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Pressurised IntraPeritoneal Aerosolised Chemotherapy (PIPAC) in the management of cancers of the bowel, ovary and stomach: a randomised controlled trial of efficacy in peritoneal metastases

Submission date 19/08/2023	**Recruitment status** Recruiting	[X] Prospectively registered [X] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 29/09/2023	**Overall study status** Ongoing	
Last Edited 15/05/2026	**Condition category** Cancer	

Plain English summary of protocol

Background and study aims

Patients with peritoneal metastases normally receive chemotherapy or biological medications either through a drip (intravenously) or by taking it in tablet form, or through combinations of these. Chemotherapy and biological medications are both types of systemic anti-cancer therapy (SACT). Even with the usual chemotherapy, peritoneal metastases can be difficult to manage as chemotherapy medicines that circulate in the bloodstream do not reach the peritoneal metastases very well and cause many side effects by acting on other areas of the body that can affect a patient's quality of life. New more effective and less severe ways of managing peritoneal metastases are urgently needed. This trial aims to find out whether using a new treatment strategy to deliver chemotherapy as a spray directly into the abdominal cavity during keyhole surgery is better at managing peritoneal metastases than the usual chemotherapy. This new way of giving chemotherapy is called Pressurised IntraPeritoneal Aerosolised Chemotherapy or PIPAC for short. It has been used across the world for a few years, however, it has only been allowed in the UK as part of research studies. The National Institute for Health and Care Excellence (NICE) reviewed the evidence for PIPAC in 2021. It found that while patients who had PIPAC may have improved survival and quality of life, higher quality evidence was needed before a decision can be made on whether or not to approve it being available to patients on the NHS. The best way of knowing whether one treatment is better than another is by carrying out a type of research called a randomised controlled trial (RCT). An RCT is a type of research study in which patients are randomly allocated into two groups - an experimental group that receives the new treatment and a control group that receives the usual treatment. Patients have an equal chance of being allocated to the experimental or control group. This enables a fair comparison to be made to see which treatment works best.

Who can participate?
Patients aged 16 years old and over with visible (measurable or non-measurable) peritoneal lesions

What does the study involve?
Because of the NICE recommendations, researchers designed the PICCOS trial – this is an RCT. Half of the patients in this trial will receive their usual chemotherapy, whilst the other half have their usual chemotherapy in addition to chemotherapy given by PIPAC.

The PICCOS trial also aims to find out whether there are differences in the quality of life in patients with peritoneal metastases who have PIPAC compared to those who do not.

What are the possible benefits and risks of participating?
Patients receiving PIPAC therapy may benefit from delayed cancer progression, improved life expectancy and better quality of life. If not randomised to receive PIPAC therapy they will be receiving what is currently the gold standard of care provided within the NHS, whilst at the same time helping the medical community worldwide understand how this new treatment affects cancer and patients' lives. Chemotherapy medicines used in this trial can cause side effects, for most people they are manageable with the support of the clinical team. Side effects include those from usual chemotherapy drugs and side effects from the PIPAC procedure which include those that come with a general anaesthetic and keyhole surgery.

Where is the study run from?
Cardiff University (UK)

When is the study starting and how long is it expected to run for?
November 2022 to October 2026

Who is funding the study?
National Institute for Health and Care Research (NIHR) (UK)

Who is the main contact?
The study team, piccos@cardiff.ac.uk (UK)

https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-looking-at-a-different-way-to-give-chemotherapy-called-pipac-for-cancer-that-has-spread-to#undefined

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Additional identifiers

Clinical Trials Information System (CTIS)
2022-003680-26

Integrated Research Application System (IRAS)
1006905

Central Portfolio Management System (CPMS)
54134

Protocol serial number
21/SEP/8237E

Study information

Scientific Title
Pressurised IntraPeritoneal Aerosolised Chemotherapy (PIPAC) in the management of cancers of the colon, ovary and stomach: a randomised controlled phase II trial of efficacy in peritoneal metastases

Acronym
PICCOS

Study objectives
Bowel, ovarian and stomach cancer will often spread (metastasise) to the lining (peritoneum) of the abdominal cavity. This trial aims to determine if a new way of delivering chemotherapy as a spray, directly into the peritoneal cavity, would improve survival in patients with peritoneal metastases, compared to conventional intravenous chemotherapy. Critically, we will also assess the impact of treatment on patient quality of life. The primary objective is to determine if PIPAC given with (colorectal, stomach) or instead of (ovarian) systematic anti-cancer treatment improves peritoneal progression-free survival compared to standard systematic anti-cancer treatment.

