Does mitogen activated protein kinase inhibition with CNI-1493 prevent post-Endoscopic retrograde cholangiopancreatography pancreatitis?

Submission date 20/12/2005	Recruitment status No longer recruiting	 Prospectively registered Protocol
Registration date 20/12/2005	Overall study status Completed	Statistical analysis planResults
Last Edited 20/08/2021	Condition category Digestive System	Individual participant dataRecord updated in last year

Plain English summary of protocol

Not provided at time of registration

Contact information

Type(s) Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers N/A

Study information

Scientific Title

Does mitogen activated protein kinase inhibition with CNI-1493 prevent post-Endoscopic retrograde cholangiopancreatography pancreatitis?

Acronym

CNI study

Study objectives

Acute pancreatitis can be due to many causes including biliary stone disease, alcohol abuse, and medication. It can also be caused by medical intervention through manipulation of area of the ampulla of Vater and diagnostic and/or therapeutic interventions in the biliary and pancreatic ductal system (endoscopic retrograde cholangiopancreaticography [ERCP]).

The overall reported incidence of post-ERCP pancreatitis is 7%, in certain subgroups with an increased risk this goes up to 20%. Local damage (temporary increased ductal pressure due to contrast injection and/or oedema due to manipulations) is followed by a local inflammatory response (Tumour Necrotising Factor [TNF], Interleukin-one [IL-1], Interleukin-six [IL-6]). In 80% of cases post-ERCP pancreatitis runs a relatively benign course with a few day of (severe) abdominal pain and an uneventful recovery. In other cases a severe pancreatitis develops with necrosis of parenchymal pancreatitis tissue (with or without infection) and a Systemic Inflammatory Response Syndrome (SIRS).

In the latter group morbidity and mortality are high. Of these patients 25% will die. Recently, a group of synthetic guanylhydrazone compounds have been developed and one of its representatives CNI-1493 (a p38 Mitogen Activated Protein [MAP] kinase inhibitor) proved to be a very powerful inhibitor of TNF-alpha. In addition, CNI-1493 inhibits a host of other macrophage induced pro-inflammatory cytokines (IL-1, IL-6, MIP-1Ñ and MIP-1Ò).

The primary question that we want to address is whether it is possible with the prophylactic administration of CNI-1493 to lower the incidence of post-ERCP pancreatitis.

Hypothesis:

Prophylactic administration of p38 MAP/c-Jun N-terminal protein Kinase (JNK) inhibitor may decrease the incidence of post-ERCP pancreatitis through inhibition of the pro-inflammatory cytokines IL-1, IL-6, TNF and Macrophage Inflammatory Protein (MIP). In animal studies CNI-1493 or related compounds have been shown to reduce the severity of experimental pancreatitis and pancreatitis associated lung injury.

Ethics approval required

Old ethics approval format

Ethics approval(s)

Ethics approval received from the local medical ethics committee

Study design

Randomised, placebo controlled, parallel group, double blinded trial

Primary study design Interventional

Secondary study design Randomised controlled trial

Study setting(s) Not specified

Study type(s) Treatment

Participant information sheet

Health condition(s) or problem(s) studied

Endoscopic Retrograde Cholangiopancreatography (ERCP), pancreatitis

Interventions

Single infusion of CNI-1493 (50 mg intravenous [IV] or placebo IV (randomised, double blind) one hour prior to start of ERCP.

Intervention Type Drug

brug

Phase Not Specified

Drug/device/biological/vaccine name(s)

CNI-1493

Primary outcome measure

Does administration of CNI-1493 decrease the incidence of post ERCP pancreatitis in high risk patients undergoing ERCP?

Secondary outcome measures

1. Is CNI-1493 administration safe in patients undergoing ERCP?

2. Does administration of CNI-1493 decrease the severity of post ERCP pancreatitis in high risk patients undergoing ERCP?

3. Does administration of CNI-1493 decrease the incidence of post ERCP hyperamylasemia in high risk patients undergoing ERCP?

4. Does administration of CNI-1493 decrease the levels of post ERCP IL-6, Interleukin-eight (IL-8), TNF and IL-1 in high risk patients undergoing ERCP?

Overall study start date

01/03/2002

Completion date 31/12/2005

Eligibility

Key inclusion criteria

1. Included are all patients who do not fit the exclusion criteria and will undergo an ERCP with the intention to:

a. cannulate and visualise the pancreatic duct

b. perform therapeutic procedures (e.g. stenting, balloon dilatation, sphincter manometry, precut papillotomy, stone extraction, (intra-luminal) endosonography, Extracorporeal Shock-Wave Lithotripsy [ESWL] and dilatation) in the pancreatic duct, common bile duct or left and right hepatic ducts

2. Patients must agree to use acceptable means of birth control for at least three months after the procedure

3. Patients must sign informed consent

Participant type(s)

Patient

Age group

Not Specified

Sex Not Specified

Target number of participants 270

270

Key exclusion criteria

- 1. Diagnostic ERCP (low risk)
- 2. Active pancreatitis at time of ERCP (confounding)
- 3. Severe abdominal pain pre ERCP (confounding)
- 4. Age less than 18 years (contra-indication)
- 5. Known or suspected pregnancy or breast-feeding (contra-indication)
- 6. ERCP for stent exchange in malignant disease (low risk)
- 7. Severe chronic pancreatitis (low risk)

8. Kidney failure i.e. serum creatinine greater than 20 mg/dl (greater than 180 μ M) (any state, contra-indication)

9. Other anti-TNF therapy (e.g. infliximab) within eight weeks of intended study treatment

Date of first enrolment

01/03/2002

Date of final enrolment 31/12/2005

Locations

Countries of recruitment Netherlands **Study participating centre Academical Medical Centre** Amsterdam Netherlands 1105 AZ

Sponsor information

Organisation Cytokine PharmaSciences, Inc (USA)

Sponsor details Walnut Hill Plaza 150 South Warner Road Suite 420 King of Prussia United States of America PA 19406

Sponsor type

Industry

Website http://www.cytokinepharmasciences.com/

ROR https://ror.org/02ytn5d60

Funder(s)

Funder type Industry

Funder Name Cytokine PharmaSciences, Inc (USA)

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