MEtoclopramide, DExamethasone or Aloxi (palonosetron) for the prevention of delayed chemotherapy-induced nausea and vomiting in moderately emetogenic non-AC-based chemotherapy: the MEDEA trial

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON44716

Source
ToetsingOnline

Brief title
MEDEA trial

Condition

- Other condition

Synonym
chemotherapy induced nausea and vomiting, nausea and vomiting caused by chemotherapy

Health condition

alle vormen van solide tumoren

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: chemotherapy, delayed CINV, prevention

Outcome measures

Primary outcome

Primary efficacy endpoint: the proportion of patients reporting complete response during the overall 24 to 160 hours after initiation of the first cycle of MEC. Complete response is defined as no vomiting and nausea and no use of rescue medication. A diary will be used to document the date and time of any emetic episodes and use of rescue medication, as well as daily nausea ratings.

Primary tolerability endpoint: the proportion of patients with minimal or no antiemetic therapy-related side effects according to the DSQ questionnaire, the AIMS and Aloxi questionnaire during the first cycle of MEC.

Primary cost-effectiveness endpoint: total antiemetic medication costs per treatment regimen during the first cycle of MEC. A diary will be used to document the use of antiemetics and rescue medication. Total medication costs will be calculated from this.

Secondary outcome

Secondary efficacy endpoint: the proportion of patients with minimal or no impact on daily life of CINV according to the FLIE questionnaire during the first cycle of MEC.

Secondary tolerability endpoint: the proportion of patients with minimal or no impact on daily life of antiemetic therapy-related side effects according to the EORTC QLQ C-30 during the first cycle of chemotherapy.

Study description

Background summary

Although significant progress has been made with the development of a number of effective and well-tolerated antiemetic treatments, chemotherapy-induced nausea and vomiting (CINV) remains among the most distressing and feared side-effects of cancer treatment. Recently, chemotherapeutic agents have been classified into four risk categories of emesis: high (> 90%, HEC), moderate (30%-90%, MEC), low (10%-30%), and minimal (< 10%). International guidelines recommend monotherapy multi-day oral dexamethasone as the preferred standard prophylaxis for delayed CINV in patients receiving MEC.
These international guidelines are not supported by studies in which dose and schedule of dexamethasone have been determined by formal testing. In addition, no studies have been performed comparing its efficacy with metoclopramide or palonosetron (aloxi) in this setting. Moreover, the administration of dexamethasone is associated with a range of side effects, which increase when administered as part of multi-day antiemetic regimens. The use of dexamethasone as an antiemetic may have a substantial deleterious effect on Quality of Life (QoL) and therefore its benefits should be evaluated when used with MEC.

Study objective

In this phase III non-inferiority trial, the aim is to evaluate whether metoclopramide and palonosetron prophylactic antiemetic treatment are non-inferior to dexamethasone with regard to its efficacy to prevent delayed CINV induced by non-AC based MEC. In addition it will be studied whether metoclopramide and palon prophylactic antiemetic treatment have a significantly lower incidence of side effects and a less negative impact on QoL than dexamethasone. The relative cost-effectiveness of the different antiemetic

regimens will also be evaluated.

Study design

Open label, multicenter, ranomised, phase III, non-inferiority study

Intervention

Dexamethasone (8 mg/day) should be taken twice daily, as two 4 mg tablets, with a sufficient amount of water during meals, on days 2 and 3.
Metoclopramide (30-60 mg/day) should be taken three-times, as single 10 mg tablets with a sufficient amount of water between meals and spread out during the day, on days 2 and 3. Metoclopramide can also be taken as a single 20 mg suppository, three times daily.
Palonosetron is administered as a single dose bolus of 125 mg on day 1, 30 minutes before chemotherapy is administered.

Study burden and risks

The burden and risks for the participants of this study are low: no extra blood samples, no extra visits or examinations are planned. A diary and seven questionnaires need to be filled in, including four self-administered questionnaires. Time of follow up is short: the end-of-treatment visit is scheduled on day 8 after initiation of the first cycle of MEC. Patients who successfully complete the first cycle are eligible to continue into the second cycle of MEC, with similar burden and risks.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

* Patient has been diagnosed with histologically or cytologically confirmed solid cancer
* Starting with first cycle of chemotherapy of moderate emetogenic risk, which does not include a combination of anthracycline plus cyclophosphamide
* Age * 18
* WHO * 1
* Patient is able to understand and speak Dutch

Exclusion criteria

* Patient with nausea and/or vomiting in 48 hours before start of chemotherapy treatment
* Patient submitted to concomitant radiotherapy or submitted to radiotherapy 15 days before start of chemotherapy or planned to receive radiotherapy during 8 days after administration of chemotherapy
* Patient with concomitant severe comorbidy, such as:
o Intestinal obstruction
o Active peptic ulcer
o Hypercalcemia
o Uncontrolled diabetes mellitus
o Pheochromocytoma
o Tardive dyskinesia
o Epilepsia
o Active infective diseases
o Brain * or leptomeningeal metastases
o Psychiatrical disorders
o Parkinsonism
* Current use of corticosteroids (similar to prednisone * 10 milligrams per day)
* Current alcohol abuse

* Pregnancy

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	16-07-2013
Enrollment:	450
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Aloxi
Generic name:	palonosetron
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	dexamethasone
Generic name:	dexamethasone
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	primperan
Generic name:	metoclopramide
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	13-12-2011
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	13-03-2012
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	10-07-2012
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	17-07-2012
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	19-09-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	05-12-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	11-02-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-05-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	04-08-2014

Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	21-08-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	06-04-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-04-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	21-12-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	09-02-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	24-11-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	30-11-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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
EudraCT	EUCTR2011-004446-17-NL
CCMO	NL38215.029.11