Primary objectives:
To determine if Pressurised IntraPeritoneal Aerosolised Chemotherapy (PIPAC) given with (colorectal, stomach) or instead of (ovarian) systemic anti-cancer therapy (SACT) improves peritoneal Progression Free Survival (PFS) compared to standard SACT

Secondary objectives:
1. To determine how PIPAC impacts quality of life (QoL) compared to standard of care (SOC)
2. To determine the safety of PIPAC in terms of the proportion of patients experiencing toxicity and/or surgical complications, compared with SACT only group
3. To determine the proportion of patients who complete three PIPAC procedures
4. To determine if disease can be reduced to the point of resectability
5. To evaluate Overall Survival (OS) in both groups
6. To evaluate overall Progression Free Survival (PFS) in both groups
7. To assess the impact on patient's symptoms (and need for intervention to relieve them – in ovarian cancer)
8. To determine peritoneal-specific overall response rate (ORR) and disease control rate (DCR)

Ethics approval required
Ethics approval required

Ethics approval(s)
1. approved 14/09/2023, Wales Research Ethics Committee 5 Bangor (Health and Care Research Wales, Castlebridge 4, 15-19 Cowbridge Road East, Cardiff, CF11 9AB, United Kingdom; +44 (0) 2922 940910; Wales.REC5@wales.nhs.uk), ref: 23/WA/0159

2. submitted 02/05/2023, Cardiff University procedure for Quality Assurance, Radiation Assurance and Pharmacy Assurance (Centre for Trials Research, College of Biomedical and Life Sciences, Cardiff University, 7th Floor, Neuadd Meirionnydd, Heath Park, Cardiff, CF14 4YS, United Kingdom; +44 (0)29 2068 7620; ctr@cardiff.ac.uk), ref: None provided

Study design
Randomized controlled phase II basket trial with intervention and control arms in each of three disease groups (colorectal, stomach and ovarian cancer)

Primary study design
Interventional

Study type(s)
Efficacy, Safety, Treatment

Health condition(s) or problem(s) studied
Colorectal, ovarian and stomach cancer with peritoneal metastasis

Interventions
Current interventions as of 19/06/2025:
The trial will test a new method to deliver chemotherapy as a spray, directly into the peritoneal cavity, to determine whether this improves survival in patients with peritoneal metastases, compared to conventional intravenous chemotherapy. This randomised controlled trial will be open to patients with bowel, ovarian or stomach cancer. Each cancer type will have individual eligibility criteria and protocols to allow for the necessary variations in treatment. In all cancer types, patients will be randomised to receive either standard chemotherapy delivered via the bloodstream or a combination of standard chemotherapy (SACT) and/or Pressurised IntraPeritoneal Aerosolised Chemotherapy (PIPAC), where three PIPAC procedures are performed (ovarian intervention arm receives PIPAC with no SACT). This trial design enables the variation required to include patients with different cancer types and the ability to stop the trial for any one cancer type if it is not working, whilst continuing with the others. Prior to randomisation, the treating Investigator will select the SACT regimen most appropriate to the individual patient from treatment options available for the patient's disease group. Following randomisation, treatment will commence within two weeks for all participants other than those in the ovarian intervention arm, for whom the first PIPAC should take place within three weeks. There is no trial-specific drug provision; all drugs used in the trial will be taken from local hospital supplies. Each disease group has specific options for the chemotherapy dose and frequency, which we have represented in our protocol with 3 separate schemas and tables for treatment options (these can be viewed in the attached synopsis). All participants will be followed up to the point of peritoneal disease progression or a minimum of six months post-randomisation, whichever comes first. Ongoing assessments will end for all patients when the last patient randomised has completed 6 months of follow-up from their randomisation date. After the end of treatment, participants will have a telephone call from the site Research Nurse every 2 months in the first year and then every 3 months thereafter, just prior to each CT scan to review progress and collect follow-up data.

