An open-label, individual study groups, fixed sequence, four-period crossover study comparing three proportionate sizes of HP 3020 patch applied for 24 hours with intravenous palonosetron injection (ALOXI®) and a one-period study with one size of HP-3020 patch applied for 168 hours, to investigate the pharmacokinetics, tolerability and safety of HP-3020 patches in healthy male subjects

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Primary: To investigate the pharmacokinetics of palonosetron in plasma from three different sizes of HP-3020 transdermal patch applied for 24 hours as compared to intravenous palonosetron (Cohort 1) and to investigate the pharmacokinetics of...

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

Summary

ID

NL-OMON34113

Source
ToetsingOnline

Brief title
HP-3020 transdermal patch study

Condition

- Miscellaneous and site unspecified neoplasms benign

Synonym
chemotherapy induced nausea, chemotherapy induced vomiting

Research involving
Human

Sponsors and support

Primary sponsor: Hisamitsu Pharmaceutical
Source(s) of monetary or material Support: farmaceutische industrie

Intervention

Keyword: chemotherapy, palonosetron, transdermal patch

Outcome measures

Primary outcome

- Pharmacokinetics

- Safety

Secondary outcome

n.a.

Study description

Background summary

The drug to be given is an existing compound, palonosetron hydrochloride (registered under the tradename Aloxi®) in a new application form (transdermal patches).

Palonosetron is used against chemotherapy induced nausea and vomiting (CINV). Palonosetron hydrochloride is a serotonin (5-hydroxytryptamine or 5-HT) receptor antagonist which exerts its effect by interacting with the 5-HT3 receptors as an antagonist.

In this study, a new administration method of palonosetron hydrochloride (palonosetron HCl), in the form of transdermal application, is tested. The advantages of this new transdermal delivery system may include the avoidance of gastrointestinal side effects after oral administration, and of complaints and complications related to administration via an injection. Thus, transdermal delivery systems may provide a wider range of therapeutic options for physicians to use in optimising their patient care

Study objective

Primary:
To investigate the pharmacokinetics of palonosetron in plasma from three different sizes of HP-3020 transdermal patch applied for 24 hours as compared to intravenous palonosetron (Cohort 1) and to investigate the pharmacokinetics of palonosetron in plasma from a 54 cm2 surface of HP-3020 transdermal patches applied for 168 hours (Cohort 2) in healthy male volunteers.
To evaluate the excreted amounts of palonosetron in urine after each application of HP-3020 transdermal patches in Cohorts 1 and 2.

Secondary :
To assess the safety and tolerability of HP-3020 transdermal system in healthy male subjects
To analyse residual palonosetron in the HP-3020 transdermal system after removal from the application site at the end of the application period.

Study design

Design:
This Phase 1 study will be conducted in two sequential Cohorts of twelve healthy male subjects per Cohort.
In Cohort 1 there will be a fixed sequence four-period crossover design: all subjects in Cohort 1 will receive a single intravenous dose of 0.25 mg palonosetron in the first period, and they will receive three sizes of HP-3020 transdermal systems (6, 18 and 54 cm2, containing a total of 0.6, 1.8 and 5.4 mg palonosetron hydrochloride, respectively) in the second to fourth period.
The transdermal patches will be removed 24 hours after application in Cohort 1.
The wash-out between applications will be at least 168 hours.
Cohort 2 will receive three 18 cm2 (so a total surface of 54 cm2 HP-3020 transdermal system (containing a total of 5.4 mg palonosetron hydrochloride)) which will be removed after 168 hours.

Procedures and assessments
Screening and follow-up:
Clinical laboratory, vital signs, full physical examination, 12-lead ECG, at eligibility screening: medical history, alcohol, nicotin metabolites and drug screen, HBsAg, anti-HCV, anti HIV 1/2; clinical laboratory, alcohol, nicotin

metabolites and drug screen, vital signs and 12-lead ECG to be repeated on admission.

