DAVINCY trial: optimal Duration of (fos)aprepitant prophylaxis for nausea and Vomiting INduced by ChemotherapY in children: a double-blind placebo-controlled crossover randomized phase III trial*

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This study has been transitioned to CTIS with ID 2024-517846-32-00 check the CTIS register for the current data. To evaluate the effect of prolonged duration of (fos)aprepitant prophylaxis on the prevention of delayed CINV (complete remission in the...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Miscellaneous and site unspecified neoplasms benign
Study type	Interventional

Summary

ID

NL-OMON50886

Source
ToetsingOnline

Brief title
DAVINCY

Condition

- Miscellaneous and site unspecified neoplasms benign

Synonym
chemotherapy induced nausea and vomiting

Research involving

Human

Sponsors and support

Primary sponsor: Prinses Máxima Centrum voor Kinderoncologie
Source(s) of monetary or material Support: ZONmw

Intervention

Keyword: aprepitant, Chemotherapy Induced Nausea and Vomiting (CINV), fosaprepitant, High/ Moderate emetogenic chemotherapy

Outcome measures

Primary outcome

Proportion of patients who achieve complete response (no vomiting, no retching

and no use of rescue medication) during the 24-72 hours after the final dose of

chemotherapy (delayed phase).

Secondary outcome

Proportion of patients who:

- achieved complete response during the course of chemotherapy until 24h af-ter

the final dose of chemotherapy (acute phase)

- achieved complete response during both the acute and delayed phase (overall

phase)

Time from initiation of emetogenic chemotherapy to:

o the first vomiting episode

o the first rescue medication use

Safety of prolonged use of (fos)aprepitant (AEs considered related by the

investiga-tors)

Pharmacokinetic (PK) parameters (i.e. clearance and volume of distribution) and

in-fluencing PK co-variates as chemotherapeutics

Improvement of CINV complaints according to the Pediatric Nausea Assessment

tool (PeNAT) for children aged 4-<=18 years

Cost-effectiveness of prolonged (fos)aprepitant dosing regimen

Study description

Background summary

Prophylaxis of chemotherapy induced nausea and vomiting (CINV) is still a major problem in children receiving moderate and highly emetogenic therapy. Compared to adults, children achieve almost 30% less control of CINV using a similar antiemetic regimen. Courses of chemotherapy in children often last longer than the approved 3-day (fos)aprepitant regimen. This will be the first randomized placebo controlled study addressing the question if prolonged duration of (fos)aprepitant treatment leads to better control of chemotherapy induced nausea and vomiting in children compared with the standard regimen.

Study objective

This study has been transitioned to CTIS with ID 2024-517846-32-00 check the CTIS register for the current data.

To evaluate the effect of prolonged duration of (fos)aprepitant prophylaxis on the prevention of delayed CINV (complete remission in the 24-72 hours after the final dose of chemotherapy) in children. The current 3-day regimen is compared to a regimen of (fos)aprepitant prophylaxis during the complete course of chemotherapy in the same patient in subsequent similar courses of chemotherapy, creating an intrapatient comparison of anti-emetic control.
See protocol section 2 objectives for het secondary objectives.

Study design

a double-blind placebo-controlled randomized cross-over phase III study

Intervention

A randomized comparison of standard of care 3-days (fos)aprepitant followed by placebo (treatment regimen A) and (fos)aprepitant prophylaxis during the

complete course of chemotherapy (treatment regimen B). Before starting the next course of similar chemotherapy patients will crossover to the second treatment regimen (A to B and B to A).

Study burden and risks

The topic of this study on improving the current protocol of anti-emetic prophylaxis will appeal children and we expect a great willingness to cooperate with this project. We hypothesize that an increase in duration of aprepitant prophylaxis from 3 days to the total duration of the course of chemotherapy will lead to a decreased number of patients experiencing nausea and vomiting. However, patients could experience side effects of longer (fos)aprepitant prophylaxes. Although considered rare, we will monitor this carefully.

Contacts

Public
Prinses Máxima Centrum voor Kinderoncologie

Heidelberglaan 25
Utrecht 3584 CS
NL
Scientific
Prinses Máxima Centrum voor Kinderoncologie

Heidelberglaan 25
Utrecht 3584 CS
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)

Children (2-11 years)
Babies and toddlers (28 days-23 months)

Inclusion criteria

these are the eligibility criteria:
- Age must be >= 6 months to <= 18 years at time of study entry and weight >=6kg
- a documented malignancy.
- Patients need to receive moderate or highly emetogenic chemotherapy blocks, or chemotherapy not previously tolerated due to vomiting, for a minimum duration of 4 days.
- Chemotherapy schedules need to contain two similar courses of chemotherapy, which do not necessarily have to be consecutive courses.
- No symptomatic primary or metastatic CNS malignancy causing nausea or vomiting.
- Patients do not receive scheduled blocks of chemotherapy containing dexamethasone as part of anti-tumour treatment during the study period.
- Patients aged 16 and greater than 16y with a Karnofsky score of 60 or more or patients aged 15y or less with a Lansky Play performance score of 60 or more.
- Patient must have a life expectancy of 3 months or more.
- Patients must not use antiemetic treatment within 48h before treatment (see appendix B).
- Patients must not receive radiation therapy to the abdomen or pelvis in the week before treatment.
- Patient must not use benzodiazepines or opioids initiated within 48h before treatment, except for single doses of triazolam, temazepam, or midazolam.
- Continuation of chronic benzodiazepine or opioid therapy is permitted provided it was initiated >=48 hours prior to study drug administration.
o In patients on chronic warfarin, acenocoumarol, tolbutamide or phenytoin (metabolised by CYP2C9) therapy should be monitored closely during treatment with (fos)aprepitant and for 14 days following each course of (fos)aprepitant.
o No use of CYP3A4 substrates/inhibitors within 7 days, or no CYP3A4 inducers within 30 days of treatment (see appendix B).

- serum creatinine must be <= 1.5 x institutional upper limit of normal (ULN) according to age.
- AST and ALT must be <= 5 x institutional ULN.
- total bilirubin must be <= 1.5 x institutional ULN
- no history of QT prolongation
- Female patients of childbearing potential must have a negative urine or serum pregnancy test confirmed prior to enrollment.
-Female patients with infants must agree not to breastfeed their infants while on this study.
-Male and female patients of child-bearing potential must agree to use a highly effective method of contraception approved by the investigator during the study, following the CTFG recommendations.

-Patients have no history of prior grade 3/4 allergic reaction to any of the study drugs.
-Patients have no underlying gastrointestinal disease that may interfere with the absorption of the medication.

Exclusion criteria

see eligibility criteria D4a.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	01-02-2022
Enrollment:	76
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	EMEND
Generic name:	aprepitant
Registration:	Yes - NL intended use
Product type:	Medicine

Brand name:	IVEMEND
Generic name:	fosaprepitant
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	09-08-2021
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	18-11-2021
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	28-12-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	30-12-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	18-07-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	02-08-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	24-06-2023
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	05-07-2023

Application type:	Amendment
Review commission:	METC NedMec

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
EU-CTR	CTIS2024-517846-32-00
EudraCT	EUCTR2021-003311-26-NL
CCMO	NL77839.041.21