Treatment Investigational Medicinal Products for the 3 disease groups are:
· Colorectal group: Oxaliplatin IP via PIPAC, Mitomycin IP via PIPAC

· Ovarian group: Cisplatin IP via PIPAC, Doxorubicin IP via PIPAC, Paclitaxel IV, Liposomal doxorubicin IV, Gemcitabine IV
· Stomach group: Cisplatin IP via PIPAC, Doxorubicin IP via PIPAC

The treatment duration for the 3 disease groups is:
· Colorectal group: Intervention arm = 18 weeks, Control arm = 18 weeks
· Ovarian group: Intervention arm = 14 or 15 weeks, Control arm = 18 or 24 weeks
· Stomach group: Intervention arm = 18 or 21 weeks, Control arm = 18 weeks

Participants will be randomised via the central PICCOS database. Sites should complete the screening Case Report Forms (CRF), answering all the questions before submitting a request to the CTR for randomisation (patients preferred PIPAC centre will need to be inputted) at the time of randomisation. Once the randomisation is completed, the database will confirm whether the participant has been allocated to the control or intervention arm. The allocation will be sent via email to those indicated as requiring it by the site. If the patient is allocated to receive PIPAC, the PIPAC site will also be notified. The database system can be accessed via: https://redcap.ctr.cardiff.ac.uk/redcap/. If the online system becomes unavailable for any reason, site staff should contact PICCOS@cardiff.ac.uk, and a manual randomisation process will be initiated. Following randomisation, participants should be provided with a Patient Card to identify them as PICCOS trial participants.
The intervention provider on each site will be a PIPAC-qualified oncology surgeon who has undergone the International Society for Study of Pleura and Peritoneum (ISSPP) approved PIPAC training and will have met the requirements of their local health board. They will be working with the qualified team designated by the site PI at each site.

Previous interventions:
The trial will test a new method to deliver chemotherapy as a spray, directly into the peritoneal cavity, for whether this improves survival in patients with peritoneal metastases, compared to conventional intravenous chemotherapy. This randomised controlled trial will be open to patients with bowel, ovarian or stomach cancer. Each cancer type will have individual eligibility criteria and protocols to allow for the necessary variations in treatment. In all cancer types, patients will be randomised to receive either standard chemotherapy delivered via the bloodstream or a combination of standard chemotherapy (SACT) and/or Pressurised IntraPeritoneal Aerosolised Chemotherapy (PIPAC), where three PIPAC procedures are performed (ovarian intervention arm receives PIPAC with no SACT). This trial design enables the variation required to include patients with different cancer types and the ability to stop the trial for any one cancer type if it is not working whilst continuing with the others. Prior to randomisation, the treating Investigator will select the SACT regimen most appropriate to the individual patient from treatment options available for the patient's disease group. Following randomisation, treatment will commence within two weeks for all participants other than those in the ovarian intervention arm, for whom the first PIPAC should take place within three weeks. There is no trial-specific drug provision, all drugs used in the trial will be taken from local hospital supplies. Each disease group has specific options for the chemotherapy dose and frequency which we have represented in our protocol with 3 separate schemas and tables for treatment options (these can be viewed in the attached synopsis). All participants will be followed up to the point of peritoneal disease progression or a minimum of six months post-randomisation whichever comes first. Ongoing assessments will end for all patients when the last patient randomised has completed 6 months of follow-up from their randomisation date. After the end of treatment, participants will have a telephone call from the site Research Nurse every 2 months in the first year and then every 3 months thereafter just prior to each CT scan to review progress and collect follow-up data.

