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Proof of mechanism study of an oral Hedgehog Inhibitor (GDC-0449) in patients with resectable pancreatic ductal adenocarcinoma in the pre-operative window period

Submission date 14/03/2011	**Recruitment status** Stopped	[ ] Prospectively registered [ ] Protocol
Registration date 14/03/2011	**Overall study status** Stopped	[ ] Statistical analysis plan [ ] Results
Last Edited 22/06/2015	**Condition category** Cancer	[ ] Individual participant data [ ] Record updated in last year

Plain English summary of protocol
http://cancerhelp.cancerresearchuk.org/trials/a-study-gdc-0449-before-srugery-for-pancreatic-cancer-hippos

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
2010-018776-24

IRAS number

ClinicalTrials.gov number
NCT01096732

Secondary identifying numbers
9531

Study information

Scientific Title
Proof of mechanism study of an oral Hedgehog Inhibitor (GDC-0449) in patients with resectable pancreatic ductal adenocarcinoma in the pre-operative window period: a non randomised study

Acronym
HIPPoS

Study objectives
This clinical trial is looking at the effect of a new drug called GDC0449 in patients with cancer of the pancreas.

Laboratory studies have shown that this drug blocks a process in pancreatic cells thought to be involved in cancer development and spread. This process is called the Hedgehog signalling pathway. As yet, it is unclear whether blocking hedgehog signalling will directly affect the tumour cells themselves or the surrounding normal tissue.

Understanding this distinction will help improve treatment strategies for pancreatic cancer. Patients will be offered to participate in this research study if they have localised pancreatic cancer that can be removed by surgery. In the period between diagnosis and surgery we do not normally treat patients, however in this trial we will ask patients to take GDC0449 during the approximately two weeks until the day of surgery. All patients that enter this study will have undergone a diagnostic biopsy of the pancreatic tumour and we will collect a second sample of the tumour at surgery. The main question of this study is whether we can detect a change in hedgehog signalling in the tumour tissue.

Furthermore we will look very carefully whether this treatment is safe for patients. All problems before and after surgery will be carefully documented and we have defined strict rules to stop the study if we observe serious problems.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Cambridgeshire 1 REC, 21/10/2010, ref: 10/H0304/76

Study design
Non-randomised, Interventional; Design type: Treatment

Primary study design
Interventional

Secondary study design

Non randomised study

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details below to request a patient information sheet

Health condition(s) or problem(s) studied
Topic: National Cancer Research Network; Subtopic: Upper Gastro-Intestinal Cancer; Disease: Pancreas

Interventions
Adverse Event Monitoring: Blood sampling, Maximum of 212ml; Concomitant Medications, electrocardiogram (ECG), endoscopic ultrasound (EUS) and contrast / elastography; Physical Exam, Urinalysis, Study Entry : Registration only

Updated 22/06/2015: The study was stopped early due to poor recruitment.

Intervention Type
Other

Phase
Phase II

Primary outcome measure
Effect on stromal cell and tumour; Timepoint(s): To study the effect of GDC0449 treatment on the stromal cell and tumour cell hedgehog signalling

Secondary outcome measures
Safety & Tolerability; Timepoint(s): To study the safety and tolerability of preoperative GDC0449 treatment in patients

Overall study start date
14/02/2011

Completion date
31/05/2012

Reason abandoned (if study stopped)
Participant recruitment issue

Eligibility

Key inclusion criteria

1. Documented tissue diagnosis of pancreatic ductal adenocarcinoma with a sufficient amount of tissue for Laser Capture Micro-dissection (LCM) of the stromal and tumour compartments
2. Confirmed eligibility for Whipple's or distal pancreatectomy procedure by Multi-Disciplinary Team (MDT) and surgeon review.
3. Adequate organ function defined as:
3.1. Creatinine clearance = 60ml/min (as defined by Cockroft-Goult)
3.2. Electrolytes (Na/K/Ca) within institutional normal limits
3.3. Alanine aminotranferease (ALT)/aspartate aminotransferase(AST) < 5*ULN
3.4. Prothrombin time test (PTT) < 2*ULN, prior supplementation with vitamin K is allowed
3.5. Adequate blood counts: neutrophils >1,500/µl, Hb > 6 mmol/L, platelets >100.000/µl
3.6. Albumin > 30mg/dL
4. Written informed consent
5. Male or female aged 18 years or over
6. WHO performance status 0-1
7. Willingness and ability to comply with scheduled visits, treatment plans, laboratory tests and other study procedures
8. Males should not donate sperm during treatment or up to 3 months after the last dose
9. Women of childbearing potential are required to have a negative serum pregnancy test (with sensitivity of at least 25 mIU/mL) within 10-14 days and within 24 hours prior to the first dose of GDC-0449

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
Planned Sample Size: 20; UK Sample Size: 20

Key exclusion criteria
1. Known Hepatitis B/C or HIV infection
2. Known hypersensitivity to GDC-0449
3. Active cardiac ischemic disease (this criterion only applies for participation in the imaging part of the study)
4. Women who are pregnant, plan to become pregnant or are lactating (during the study or for up to 12 months after the last dose)
5. Concurrent participation in another clinical trial using an investigational medicinal product
6. Other severe acute or chronic medical or psychiatric condition, or laboratory abnormality that may increase the risk associated with study participation or study drug administration or in the judgment of the investigator would make it undesirable for the patient to enter the trial (i.e. patients is not able to swallow tablets)

Date of first enrolment

14/02/2011

Date of final enrolment
31/05/2012

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Cambridge Cancer Trials Centre
Cambridge
United Kingdom
CB2 0QQ

Sponsor information

Organisation
Cambridge University Hospitals NHS Foundation Trust (UK)

Sponsor details
Addenbrookes Hospital,
Hills Road
Cambridge
England
United Kingdom
CB2 0QQ

Sponsor type
Hospital/treatment centre

ROR
https://ror.org/04v54gj93

Funder(s)

Funder type
Government

Funder Name
Cambridge University Hospitals NHS Foundation Trust (UK)

Funder Name
Roche Products Ltd (UK)

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

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