Does MAP kinase inhibition with CNI-1493 prevent post-ERCP pancreatitis?

No registrations found.

Ethical review	Positive opinion
Status	Recruitment stopped
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON23715

Source
NTR

Brief title
CNI study

Health condition

Patients with a need to undergo ERCP and a relatively high risk to develop post-ERCP pancreatitis.

Sponsors and support

Primary sponsor: Cytokine PharmaSciences, Inc
King of Prussia, PA
United States of America

Source(s) of monetary or material Support: N/A

Intervention

Outcome measures

Primary outcome

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

Secondary outcome

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, IL-8, TNF and IL-1 in high risk patients undergoing ERCP?

Study description

Background summary

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 andor oedema due to manipulations) is followed by a local inflammatory response (TNF, IL-1, IL-6). In 80% of cases post-ERCP pancreatitis runs a relatively benign course with a few day o (severe) abdominal pain and a 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 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-1ƒÑ en MIP-1ƒÒ).

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.

The study is double blind and randomized. Patients with a increased risk to develop post-ERCP pancreatitis will be randomized between prophylactic administration of CNI-1493 (50 mg IV) and placebo.

Patients will be follow-up for 48 hours. Blood samples will be taken at regular intervals for amylase and lipase (and CRP, IL-6, IL-1, TNF, IL-8). Clinical symptoms such as pain are quantified by means of VAS scores and noted.
The primary endpoint is the incidence of post-ERCP pancreatitis.
Other (secondary) endpoints include morbidity, mortality, incidence of post-ERCP hyper hyperamylasemia, serum concentrations of cytokines/chemokines.

Study objective

Prophylactic administration of p38 MAP/JNK kinase inhibitor may decrease the incidence of post-ERCP pancreatitis through inhibition of the pro-inflammatory cytokines IL-1, IL-6, TNF and MIP. In animal studies CNI-1493 or related compounds have been shown to reduce the severity of experimental pancreatitis and pancreatitis associated lung injury.

Study design

N/A

Intervention

Single infusion of CNI-1493 (50 mg IV or placebo IV (randomized, double blind) 1 h prior to start of ERCP.

Contacts

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Eligibility criteria

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 visualize the pancreatic duct;

b. Perform therapeutic procedures (e.g. stenting, balloon dilatation, sphincter manometry, precut papillotomy, stone extraction, (intra-luminal) endosonography, 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 3 months after the procedure;

3. Patients must sign informed consent.

Exclusion criteria

1. Diagnostic ERCP (low risk);

2. Active pancreatitis at time of ERCP (confounding);

3. Severe abdominal pain pre ERCP (confounding);

4. Age < 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, ie, serum creatinine > 2.0 mg/dl (> 180 ƒÝM) (any state, contra indication);

9. Other anti-TNF therapy (eg, infliximab) within 8 weeks of intended study treatment.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-03-2002
Enrollment:	270
Type:	Actual

Ethics review

Positive opinion

Date:	09-09-2005

Application type: First submission

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
NTR-new	NL161
NTR-old	NTR196
Other	: N/A
ISRCTN	ISRCTN26235881

Study results

Summary results
Gastrointest Endosc. 2008 Aug;68(2):246-54. Epub 2008 May 2.