Treatment Investigational Medicinal Products for the 3 disease groups are:
• Colorectal group: Oxaliplatin IP via PIPAC, Mitomycin IP via PIPAC
• Ovarian group: Cisplatin IP via PIPAC, Doxorubicin IP via PIPAC, Paclitaxel IV, Liposomal doxorubicin IV, Gemcitabine IV
• Stomach group: Cisplatin IP via PIPAC, Doxorubicin IP via PIPAC

The treatment duration for the 3 disease groups is:
• Colorectal group: Intervention arm = 18 weeks, Control arm = 18 weeks
• Ovarian group: Intervention arm = 14 or 15 weeks, Control arm = 18 or 24 weeks
• Stomach group: Intervention arm = 18 or 21 weeks, Control arm = 18 weeks

Participants will be randomised via the central PICCOS database. Sites should complete the first part of the randomisation Case Report Form (CRF), answering all the questions before submitting the randomisation (patients preferred PIPAC centre will need to be inputted) at the time of randomisation. Once the randomisation is completed, the database will confirm whether the participant has been allocated to the control or intervention arm. The allocation will be sent via email to those indicated as requiring it by the site. If the patient is allocated to receive PIPAC, the PIPAC site will also be notified. The randomisation system can be accessed via: https://redcap.ctr.cardiff.ac.uk/redcap/. If the online system becomes unavailable for any reason, site staff should contact PICCOS@cardiff.ac.uk and a manual randomisation process will be initiated. Following randomisation, participants should be provided with a Patient Card to identify them as PICCOS trial participants.

The intervention provider on each site will be PIPAC qualified oncology surgeon who has undergone the International Society for Study of Pleura and Peritoneum (ISSPP) approved PIPAC training and will have met the requirements of their local health board. They will be working with the qualified team designated by the site PI at each site.

Intervention Type
Procedure/Surgery

Primary outcome(s)
Peritoneal progression-free survival (pPFS) measured using Response Evaluation Criteria in Solid Tumours (RECIST) V1.1 criteria based on CT scans performed at baseline, prior to each cycle of chemotherapy, prior to each cycle of PIPAC, 30 days after each PIPAC, every two months for the first year after of trial treatment and every three months thereafter until the end of the trial

Key secondary outcome(s))
1. Oncology patients' core quality of life measures using the EORTC QLQ C30 questionnaire at baseline, after each PIPAC cycle, 2 months follow up, 4 monthly thereafter
2. Safety and surgical complication rates measured using 2.1 and 2.1.1 below prior to and post each PIPAC cycle:
2.1. Toxicity and grade according to NCI Common Terminology Criteria for Adverse Events (CTCAE) V5.0
2.1.1. Episodes of neutropenic sepsis
2.2. Clavien Dindo Classification (within 30 days of each PIPAC)
2.3. Incidence of radiologically proven bowel obstruction every 2 months in the first year then every 3 months
3. Proportion of patients completing 3 PIPAC procedures, and reasons why not if <3 completed
4. Number of conversions to operable disease in the stomach or colorectal cancer
5. OS, defined as days from randomisation to death for any reason

6. PFS. This is defined as the time from the date of randomisation to the date of progression (anywhere in the patient) or death from any cause
6.1. Extraperitoneal PFS (ePFS), defined as the time from the date of randomisation to the date of progression (outside of the peritoneum) or death from any cause
6.2. Episodes of therapeutic ascitic drainages (in ovarian cancer)
7. Peritoneal specific ORR observed at any time during treatment and follow-up
8. Peritoneal-specific DCR, defined as the proportion of patients with complete response, partial response or stable disease maintained at the end of treatment scan (i.e. 3rd scan)

Completion date
31/10/2028

Eligibility

Key inclusion criteria
Current key inclusion criteria as of 01/04/2026:

All disease groups:
1. 16 years and older
2. Visible (measurable or non-measurable) peritoneal lesion(s) on computerised tomography (CT) imaging as per Response Evaluation
Criteria in Solid Tumours (RECIST) v1.1
3. Eastern Cooperative Oncology Group (ECOG) performance status 0–1
4. Adequate bone marrow, liver and kidney function (within 7 days prior to randomisation):
4.1. Neutrophil ≥1.5×10"9/L
4.2. White blood cells ≥3.0 x 10"9/L
4.3. Platelets ≥100×10"9/L
4.4. Haemoglobin ≥90 g/l
4.5. Serum bilirubin <30 micromol/L
4.6. ALT/AST ≤2.5 x ULN (if both done, both must meet criteria)
4.7. Creatinine clearance ≥50 ml/min (Creatinine clearance should be estimated using the online ClinCalc calculator: https://clincalc.com/kinetics/crcl.aspx)
5. Fit enough to receive full dose of systemic anti-cancer therapy (SACT) in cycle 1 as defined in the protocol.
6. Ability to provide informed consent obtained prior to any trial-specific screening procedures.

Colorectal group only:
1. Peritoneal Metastasis (PM) from MDT confirmed primary adenocarcinoma (this may include “suspicious” if agreed by MDT) of the colorectum or appendiceal cancer (not pseudomyxoma).
Ovarian group only:
1. PM from MDT confirmed primary epithelial ovarian, tubal, or primary peritoneal platinum-resistant carcinoma (including clinical recurrence, refractory disease, or persistent disease within 6 months of last chemotherapy). (This may include “suspicious” if agreed by MDT).
Stomach group only:
1. PM from histologically proven primary adenocarcinoma (any subtype) of stomach or Siewert type 3 gastro-oesophageal junction tumour (any Human Epidermal Growth Factor Receptor 2 [HER2] status or Combined Positive Score [CPS]).

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Previous participant inclusion criteria as of 19/06/2025:

All disease groups:
1. 16 years and older
2. Visible (measurable or non-measurable) peritoneal lesion(s) on computerised tomography (CT) imaging as per Response Evaluation
Criteria in Solid Tumours (RECIST) v1.1
3. Eastern Cooperative Oncology Group (ECOG) performance status 0–1
4. Adequate bone marrow, liver and kidney function (within 7 days prior to randomisation):
4.1. Neutrophil ≥1.5×10"9/L
4.2. White blood cells ≥3.0 x 10"9/L
4.3. Platelets ≥100×10"9/L
4.4. Haemoglobin ≥90 g/l
4.5. Serum bilirubin <30 micromol/L
4.6. ALT/AST ≤2.5 x ULN (if both done, both must meet criteria)
4.7. Creatinine clearance ≥50 ml/min (Creatinine clearance should be estimated using the online ClinCalc calculator: https://clincalc.com/kinetics/crcl.aspx)
5. Fit enough to receive full dose of systemic anti-cancer therapy (SACT) in cycle 1 as defined in the protocol.
6. Ability to provide informed consent obtained prior to any trial-specific screening procedures.

Colorectal group only:
1. PM from histologically proven primary adenocarcinoma of the colorectum.
Ovarian group only:
1. PM from histologically confirmed primary epithelial ovarian, tubal, or primary peritoneal platinum-resistant carcinoma (including clinical recurrence, refractory disease, or persistent disease within 6 months of last chemotherapy).
Stomach group only:
1. PM from histologically proven primary adenocarcinoma (any subtype) of stomach or Siewert type 3 gastro-oesophageal junction tumour (any Human Epidermal Growth Factor Receptor 2 [HER2] status or Combined Positive Score [CPS]).

