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A study for patients with advanced pancreatic cancer looking at adding olaparib to chemotherapy with radiotherapy (chemoradiation)

Submission date
20/04/2015

Recruitment status
No longer recruiting

Registration date
20/04/2015

Overall study status
Completed

Last Edited
22/09/2023

Condition category
Cancer

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] Record updated in last year

Plain English summary of protocol
http://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-looking-at-olaparib-with-chemoradiation-for-pancreatic-cancer-pioneer

Contact information

Type(s)
Public

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Additional identifiers

Clinical Trials Information System (CTIS)
2014-002074-37

Integrated Research Application System (IRAS)

159690

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
PIONEER-2014, IRAS 159690

Study information

Scientific Title
A Phase I study of olaparib in combination with chemoradiation in locally advanced pancreatic cancer

Acronym
PIONEER

Study objectives
The hypothesis to be tested is that olaparib can be safely combined with a standard chemoradiation regimen in locally advanced, non-metastatic pancreatic cancer and that the addition of a PARP inhibitor to the standard fluoropyrimidine - based chemo-radiation backbone might potentiate the effects of this combined modality therapy in patients with both locally advanced, inoperable pancreatic cancer as well in those with borderline resectable disease.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 03/03/2015, Scotland A Research Ethics Committee (2nd Floor Waverley Gate, 2-4 Waterloo Place, Edinburgh, EH1 3EG, United Kingdom; +44 (0)1314655680; Manx. Neill@nhslothian.scot.nhs.uk), ref: 15-SS-0011

Study design
Interventional

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Locally advanced pancreatic cancer

Interventions
Current interventions as of 08/04/2020:

Patients will be treated as follows:
1. Olaparib (starting day three days prior to chemo-radiation in escalating doses* orally twice daily (Mon-Fri) until final day of radiation therapy

2. Capecitabine 830mg/m2 PO twice daily Mon-Fri until the final date of radiation therapy.
3. Radiotherapy (50.4 Gy in 28 fractions) Mon-Fri

*Expansion cohort of up to 12 patients (minimum of 6) with borderline resectable disease will be treated at the Olaparib MTD. The MTD of Olaparib in the dose escalation phase is 100mg bd

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Previous interventions:

Patients will be treated as follows:
1. Olaparib (starting day three days prior to chemo-radiation in escalating doses* orally twice daily (Mon-Fri) until final day of radiation therapy
2. Capecitabine 830mg/m2 PO twice daily Mon-Fri until the final date of radiation therapy.
3. Radiotherapy (50.4 Gy in 28 fractions) Mon-Fri

*Expansion cohort of 12 patients with borderline resectable disease will be treated at the Olaparib MTD

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
Olaparib

Primary outcome(s)
The primary objective is to determine the Maximum Tolerated Dose (MTD) of olaparib when administered in combination with standard capecitabine-based chemo-radiation in patients with pancreatic cancer. Toxicity will be assessed on an ongoing basis throughout the treatment phase of the study.

Key secondary outcome(s))
1. To identify the DLT (Dose-Limiting Toxicity) of olaparib when administered in combination with standard capecitabine-based chemo-radiation in these patients. DLTs will be assessed weekly for six weeks during patient treatment in the dose escalation phase.
2. To explore the safety and tolerability of olaparib when administered in combination with standard capecitabine-based chemo-radiation including in a cohort of patients with “borderline” resectable pancreatic ductal adenocarcinoma. This will be assessed on an ongoing basis during the six week treatment period of the patients in the dose expansion phase.

Completion date
31/03/2022

Eligibility

Key inclusion criteria
1. Histologically or cytologically confirmed locally advanced inoperable pancreatic ductal adenocarcinoma
2. Patients with clearly un-resectable disease on anatomical criteria as determined by a multi-disciplinary team and considered to be candidates for combined modality treatment with chemo-

radiation
3. Patients must have had a partial response or stable disease following 3 cycles of induction chemotherapy with gemcitabine and capecitabine as described in Appendix 1, and have a tumour diameter of 6cm or less
4. Performance status ≤ 1 (ECOG, Appendix 3)
5. Age ≥ 16 years
6. Evaluable or measurable disease
7. Estimated life expectancy greater than 3 months
8. Adequate haematological function as defined by:
8.1. Haemoglobin (Hb) > 10g/dl (no blood transfusions in the 28 days prior to trial entry)
8.2. Neutrophil Count > 1.5 x 109/l (no features suggestive of MDS/AML on peripheral blood smear)
8.3. White Blood Cells (WBC) >3x109/L
8.4. Platelets > 100 x 109/l
8.5. Bilirubin < 1.5 x upper limit of normal (ULN)
8.6. Alanine aminotransferase (ALT) or aspartate aminotransferase (AST) < 2.5 x ULN
8.7. Adequate renal function with creatinine clearance / glomerular filtration rate > 50 ml/min. If the creatinine clearance / glomerular filtration rate is less than 50 ml/min as calculated by the Cockcroft-Gault/Wright formula, then the creatinine clearance / glomerular filtration rate should be measured by either a radio-isotope technique or by 24-hour urine collection
9. Able to swallow oral tablets/capsules
10. Able to comply with study procedures
11. Written informed consent
12. Evidence of non-childbearing status for women of childbearing potential: negative urine or serum pregnancy test within 7 days of trial treatment
13. Postmenopausal as defined as:
13.1. Amenorrheic for 1 year or more following cessation of exogenous hormonal treatments,
13.2. LH and FSH levels in the post-menopausal range for women under 50,
13.3. Surgical sterilisation (bilateral oophorectomy or hysterectomy).

