An Investigation of the Mass Balance, Pharmacokinetics, Excretion and Metabolism of [14C]-Nanatinostat in Patients with Advanced Solid Tumors: A Phase 1, Open-Label Study

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Primary objective:• To assess the mass balance of nanatinostat (ie, evaluate clearance mechanisms of nanatinostat and drug-related metabolites) following a single oral dose of [14C]-nanatinostat in patients with advanced cancer.Secondary objectives...

Ethical review	Approved WMO
Status	Will not start
Health condition type	Metastases
Study type	Interventional

Summary

ID

NL-OMON51840

Source
ToetsingOnline

Brief title
CS0383-210288 VT3996-101

Condition

- Metastases

Synonym
metastatic or advanced solid tumors

Research involving
Human

Sponsors and support

Primary sponsor: Viracta Therapeutics, Inc.
Source(s) of monetary or material Support: Viracta Therapeutics Inc.

Intervention

Keyword: excretion, mass balance, metabolism, pharmacokinetics

Outcome measures

Primary outcome

Primary endpoints

• The amount of radioactivity excreted in urine and feces with an objective to recover >=90% of the radiolabeled nanatinostat.

Secondary outcome

Secondary:

• Concentration-time profile and PK parameters of total radioactivity from analysis of plasma, urine, and feces collected at identified timepoints.

• PK parameter estimates for nanatinostat and metabolites M1 and M2 in plasma.

• The amount of radioactivity in plasma and whole blood, including the erythrocyte transfer ratio (ETR) and erythrocyte/plasma partition coefficient (EPPC).

• [14C]-metabolic profile and identification of metabolites in plasma and/or blood

• Major radioactive peak/metabolites in the urine and fecal radiochromatograms as a percentage of the radioactive dose.

• Incidence and severity of treatment-emergent adverse events (TEAEs). Adverse events (AEs) will be graded according to National Cancer Institute (NCI) Common

Terminology Criteria for Adverse Events (CTCAE), version 5.0.

Study description

Background summary

Nanatinostat (also known as VRx-3996 and CHR-3996) is an orally administered hydroxamic acid-based, class-I selective histone deacetylase (HDAC) inhibitor that is currently in development in combination with the antiviral drug valganciclovir for the treatment of patients with advanced Epstein-Barr virus (EBV)-associated malignancies.

The safety, tolerability and pharmacokinetics (PK) of nanatinostat were initially evaluated in a Phase 1 dose-escalation safety trial in 39 patients with advanced solid tumors. Nanatinostat was generally well-tolerated, and preliminary clinical activity was shown; a partial response was seen in one patient with metastatic acinar pancreatic carcinoma, and 9 patients had a best response of stable disease.

The combination of nanatinostat and valganciclovir (VALCYTE®), an oral prodrug of ganciclovir, is currently under investigation in 3 ongoing studies including a Phase 1b/2 study (VT3996-201) in patients with relapsed/refractory EBV-positive (EBV+) lymphoma, a Phase 2 study (VT3996-202) in patients with EBV+ relapsed/refractory lymphomas, and a Phase 1b/2 study (VT3996-301) in patients with advanced EBV+ solid tumors.

Study objective

Primary objective:
• To assess the mass balance of nanatinostat (ie, evaluate clearance mechanisms of nanatinostat and drug-related metabolites) following a single oral dose of [14C]-nanatinostat in patients with advanced cancer.

Secondary objectives:
• To evaluate the pharmacokinetics (PK) of nanatinostat and metabolites M1 (NT-IM-1, hydrolysis product) and M2 (NT-IM-2, N-hydroxyl reduction product) in plasma.
• To screen and identify for profiling purposes potential nanatinostat metabolites in selected and pooled plasma, feces, and urine samples.
• To assess safety and tolerability of [14C]-nanatinostat in patients with advanced cancer.

Study design

This is a Phase 1, single-center, open-label, mass balance study.

Intervention

radiolabeled nanatinostat: [14C]-Nanatinostat

Study burden and risks

The proposed clinical trial is a human mass balance study of an investigational medicinal product belonging to the well characterized class of HDAC inhibitors. The risks associated with HDAC inhibitors are considered ethically acceptable in the proposed study population, patients with metastatic or advanced solid tumors refractory to standard therapy, albeit a potential treatment benefit is unlikely after a single dose of nanatinostat monotherapy.
The overall risk assessments are acceptable in this patient population with the dose level of 40 mg oral dose of nanatinostat, containing 88 µCi [14C]-nanatinostat, given the available clinical data and with the supervision and medical monitoring of participants during the study period in the unit.

Nanatinostat has been in clinical development as a monotherapy as well as in combination, is oral, and over 100 patients have been dosed with this drug, and thus its safety profile is well-established. Further, it is tolerated at much larger daily doses with nearly all toxicities being reversible given its short half-life, thus carrying little risk in a single-dose study. Results from this phase 1 study will support further development of new therapies for cancer patients who may not have other options for therapy at the present.

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

1. Men or women that are at least 18 years of age at the time of informed consent.
2. Has histologically confirmed metastatic or advanced solid tumors refractory to standard therapy, and for whom no standard curative therapy exists.
3. Eastern Cooperative Oncology Group (ECOG) performance status: 0-2.
4. Adequate laboratory parameters (in absence of transfusion support within three weeks or growth factor within two weeks of Screening), including:
Absolute neutrophil count (ANC) >=1500/mm3 = 1.5 × 109/L.
Platelets count >=90,000/mm3 = 90 × 109/L.
Hemoglobin >=9.0 g/dL.
Aspartate aminotransferase (AST), alanine aminotransferase (ALT) <=2.5 × upper limit of normal (ULN), or < 5x ULN in the presence of liver metastases.
Total bilirubin <=1.5 × ULN unless considered due to Gilbert*s syndrome, in which case, <=3.0 × ULN.
Estimated glomerular filtration rate (eGFR) >=60 mL/min by CKD-EPI equation.
Serum potassium, magnesium, and corrected calcium outside normal limits for institution that are assessed as clinically significant by the Investigator should be treated to correct abnormalities with confirmation on repeat lab studies.
5. Life expectancy >3 months, as determined by the treating physician.

Exclusion criteria

1. Known history of central nervous system and/or leptomeningeal disease.
2. Prior treatment with [14C]-nanatinostat or history of allergic reactions attributed to compounds
of similar chemical or biologic composition to [14C]-nanatinostat.

3. Inability to take or tolerate oral medication.
4. Any gastrointestinal, liver, or kidney condition that may affect drug absorption and metabolism.
5.Is currently participating in or has participated in an interventional study of an investigational agent or has used an investigational device within 4 weeks or 5 half-lives prior to dosing, whichever is longer.

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	6
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Nap.
Generic name:	[14C]-Nanatinostat

Ethics review

Approved WMO Date:	29-06-2022
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	22-08-2022

Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	05-11-2022
Application type:	Amendment
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	EUCTR2022-001630-11-NL
CCMO	NL81579.056.22