sensory or motor neuropathy grade =2
- 7. Evidence of any other disease/metabolic dysfunction that in the opinion of the investigator would put the subject at highrisk of treatment-related complications or prevent compliance with

the trial protocol

- 8. Planned intraperitoneal cytotoxic chemotherapy
- 9. Any previous radiotherapy to the abdomen or pelvis
- 10. Sexually active women of childbearing potential not willing to use adequate contraception (eg. oral contraceptives, intrauterine device or barrier method of contraception in conjunction with spermicidal jelly or surgically sterile) for the study duration and at least six months afterwards
- 11. Pregnant or lactating women
- 12. Treatment with any other investigational agent prior to protocol defined progression
- 13. Known hypersensitivity to carboplatin, paclitaxel or their excipients (including cremophor)
- 14. History or clinical suspicion of brain metastases or spinal cord compression. CT/MRI of the brain is mandatory in the case of suspected brain metastases. Spinal MRI is mandatory in the case of suspected spinal cord compression. Patients with brain or meningeal metastases are not eligible

Current ICON8 exclusion criteria as of 12/09/2018:

- 1. Non-epithelial ovarian cancer
- 2. Peritoneal cancer that is not of Müllerian origin, including mucinous histology
- 3. Borderline tumours (i.e. tumours of low malignant potential)
- 4. Clinical symptoms or radiological evidence of bowel obstruction (including sub-acute obstruction) or extensive recto-sigmoid involvement on imaging related to ovarian cancer
- 5. Prior systemic anti-cancer therapy for ovarian cancer (for example chemotherapy, monoclonal antibody therapy, tyrosine kinase inhibitor therapy or hormonal therapy)
- 6. Previous malignancies within 5 years prior to randomisation apart from:
- 6.1. adequately treated carcinoma in-situ of the cervix, breast ductal carcinoma in-situ, non-melanomatous skin cancer; or
- 6.2. previous/synchronous early-stage endometrial cancer defined as stage IA (FIGO 2009) grade 1 or 2 endometrioid cancers with no lymphovascular space invasion
- 7. Pre-existing sensory or motor neuropathy CTCAE grade ≥2
- 8. Proteinuria at baseline: >1 g protein/24 h by a 24-hour urine collection
- 9. Significant co-existing or previous medical conditions that are contra-indications to treatment with bevacizumab, including:
- 9.1. Cerebrovascular disease, including transient ischaemic attacks (TIAs), cerebrovascular accident (CVA; i.e. stroke) and intracranial bleeds (i.e. intra-cerebral haemorrhage, sub-arachnoid haemorrhage or sub-dural haemorrhage) within 6 months before trial entry
- 9.2. Cardiovascular disease as follows:
- 9.2.1. Uncontrolled hypertension, defined as sustained BP >150/100 mmHg while receiving anti-hypertensive medication
- NB. Patients with a BP>150/100 mmHg prior to randomisation should be commenced on a calcium-channel blocker or other anti-hypertensive agent; or in the case of patients already on anti-hypertensives, medical therapy should be optimised. The BP should then be re-checked a few days later, if BP is controlled to ≤150/100 mmHg the patient may be entered into the trial
- 9.2.2. Myocardial infarction or unstable angina within 6 months prior to randomization
- 9.2.3. New York Heart Association (NYHA) grade ≥2 congestive heart failure
- 9.2.4. Poorly controlled cardiac arrhythmia despite medication
- NB. Patients with rate-controlled atrial fibrillation are eligible
- 9.2.5. Peripheral vascular disease grade ≥3, i.e. symptomatic and interfering with activities of daily living requiring repair or revision
- 9.3. History or evidence of bleeding diathesis or coagulopathy (in patients not on therapeutic anti-coagulant medication)
- 10. Chronic daily use of high-dose aspirin, >325 mg/day, within 10 days prior to study entry
- 11. Surgery (including open biopsy) or significant traumatic injury within 28 days prior to

