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ICON8 Trials Programme

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

Study website
http://www.icon8trial.org

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
2010-022209-16

IRAS number

64812

ClinicalTrials.gov number
NCT01654146

Secondary identifying numbers
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

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please email mrcctu.icon8and8b@ucl.ac.uk to request a patient information sheet

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 measure
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

Secondary outcome measures
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

Overall study start date
29/04/2011

Completion date
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) ≥100 x 10(9)/l
8.3. Haemoglobin (Hb) ≥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 x 10^9/l
8.2. Platelets (Plt) > 100 x 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 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 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) ≥100 x 10(9)/l
9.3. Haemoglobin (Hb) ≥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) ≤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) ≥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 ≥ 60 ml/min.

10. Adequate coagulation profile:
10.1. International normalised ratio (INR) ≤1.5
10.2. Activated prothrombin time (APTT) ≤1.5xULN.
11. Able to start chemotherapy within 8 weeks after IPS (where applicable).

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Female

Target number of participants
1485 (ICON8); 590 (ICON8B)

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
08/04/2020

Locations

Countries of recruitment
Australia

England

Ireland

Korea, South

Mexico

New Zealand

Northern Ireland

Scotland

Switzerland

United Kingdom

Wales

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
SS0 0RY

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)

Sponsor details
Institute of Clinical Trials & Methodology
90 High Holborn 2nd Floor
London
England
United Kingdom
WC1V 6LJ

Sponsor type

University/education

Website
http://www.mrc.ac.uk/index.htm

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

Publication and dissemination plan
For ICON8, results of the stage 1 feasibility and safety analysis will be published. After the stage 2 analysis, advice will be sought from the Trial Steering Committee with regard to the publication of those results. The progression-free survival analysis is expected to occur 1 year after the last patient is randomised, and the overall survival analysis is expected to occur 3 years after the last patient is randomised. The results of the progression-free and overall survival analyses will be published separately, and as soon as possible after each analysis has occurred.

For the ICON8B cohort, results of the safety analysis in Delayed Primary Surgery patients will be published. The progression-free survival analysis is expected to occur 1 year after the last patient is randomised, and the overall survival analysis is expected to occur 3 years after the last patient is randomised. The results of the progression-free and overall survival analyses will be published separately, and as soon as possible after each analysis has occurred.

Intention to publish date
24/12/2025

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?

Results article	ICON8 results	07/12/2019	04/12/2019	Yes	No
Results article	ICON8 quality-of-life results	01/07/2020	05/07/2020	Yes	No
Plain English results	ICON8	11/01/2018	25/01/2022	No	Yes
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