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Previous participant inclusion criteria as of 20/09/2024:

All disease groups:
1. 16 years and older
2. Visible (measurable or non-measurable) peritoneal lesion(s) on computerised tomography (CT) imaging as per Response Evaluation
Criteria in Solid Tumours (RECIST) v1.1
3. Eastern Cooperative Oncology Group (ECOG) performance status 0–1
4. Adequate bone marrow, liver and kidney function (within 7 days prior to randomisation):
4.1. Neutrophil ≥1.5×10^9/L
4.2. White blood cells ≥3.0 x 10^9/L
4.3. Platelets ≥100×10^9/L
4.4. Haemoglobin ≥90 g/l
4.5. Serum bilirubin ≤3 x ULN
4.6. ALT/AST ≤2.5 x ULN (if both done, both must meet criteria)
4.7. Creatinine clearance ≥50 ml/min
5. Fit enough to receive full dose of systemic anti-cancer therapy (SACT) in cycle 1 as defined in the protocol.
6. Ability to provide informed consent obtained prior to any trial-specific screening procedures.

Colorectal group only:
1. PM from histologically proven primary adenocarcinoma of the colorectum.

Ovarian group only:
1. PM from histologically confirmed primary epithelial ovarian, tubal, or primary peritoneal platinum-resistant carcinoma (including clinical recurrence, refractory disease, or persistent disease within 6 months of last chemotherapy).

Stomach group only:
1. PM from histologically proven primary adenocarcinoma (any subtype) of stomach or Siewert type 3 gastro-oesophageal junction tumour (any Human Epidermal Growth Factor Receptor 2 [HER2] status or Combined Positive Score [CPS]).

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Previous participant inclusion criteria:

All disease groups:
1. 16 years and older
2. Visible (measurable or non-measurable) peritoneal lesion(s) on computerised tomography (CT) imaging as per Response Evaluation
Criteria in Solid Tumours (RECIST) v1.1
3. Eastern Cooperative Oncology Group (ECOG) performance status 0–1
4. Adequate bone marrow, liver and kidney function (within 7 days prior to randomisation):
4.1. Neutrophil ≥1.5×10^9/L
4.2. White blood cells ≥3.0 x 10^9/L
4.3. Platelets ≥100×10^9/L
4.4. Haemoglobin ≥90 g/l
4.5. Serum bilirubin ≤3 x ULN
4.6. ALT/AST ≤2.5 x ULN (if both done, both must meet criteria)
4.7. Creatinine clearance ≥60 ml/min
5. Fit enough to receive full dose of systemic anti-cancer therapy (SACT) in cycle 1 as defined in the protocol.
6. Ability to provide informed consent obtained prior to any trial-specific screening procedures.

Colorectal group only:
1. PM from histologically proven primary adenocarcinoma of the colorectum.

Ovarian group only:
1. PM from histologically confirmed primary epithelial ovarian, tubal, or primary peritoneal platinum-resistant carcinoma (including clinical recurrence, refractory disease, or persistent disease within 6 months of last chemotherapy).

Stomach group only:
1. PM from histologically proven primary adenocarcinoma (any subtype) of stomach or Siewert type 3 gastro-oesophageal junction tumour (any Human Epidermal Growth Factor Receptor 2 [HER2] status or Combined Positive Score [CPS]).

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
16 years

Upper age limit
110 years

Sex
All

Total final enrolment
0

Key exclusion criteria
Current key exclusion criteria as of 01/04/2026:
All disease groups:
1. Any prior malignancy not considered in complete remission for at least 2 years, excluding non-melanoma skin cancer
2. Pregnant or breastfeeding
3. Untreated central nervous system disease or symptomatic central nervous system metastasis, history, or evidence of thrombotic or haemorrhagic disorders not considered currently in complete remission
4. Contraindication to any drug contained in the chemotherapy regimen
5. Medical, geographical, sociological, psychological, or legal conditions that would prevent the patient from completing the study or signing the informed consent
6. Unresolved bowel obstruction or parenteral nutrition or gastric tube
7. Contraindication to surgery
8. Participating in other oncological trials that may impact on endpoint
9. Life expectancy <3 months

*Note a minimum of 4 weeks washout between date of PIPAC 1 and last dose of bevacizumab / aflibercept (if applicable) must be complied with should a patient be randomised to the intervention arm.