anticipated date of first dose of bevacizumab

- 12. Serious non-healing wound, worse than CTCAE Wound Complication or Wound Dehiscence grade 1
- 13. Active ulcer or bone fracture
- 14. Anticipated to require extensive dental work during protocol treatment
- 15. Evidence of any other disease/metabolic dysfunction that in the opinion of the investigator would put the subject at high-risk of treatment-related complications or prevent compliance with the trial protocol
- 16. Evidence of intra-abdominal free air not explained by paracentesis or recent surgical procedure
- 17. Symptomatic abdominal fistulae
- 18. History or clinical suspicion of brain metastases or spinal cord compression. CT/MRI of the brain is mandatory in the case of suspected brain metastases. Spinal MRI is mandatory in the case of suspected spinal cord compression. Patients with brain or meningeal metastases are not eligible
- 19. Sexually active women of childbearing potential not willing to use adequate contraception (e. g. oral contraceptives, intrauterine device or barrier method of contraception in conjunction with spermicidal jelly or surgically sterile) for the study duration and at least six months afterwards
- 20. Pregnant or lactating women who are currently breastfeeding
- 21. Known hypersensitivity to carboplatin, paclitaxel, bevacizumab or their excipients (including cremophor)
- 22. Planned intraperitoneal cytotoxic chemotherapy
- 23. Planned treatment with any other systemic anti-cancer therapy following completion of protocol treatment and prior to protocol defined progression
- 24. Any previous radiotherapy to the abdomen or pelvis
- 25. Treatment with any other investigational agent prior to protocol defined progression.

Previous ICON8B exclusion criteria (added 12/08/2015):

- 1. Non-epithelial ovarian cancer
- 2. Peritoneal cancer that is not of Müllerian origin, including mucinous histology
- 3. Borderline tumours (i.e. tumours of low malignant potential)
- 4. Prior systemic anti-cancer therapy for ovarian cancer (for example chemotherapy, monoclonal antibody therapy, tyrosine kinase inhibitor therapy or hormonal therapy)
- 5. Previous malignancies within 5 years prior to randomisation apart from:
- 5.1. Adequately treated carcinoma in-situ of the cervix, breast ductal carcinoma in-situ, non-melanomatous skin cancer; or
- 5.2. Previous/synchronous early-stage endometrial cancer defined as stage IA (FIGO 2009) grade 1 or 2 endometrioid cancers with no lymphovascular space invasion.
- 6. Pre-existing sensory or motor neuropathy CTCAE grade ≥2
- 7. Proteinuria at baseline: >1gm protein/24h by a 24-hour urine collection. NB. Proteinuria should be initially assessed by urine dipstick. If urine protein is ≥2+ on urine dipstick, a 24-hour urine protein collection must be performed.
- 8. Significant co-existing or previous medical conditions that are contra-indications to treatment with bevacizumab, including:
- 8.1. Cerebrovascular disease, including transient ischaemic attacks (TIAs), cerebrovascular accident (CVA; i.e. stroke) and intracranial bleeds (i.e. intra-cerebral haemorrhage, sub-arachnoid haemorrhage or sub-dural haemorrhage) within 6 months before trial entry
- 8.2. Cardiovascular disease as follows:
- 8.2.1. Uncontrolled hypertension, defined as sustained BP>150/100mmHg while receiving anti-hypertensive medication. NB. Patients with a BP>150/100 mmHg prior to randomisation should be commenced on a calcium-channel blocker or other anti-hypertensive agent; or in the case of

patients already on anti-hypertensives, medical therapy should be optimised. The BP should then be re-checked a few days later, if BP is controlled to ≤150/100mmHg the patient may be entered into the trial

- 8.2.2. Myocardial infarction or unstable angina within 6 months prior to randomization
- 8.3.3. New York Heart Association (NYHA) grade ≥2 congestive heart failure
- 8.3.4. Poorly controlled cardiac arrhythmia despite medication. NB. Patients with rate-controlled atrial fibrillation are eligible
- 8.3.5. Peripheral vascular disease grade ≥3, i.e. symptomatic and interfering with activities of daily living requiring repair or revision
- 8.3. History or evidence of bleeding diathesis or coagulopathy (in patients not on therapeutic anti-coagulant medication)
- 8.4. Recent history of proven active peptic ulcer disease, diverticulitis or inflammatory bowel disease (Crohns' Disease and ulcerative colitis)
- 8.5. Previous gastrointestinal perforation.
- 9. Chronic daily use of high-dose aspirin, >325mg/day, within 10 days prior to study entry
- 10. Surgery (including open biopsy) or significant traumatic injury within 28 days prior to anticipated date of first dose of bevacizumab. NB. If IPS was performed within 28 days of planned start of treatment, patients are eligible but bevacizumab must be omitted from cycle 1.
- 11. Serious non-healing wound, worse than CTCAE Wound Complication or Wound Dehiscence grade 1
- 12. Active ulcer or bone fracture
- 13. Anticipated to require extensive dental work during protocol treatment
- 14. Evidence of any other disease/metabolic dysfunction that in the opinion of the investigator would put the subject at high-risk of treatment-related complications or prevent compliance with the trial protocol
- 15. Clinical symptoms or radiological evidence of bowel obstruction (including sub-acute obstruction) or extensive recto-sigmoid involvement on imaging related to ovarian cancer
- 16. Evidence of intra-abdominal free air not explained by paracentesis or recent surgical procedure
- 17. Symptomatic abdominal fistulae
- 18. History or clinical suspicion of brain metastases or spinal cord compression. CT/MRI of the brain is mandatory in the case of suspected brain metastases. Spinal MRI is mandatory in the case of suspected spinal cord compression. Patients with brain or meningeal metastases are not eligible
- 19. Sexually active women of childbearing potential not willing to use adequate contraception (e. g. oral contraceptives, intrauterine device or barrier method of contraception in conjunction with spermicidal jelly or surgically sterile) for the study duration and at least six months afterwards
- 20. Pregnant or lactating women who are currently breastfeeding
- 21. Known hypersensitivity to carboplatin, paclitaxel, bevacizumab or their excipients (including cremophor)
- 22. Planned intraperitoneal cytotoxic chemotherapy
- 23. Planned treatment with any other systemic anti-cancer therapy following completion of protocol treatment and prior to protocol defined progression
- 24. Any previous radiotherapy to the abdomen or pelvis
- 25. Treatment with any other investigational agent prior to protocol defined progression