Cohort 1:
Observation period:
Admission in clinic from -17 hours before the first drug administration up to 168 hours after removal of the last patch (Day 33).

Blood sampling:
For pharmacokinetics of palonosetron: pre-dose and 1, 3, 5, 15 and 30 minutes and 1, 2, 4, 6, 12, 24, 48, 72, 96, 120, 144, 168 and 192 hour post-dose (Period 1, Aloxi® injection) and at 0, 2, 4, 6, 12, 18, 24 (before removal of the patches), 28, 32, 40, 48, 72, 96, 120, 144, 168 and 192 hours post-dose (Periods 2, 3 and 4)

Urine collection:
For pharmacokinetics of palonosetron: during each period pre-dose and intervals 0-24, 24-48, 48-72, 72-96, 96-120, 120-144, 144 168 and 168-192 hours post-dose.

Safety assessments:
Adverse events (throughout the study); vital signs and ECG: pre-dose and 2, 4, 12, 24, 48, 72, 96, 120 and 192 hours post-dose (all 4 study periods, for periods 2-4 the 192 hour recording of the previous period is the pre-dose); visual inspections of the application sites 0 hr (immediately prior to the patch application), 25, 48, 72, 96, 120, 144, 168 and 192 hours after the application of each transdermal patch; clinical laboratory: on Day -1 and 48 and 168 hours post-dose in Periods 1-3 and at 48 and 192 hours post-dose in Period 4.

Adhesion Evaluation:
2, 4, 8 and 24 hours after the application of each transdermal patch; Adhesive Residue.

Bioanalysis:
Analysis of plasma and urine samples for palonosetron using a validated method by PRA International.

Cohort 2:
Observation period:
Admission in clinic from -17 hours before patch application up to 168 hours after removal of the patch (Day15).

Blood sampling:
For pharmacokinetics of palonosetron : pre-dose and 2, 4, 6, 12, 18, 24, 28, 32, 40, 48, 72, 96, 120, 144 and 168 (before removal of the patches), 172, 176,

184, 192, 216, 240, 264, 288, 312, 336 hours post dose.

Urine collection:
For pharmacokinetics of palonosetron: pre-dose and intervals 0-24, 24-48, 48-72, 72-96, 96-120, 120-144, 144 168, 168-192, 192-216, 216-240, 240-264, 264-288, 288- 312 and 312-336 hours.

Safety assessments:
Adverse events (throughout the study); vital signs and ECG: pre-dose and 4, 12, 24, 48, 72, 96, 120, 168, 192 hour post-dose (before removal of the patches) and 216, 240, 288 and 336 hour post-dose; visual inspections of the application sites 0 hr (immediately prior to the patch application), 169, 192, 216, 240, 264, 288, 312 and 336 hours after the application of the transdermal patch; clinical laboratory: day -1 and 48 and 192, 240 and 336 hour post-dose.

Adhesion Evaluation:
2, 4, 8, 24, 48, 72, 96, 120, 144 and 168 hours after the application of each transdermal patch; Adhesive Residue.

Bioanalysis:
Analysis of plasma and urine samples for palonosetron using a validated method by PRA International

Intervention

Study madication: palonosetron in transdermal patch (HP-3020, 0.6 mg palonosetron HCl per 6 cm2) and solution for intravenous injection (Aloxi®, 0.25 mg).

Study burden and risks

Procedures: pain, light bleeding, heamatoma, possibly an infection, irritation patch.

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

- age 18- 55 year
- BMI 18.0 - 29.9
- caucasian

Exclusion criteria

Suffering from: hepatitis B, cancer or HIV/AIDS. In case of participation in another drug study within 60 days before the start of this study or being a blood donor within 60 days from the start of the study or in case of donating more than 1 liter of blood in the 10 months prior the start of this study.

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial

Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	21-09-2010
Enrollment:	24
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Aloxi
Generic name:	Palonosetron
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	03-09-2010
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	09-09-2010
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

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	EUCTR2010-021511-16-NL
CCMO	NL33664.056.10