Colorectal group only:
1. Extra-peritoneal metastases except for:
1.1. Retroperitoneal lymph nodes <2cm
1.2. Lung metastases; with < 5 lung metastases none >1cm
1.3. Solid organ metastases deemed asymptomatic and non-progressive by MDT
2. Eligible for and chooses cytoreductive surgery (CRS) and Hyperthermic Intraperitoneal Chemotherapy (HIPEC) upfront
3. Dihydropyrimidine Dehydrogenase Deficiency (DPYD) variant detected
4. Microsatellite instability (MSI) high or MMR-deficient (unless progressed on immunotherapy)
5. Previous cytoreductive surgery (CRS) or Hyperthermic Intraperitoneal Chemotherapy (HIPEC) and felt to be surgically suitable by MDT

Ovarian group only:
1. Extra-peritoneal metastases (with the exception of retroperitoneal lymph nodes)
2. Parenchymal liver or spleen metastases
3. Malignant pleural effusion
4. Non-epithelial pathology subtype
5. Peritoneal disease, amenable to surgical resection

Stomach group only:
1. Extra-peritoneal metastases (with the exception of retroperitoneal lymph nodes)
2. Prior systemic anti-cancer therapy, radiotherapy or surgery for stomach cancer
3. Gastric or duodenal stent in-situ
4. Gastro-oesophageal junction Sievert Type 1 or Type 2 tumour
5. Symptoms and/or radiology suggestive of impending and/or current bowel obstruction
6. Uncontrolled and persistent ascites
7. MSI high
8. DPYD variant detected
6. Previous cytoreductive surgery (CRS) or Hyperthermic Intraperitoneal Chemotherapy (HIPEC) and felt to be surgically suitable by MDT.

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Previous key exclusion criteria as of 28/10/2025:

All disease groups:
1. Any prior malignancy not considered in complete remission for at least 2 years, excluding non-melanoma skin cancer
2. Pregnant or breastfeeding
3. Untreated central nervous system disease or symptomatic central nervous system metastasis, history, or evidence of thrombotic or haemorrhagic disorders not considered currently in complete remission
4. Contraindication to any drug contained in the chemotherapy regimen
5. Medical, geographical, sociological, psychological, or legal conditions that would prevent the patient from completing the study or signing the informed consent
6. Unresolved bowel obstruction or parenteral nutrition or gastric tube
7. Contraindication to surgery
8. Participating in other oncological trials that may impact on endpoint
9. Life expectancy <3 months

*Note a minimum of 4 weeks washout between date of PIPAC 1 and last dose of bevacizumab / aflibercept (if applicable) must be complied with should a patient be randomised to the intervention arm.

Colorectal group only:
1. Extra-peritoneal metastases except for:
1.1. retroperitoneal lymph nodes <2cm
1.2. lung metastases; with < 5 lung metastases none >1cm
2. Eligible for and chooses cytoreductive surgery (CRS) and Hyperthermic Intraperitoneal Chemotherapy (HIPEC) upfront
3. Prior systemic therapy for colorectal cancer in the last 3 months (prior to the date of randomisation)

4. Dihydropyrimidine Dehydrogenase Deficiency (DPYD) variant detected
5. Microsatellite instability (MSI) high
6. Previous cytoreductive surgery (CRS) or Hyperthermic Intraperitoneal Chemotherapy (HIPEC)

Ovarian group only:
1. Extra-peritoneal metastases (with the exception of retroperitoneal lymph nodes)
2. Parenchymal liver or spleen metastases
3. Malignant pleural effusion
4. Non-epithelial pathology subtype
5. Peritoneal disease, amenable to surgical resection

Stomach group only:
1. Extra-peritoneal metastases (with the exception of retroperitoneal lymph nodes)
2. Prior systemic anti-cancer therapy, radiotherapy or surgery for stomach cancer
3. Gastric or duodenal stent in-situ
4. Gastro-oesophageal junction Sievert Type 1 or Type 2 tumour
5. Symptoms and/or radiology suggestive of impending and/or current bowel obstruction
6. Uncontrolled and persistent ascites
7. MSI high
8. DPYD variant detected
6. Previous cytoreductive surgery (CRS) or Hyperthermic Intraperitoneal Chemotherapy (HIPEC)