Date of first enrolment

29/04/2011

Date of final enrolment

Locations

Countries of recruitment

United Kingdom

England

Northern Ireland

Scotland

Wales

Australia

Ireland

Korea, South

Mexico

New Zealand

Switzerland

Study participating centre Aberdeen Royal Infirmary

Foresterhill Health Campus Foresterhill Road Aberdeen United Kingdom AB25 2ZN

Study participating centre Addenbrooke's Hospital

Hills Road Cambridge United Kingdom CB2 0QQ

Study participating centre Airedale General Hospital Skipton Road Steeton Keighley United Kingdom BD20 6TD

Study participating centre Beatson West of Scotland Cancer Centre

1053 Great Western Road Glasgow United Kingdom G12 0YN

Study participating centre Bedford Hospital

Kempston Road Bedford United Kingdom MK42 9DJ

Study participating centre Belfast City Hospital

51 Lisburn Road Belfast United Kingdom BT9 7AB

Study participating centre Birmingham Heartlands Hospital

Bordesley Green E Birmingham United Kingdom B9 5SS

Study participating centre Blackpool Victoria Hospital

Whinney Heys Road Blackpool United Kingdom FY3 8NR

Study participating centre Bradford Royal Infirmary

Duckworth Lane Bradford United Kingdom BD9 6RJ

Study participating centre Bristol Haematology & Oncology Centre

Horfield Road Avon Bristol United Kingdom BS2 8ED

Study participating centre Broomfield Hospital

Court Road Broomfield Chelmsford United Kingdom CM1 7ET

Study participating centre Huddersfield Royal Infirmary

Acre Street Huddersfield United Kingdom HD3 3EA

Study participating centre Castle Hill Hospital

Castle Road Cottingham United Kingdom HU16 5JQ

Study participating centre Cheltenham General Hospital Sandford Road

Cheltenham United Kingdom GL53 7AN

Study participating centre Christie Hospital

Wilmslow Road Manchester United Kingdom M20 4BX

Study participating centre Churchill Hospital

Old Road Oxford United Kingdom OX3 7LE

Study participating centre City Hospital

Dudley Road Birmingham United Kingdom B18 7QH

Study participating centre The Clatterbridge Cancer Centre

Clatterbridge Road Birkenhead United Kingdom CH63 4JY

Study participating centre County Hospital

151 Weston Road Stafford United Kingdom ST16 3SA

Study participating centre Cumberland Infirmary

Newtown Road Carlisle United Kingdom CA2 7HY

Study participating centre
Diana, Princess of Wales Hospital
Scartho Road
Grimsby
United Kingdom
DN33 2BA

