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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 plan [_] Results
Last Edited 20/08/2021	**Condition category** Digestive System	[_] Individual participant data [_] Record 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

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

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 µM) (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
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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