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Previous key exclusion criteria:

All disease groups:
1. Any prior malignancy not considered in complete remission for at least 2 years, excluding non-melanoma skin cancer
2. Pregnant or breastfeeding
3. Untreated central nervous system disease or symptomatic central nervous system metastasis, history, or evidence of thrombotic or haemorrhagic disorders not considered currently in complete remission
4. Bevacizumab/aflibercept should not be used in either arm (minimum 4 weeks from any prior bevacizumab/aflibercept)
5. Contraindication to any drug contained in the chemotherapy regimen
6. Medical, geographical, sociological, psychological, or legal conditions that would prevent the patient from completing the study or signing the informed consent
7. Unresolved bowel obstruction or parenteral nutrition or gastric tube
8. Contraindication to surgery
9. Participating in other oncological trials that may impact on endpoint
Added 26/03/2024: 10. Life expectancy <3 months

Colorectal group only:
1. Extra-peritoneal metastases except for:
1.1. retroperitoneal lymph nodes <2cm
1.2. lung metastases; with < 5 lung metastases none >1cm
2. Eligible for and chooses cytoreductive surgery (CRS) and Hyperthermic Intraperitoneal Chemotherapy (HIPEC) upfront
3. Prior systemic therapy for colorectal cancer in the last 6 months
4. Dihydropyrimidine Dehydrogenase Deficiency (DPYD) variant detected
5. Microsatellite instability (MSI) high

Added 26/03/2024: 6. Previous cytoreductive surgery (CRS) or Hyperthermic Intraperitoneal Chemotherapy (HIPEC)

Ovarian group only:
1. Extra-peritoneal metastases (with the exception of retroperitoneal lymph nodes)
2. Parenchymal liver or spleen metastases
3. Malignant pleural effusion
4. Non-epithelial pathology subtype
5. Peritoneal disease, amenable to surgical resection

Stomach group only:
1. Extra-peritoneal metastases (with the exception of retroperitoneal lymph nodes)
2. Prior systemic anti-cancer therapy, radiotherapy or surgery for stomach cancer
3. Gastric or duodenal stent in-situ
4. Gastro-oesophageal junction Sievert Type 1 or Type 2 tumour
5. Symptoms and/or radiology suggestive of impending and/or current bowel obstruction
6. Uncontrolled and persistent ascites
7. MSI high
8. DPYD variant detected
Added 26/03/2024: 6. Previous cytoreductive surgery (CRS) or Hyperthermic Intraperitoneal Chemotherapy (HIPEC)

Date of first enrolment
22/01/2024

Date of final enrolment
31/10/2027

Locations

Countries of recruitment
United Kingdom

England

Northern Ireland

Scotland

Wales

Study participating centre
Cardiff & Vale UHB
Joint Research Office
2nd Floor Lakeside Building
University of Wales
Heath Hospital

Cardiff
Wales
CF14 4XW

Study participating centre
Imperial College Healthcare NHS Trust
The Bays
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South Wharf Road
London
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W2 1BL

Study participating centre
Swansea NHS Trust
Singleton Hospital
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Study participating centre
Royal United Hospitals Bath NHS Foundation Trust
Combe Park
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BA1 3NG

Sponsor information

Organisation
Cardiff and Vale University Health Board

ROR
https://ror.org/0489f6q08

Funder(s)

Funder type

Government

Funder Name
National Institute for Health and Care Research

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be stored in a non-publicly available repository (https://redcap.ctr.cardiff.ac.uk/redcap/).

IPD sharing plan summary
Stored in non-publicly available repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Other files	version 2	05/05/2023	21/08/2023	No	No
Protocol file	version 1.0	26/04/2023	21/08/2023	No	No
Protocol file	version 5.0	05/12/2024	16/06/2025	No	No
Protocol file	version 6.0	02/07/2025	28/10/2025	No	No
Protocol file	version 7.0	17/11/2025	01/04/2026	No	No