Study participating centre Doncaster Royal Infirmary

Thorne Road Doncaster United Kingdom DN2 5LT

Study participating centre Dorset County Hispital

Williams Avenue Dorchester United Kingdom DT1 2JY

Study participating centre Essex County Hospital

Lexden Road Colchester United Kingdom CO3 3NB

Study participating centre Freeman Hospital

Freeman Road High Heaton Newcastle upon Tyne United Kingdom NE7 7DN

Study participating centre George Eliot Hospital

College Street Nuneaton United Kingdom CV10 7DJ

Study participating centre Glan Clwyd Hospital

Rhuddlan Road Bodelwyddan Rhyl United Kingdom LL18 5UJ

Study participating centre Gloucestershire Royal Hospital

Great Western Road Gloucester United Kingdom GL1 3NN

Study participating centre Great Western Hospital

Marlborough Road Swindon United Kingdom SN3 6BB

Study participating centre Guy's & St. Thomas' Hospital

Great Maze Pond London United Kingdom SE1 9RT

Study participating centre Hammersmith Hospital

150 Du Cane Road White City London United Kingdom W12 0HS

Study participating centre Hereford County Hospital

Stonebow Road Hereford United Kingdom HR1 2BN

Study participating centre Hinchingbrooke Hospital

Parkway Hinchingbrooke Huntingdon United Kingdom PE29 6NT

Study participating centre Ipswich Hospital

Heath Road Ipswich United Kingdom IP4 5PD

Study participating centre James Cook University Hospital

Marton Road Middlesbrough United Kingdom TS4 3BW

Study participating centre James Paget Hospital

Lowestoft Road

Gorleston-on-Sea Great Yarmouth United Kingdom NR31 6LA

Study participating centre Leicester Royal Infirmary

Infirmary Square Leicester United Kingdom LE1 5WW

Study participating centre Lincoln County Hospital

Greetwell Road Lincoln United Kingdom LN2 5QY

Study participating centre Lister Hospital

Stevenage United Kingdom SG1 4AB

Study participating centre Liverpool Women's Hospital

Crown Street Liverpool United Kingdom L8 7SS

Study participating centre Maidstone Hospital

Hermitage Lane Maidstone United Kingdom ME16 9QQ

Study participating centre Walsall Manor Hospital

Moat Road Walsall United Kingdom WS2 9PS

Study participating centre Mount Vernon Hospital

Rickmansworth Road Northwood United Kingdom HA6 2RN

Study participating centre Musgrove Park Hospital

Parkfield Drive Taunton United Kingdom TA1 5DA

Study participating centre New Cross Hospital

Wolverhampton Road Heath Town Wolverhampton United Kingdom WV10 0QP

Study participating centre Ninewells Hospital

James Arrott Drive Dundee United Kingdom DD2 1SY

Study participating centre Norfolk & Norwich University Hospital

Colney Lane

Norwich United Kingdom NR4 7UY

Study participating centre North Devon District Hospital

Raleigh Park Barnstaple United Kingdom EX31 4JB

Study participating centre Northampton General Hospital

Cliftonville Northampton United Kingdom NN1 5BD

Study participating centre Nottingham City Hospital

Hucknall Road Nottingham United Kingdom NG5 1PB

Study participating centre Peterborough City Hospital

Edith Cavell Campus Bretton Gate Peterborough United Kingdom PE3 9GZ

Study participating centre Pilgrim Hospital

Sibsey Road Boston United Kingdom PE21 9QS

Study participating centre Dorset Cancer Centre

Poole Hospital NHS Foundation Trust Longfleet Road Poole United Kingdom BH15 2JB

Study participating centre Queen Alexandra Hospital

Portsmouth United Kingdom PO6 3LY

Study participating centre Queen Elizabeth, The Queen Mother Hospital

St Peter's Road Margate United Kingdom CT9 4AN

Study participating centre Queen Elizabeth Hospital, King's Lynn

Gayton Road King's Lynn United Kingdom PE30 4ET

Study participating centre Queen Elizabeth Hospital, Birmingham

Mindelsohn Way Birmingham United Kingdom B15 2TH

Study participating centre Queen's Hospital, Burton-on-Trent

Belvedere Road

Burton-on-Trent United Kingdom DE13 0RB

Study participating centre Queen's Hospital, Romford

Rom Valley Way Romford United Kingdom RM7 0AG

Study participating centre Royal Berkshire Hospital

21 Craven Road Reading United Kingdom RG1 5LE

Study participating centre Royal Blackburn Hospital

Haslingden Road Blackburn United Kingdom BB2 3HH

Study participating centre Royal Cornwall Hospital

Treliske Truro United Kingdom TR1 3LQ

Study participating centre Royal Derby Hospital

Uttoxeter Road Derby United Kingdom DE22 3NE

Study participating centre Royal Devon & Exeter Hospital

Barrack Road Exeter United Kingdom EX2 5DW

Study participating centre Royal Lancaster Infirmary

Ashton Road Lancaster United Kingdom LA1 4RP

Study participating centre Furness General Hospital

Dalton Lane Barrow-in-Furness United Kingdom LA14 4LF

Study participating centre The Royal Marsden Hospital

203 Fulham Road Chelsea London United Kingdom SW3 6JJ

Study participating centre The Royal Marsden Hospital (Sutton)

