Pharmacokinetics and –dynamics of Dabigatran Etexilate and Rivaroxaban in patients requiring PArenteral Nutrition (the PDER PAN study)

No registrations found.

Ethical review	Positive opinion
Status	Recruiting
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON26342

Source
Nationaal Trial Register

Brief title
the PDER PAN study

Health condition

parenteral nutrition, thrombosis, pharmacokinetics, pharmacodynamics, anticoagulant

Sponsors and support

Primary sponsor: Academic Medical Center, Amsterdam, The Netherlands
Source(s) of monetary or material Support: Academic Medical Center, Amsterdam, The Netherlands

Intervention

Outcome measures

Primary outcome

The primary outcome is the assessment of PK and PD parameters of the two drugs and the comparison to published values.

Secondary outcome

The secondary outcome is the comparison between rivaroxaban PK parameters and dabigatran PK parameters (AUC, Cmax and Tmax).

Study description

Background summary

Chronic intestinal failure (IF) is caused by either surgically induced anatomical short bowel, severe motility, or absorption disorders. These patients require partial or total parenteral nutrition (PN and TPN, respectively) and are thereby critically dependent on maintaining venous access with a central venous catheter (CVC). Recurrent CVC-related thrombosis will ultimately lead to loss of central venous access with intestinal transplantation being the only treatment option left. Therefore, patients at risk for recurrent thrombosis and requiring (T)PN are often treated with long-term anticoagulants to prevent CVC-thrombosis, such as INR-adjusted vitamin K antagonists (VKAs) or low-molecular-weght heparins (LMWHs).
A new generation of oral anticoagulants (NOACs), including dabigatran etexilate and rivaroxaban, has recently been approved for several indications. In contrast with VKAs, these drugs do not interact with vitamin K metabolism, have a more predictable pharmacokinetic profile, have less interaction with other drugs, and are prescribed at a fixed dose without routine laboratory monitoring. Importantly, these drugs are absorbed proximally in the gastrointestinal tract (stomach, duodenum, and proximal small bowel). Therefore, NOACs may be an attractive oral alternative to both LMWH injections and VKAs in these patients.
The aim of the PDER PAN phase I study is to assess the extent of intestinal absorption of rivaroxaban 20 mg once-daily and dabigatran etexilate 150 mg twice-daily at steady state in adult patients with short bowel syndrome requiring long-term TPN.
The primary outcome is the assessment of pharmacokinetics and -dynamics parameters of the two drugs, and the comparison to published values from studies in healthy volunteer.

Study objective

The aim of this phase I study is to assess the extent of intestinal absorption of rivaroxaban and dabigatran etexilate in adult patients with short bowel syndrome requiring long-term TPN.

Study design

Blood samples will be collected at the research unit at the following times:

1) after rivaroxaban administration:

- Day 0: T = 0 (= blank), T = 3 hours following the first dose;

- Day 4 at steady state: T = 0 (= trough), T = 1, 2, 3, 4, 5, 6, 8, 10, 24 hour(s) following the fifth dose.

2) after dabigatran etexilate administration:

- Day 0: T = 0 (= blank), T = 3 hours following the first dose;

- Day 4 at steady state: T = 0 (= trough), T = 1, 2, 3, 4, 5, 6, 8, 12 hour(s) following the ninth dose.

Intervention

In a cross-over design, patients will be treated with either rivaroxaban 20 mg once daily for five days or dabigatran etexilate 150 mg twice daily for five days. Between the two treatment periods, a wash out period of at least 4 days will be applied. After each 5-day period of NOAC use, patients will be admitted for a full pharmacokinetic and –dynamic profile will be obtained with 10 blood samples.

Contacts

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Eligibility criteria

Inclusion criteria

Inclusion criteria are:

- clinically stable adult male and female patients (age between 18 and 75 years),

- body weight between 50 and 100 kg,

- chronic (>3 months) use of home TPN due to short bowel syndrome after surgical resection and small bowel shorter than 160 cm after ligamentum of Treitz, irrespective of the presence of colon

Exclusion criteria

Exclusion criteria are:

- moderate/severe renal impairment (CKD EPI Creatinine Clearance < 50 mL/min according to http://www.nephron.com/MDRD_GFR.cgi), or moderate/severe hepatic impairment (class B (7-9 points) or class C (10-15 points) at the Child-Pugh score),

- major bleeding events in the previous 6 months (according with the International Society on Thrombosis and Haemostasis definition of major bleeding in non-surgical patients, defined as symptomatic bleeding in a critical area or organ, such as intracranial, intraspinal, intraocular, retroperitoneal, intra- articular or pericardial, or intramuscular with compartment syndrome, and/or bleeding causing a fall in hemoglobin level of 20 g/L or more, or leading to transfusion of two or more units of whole blood or red cells),

- cytochrome P450 3A4 and/or P-gp-dependent co-medications in the last 14 days (verapamil, azoles, amiodarone, dronedarone, azithromycin, erythromycin, clarythromycin, quinidine, ritonavir, cyclosporine, propafenone, isoniazid, rifampin, rifapentine, primidone, St. John’s wort, carbamazepine, oxcarbazepine, phenobarbital, pentobarbital, nevirapine, nafcillin, fosphenonytoin),

- ongoing anticoagulant treatment for an acute thrombotic event (prior 6 months) or for a condition estimated to be at high risk of recurrence (i.e., presence of mechanical heart valve),

- use of phenprocoumon, due to the difficulties of a proper bridging (drug half-life = 7 days),

- chronic treatment with non-aspirin non-steroidal anti-inflammatory drugs (NSAIDs), or chronic treatment with aspirin (>100 mg/day), or dual antiplatelet therapy
,
- current participation in any other investigational drug study or within the past 30 days,

- pregnancy,

- partial or total gastrectomy, and/or resection of the duodenum for any cause,

- presence of any condition that, as judged by the investigator, would place the subject at increased risk of harm if he participated in the study (i.e., recent CVC-related infection, sepsis)

- presence of significant haemostatic abnormalities (i.e., severe thrombocytopenia, severe prolongation of haemostatic tests PT and aPTT) in patients not currently on anticoagulant.

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Single blinded (masking used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	01-10-2013
Enrollment:	6
Type:	Anticipated

Ethics review

Positive opinion

Date:	01-10-2013
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	NL3978
NTR-old	NTR4192
Other	42865 : ABR
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Study results

Summary results
N/A