Dose Expansion Cohort
Additional Eligibility Criteria
1. Patients with pancreatic ductal adenocarcinoma who are considered by a multi-disciplinary team to have “borderline” resectable disease based on their anatomical findings during pre-operative staging

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Key exclusion criteria
1. Any prior anti-cancer therapy for pancreatic cancer including chemotherapy, radiotherapy, endocrine therapy, immunotherapy or use of other investigational agents (except induction

chemotherapy)
2. Patients with known metastatic disease
3. Pregnant or lactating women
4. Women of childbearing age and potential who are not willing to use an two highly effective methods of contraception as detailed in section 11.3. Male patients of childbearing potential will also be excluded if either they or their female partner are not willing to use two highly effective methods of contraception as detailed in section 11.3. In addition, both of the above will be excluded if they are not willing to use contraception for 12 months after the last dose. Men with pregnant or lactating partners should be advised to user barrier contraception to prevent exposure to the foetus or neonate.
5. Patients who are known to be HIV positive, or who are known to have positive Hepatitis B or C serology
6. Any evidence of uncontrolled cardiac disease or any other serious medical or psychiatric disorder that would be, in the opinion of the investigator, a contra-indication to either the trial procedures or to therapy with olaparib or capecitabine
7. Patients with second or third degree heart block, family history of QT prolongation or shortening, history of arrhythmia, or familial sudden death or QT interval at screening of >450 ms (male) / >470 ms (female)
8. Patients receiving concomitant medications known to cause QT prolongation
9. Patients with known DPD deficiency
10. Patients with a lack of physical integrity of the GI tract leading to a malabsorption syndrome or intestinal obstruction that would impair the administration and absorption of oral therapy
11. Participation in another clinical trial with an investigational product during the last 12 months
12. Any previous treatment with a PARP inhibitor, including olaparib.
13. Concomitant use of known CYP3A4 inhibitors such as ketoconazole, itraconazole, ritonavir, indinavir, saquinavir, telithromycin, clarithromycin and nelfinavir. In addition , to avoid potential reductions in exposure due to drug interactions and, therefore, a potential reduction in efficacy, the following CYP3A4 inducers are excluded: Phenytoin, fiampicin, rifapentin, rifabutin, carbamazepine, phenobarbitone, nevirapine, modafinil and St John's Wort (Hypericum perforatum; wash-out period for phenobarbitone 5 weeks and for any of the others 3 weeks)
14. Blood transfusions within 1 month prior to trial start
15. Patients with myelodysplastic syndrome/acute myeloid leukaemia
16. Major surgery within 14 days of starting trial treatment and patients must have recovered from any effects of major surgery
17. Patients with a known hypersensitivity to olaparib or any of the excipients of the product
18. Patients with uncontrolled seizures
19. Patients with grade III / IV non-haematological toxicity related to capecitabine during induction chemotherapy except for alopecia or nausea and vomiting unless not controlled with maximal anti-emetics support
20. Patients unable to tolerate standard dose of capecitabine during induction chemotherapy

Date of first enrolment
01/05/2015

Date of final enrolment
31/07/2021

Locations

Countries of recruitment
United Kingdom

Northern Ireland

Scotland

Study participating centre
The Beatson West of Scotland Cancer Centre
1053 Great Western Road
Glasgow
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Study participating centre
Belfast City Hospital
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Sponsor information

Organisation
NHS Greater Glasgow and Clyde

ROR
https://ror.org/05kdz4d87

Organisation
The Unversity of Glasgow

Funder(s)

Funder type
Charity

Funder Name
Cancer Research UK

Alternative Name(s)

CR_UK, Cancer Research UK - London, Cancer Research UK (CRUK), CRUK

Funding Body Type
Private sector organisation

Funding Body Subtype
Other non-profit organizations

Location
United Kingdom

Funder Name
AstraZeneca

Alternative Name(s)
AstraZeneca PLC, Pearl Therapeutics, AZ

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No