Downs Road Sutton United Kingdom SM2 5PT

Study participating centre Royal Preston Hospital

Sharoe Green Lane North Fulwood Preston United Kingdom PR2 9HT

Study participating centre Royal Shrewsbury Hospital

Mytton Oak Road Shrewsbury United Kingdom SY3 8XQ

Study participating centre Royal Stoke Hospital

Newcastle Road Stoke-on-Trent United Kingdom ST4 6QG

Study participating centre Royal Surrey County Hospital

Egerton Road Guildford United Kingdom GU2 7XX

Study participating centre Royal Sussex County Hospital

Barry Building Eastern Road Brighton United Kingdom BN2 5BE

Study participating centre Royal United Hospital

Combe Park Avon Bath United Kingdom BA1 3NG

Study participating centre Scunthorpe General Hospital

Cliff Gardens Scunthorpe United Kingdom DN15 7BH

Study participating centre Singleton Hospital

Sketty Lane Sketty Swansea United Kingdom SA2 8QA

Study participating centre Southampton General Hospital

Tremona Road Southampton United Kingdom SO16 6YD

Study participating centre Southend Hospital

Prittlewell Chase Southend-on-Sea United Kingdom SSO ORY

Study participating centre St Bartholomew's Hospital

W Smithfield London United Kingdom EC1A 7BE

Study participating centre St George's Hospital Blackshaw Road

London

United Kingdom SW17 0QT

Study participating centre Whiston Hospital

Warrington Road Rainhill Prescot United Kingdom L35 5DR

Study participating centre St James's University Hospital

Beckett Street Leeds United Kingdom LS9 7TF

Study participating centre Torbay Hospital

Newton Road Torquay United Kingdom TQ2 7AA

Study participating centre University Hospital Coventry

Clifford Bridge Road Coventry United Kingdom CV2 2DX

Study participating centre Velindre Cancer Centre

Velindre Road Cardiff United Kingdom CF14 2TL

Study participating centre Warwick Hospital

Lakin Road Warwick United Kingdom CV34 5BW

Study participating centre West Cumberland Hospital

Homewood Road Whitehaven United Kingdom CA28 8JG

Study participating centre Weston General Hospital

Grange Road Weston-super-Mare United Kingdom BS23 4TG

Study participating centre Weston Park Hospital

Whitham Road Sheffield United Kingdom S10 2SJ

Study participating centre Wexham Park Hospital

Wexham Street Slough United Kingdom SL2 4HL

Study participating centre Worthing Hospital

Lyndhurst Road Worthing United Kingdom BN11 2DH

Study participating centre Wrexham Maelor Hospital

Croesnewydd Road Wrexham United Kingdom LL13 7TD

Study participating centre Yeovil District Hospital

Higher Kingston Yeovil United Kingdom BA21 4AT

Study participating centre York Hospital

Wigginton Road York United Kingdom YO31 8HE

Study participating centre Ysbyty Gwynedd Hospital

Bangor United Kingdom LL57 2PW

Study participating centre Good Hope Hospital

Rectory Road Sutton Coldfield United Kingdom B75 7RR

Study participating centre Pinderfields General Hospital Aberford Road Wakefield

United Kingdom WF1 4DG

Study participating centre Kantonsspital Frauenfeld Pfaffenholzstrasse 4 Frauenfeld Switzerland CH-8501

Sponsor information

Organisation

MRC Clinical Trials Unit at UCL (UK)

ROR

https://ror.org/001mm6w73

Funder(s)

Funder type

Charity

Funder Name

Cancer Research UK Clinical Trials Advisory and Awards Committee (UK)

Results and Publications

Individual participant data (IPD) sharing plan

Data will be made available on request following the MRC CTU Data Sharing Policy. Data release applications will be reviewed by the Trial Management Group and Trial Steering Committee before final approval. Data-sharing contracts will be put in place between the applicant and UCL.

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient- facing?
	ICONS results	07/12	04/12		

Results article		/2019	/2019	Yes	No
Results article	ICON8 quality-of-life results	01/07 /2020	05/07 /2020	Yes	No
Results article	ICON8 overall survival and progression-free survival results	08/06 /2022	13/06 /2022	Yes	No
HRA research summary	ICON8		28/06 /2023	No	No
Participant information sheet	Participant information sheet	11/11 /2025	11/11 /2025	No	Yes
Plain English results	ICON8	11/01 /2018	25/01 /2022	No	Yes
Study website	Study website	11/11 /2025	11/11 /2025	No	Yes