A Rollover Protocol to allow continued access to Tivozanib Hydrochloride (AV-951) for subjects enrolled in other Tivozanib Hydrochloride Protocols

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Objectives:• To allow continued access to tivozanib for subjects who have participated in other tivozanib (monotherapy orcombination) protocols, who are tolerating study drug and displaying clinical benefit.• To assess long-term safety and...

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

Summary

ID

NL-OMON39584

Source
ToetsingOnline

Brief title
Continued Access to Tivozanib

Condition

- Miscellaneous and site unspecified neoplasms benign

Synonym
gastrointestinal cancer

Research involving
Human

Sponsors and support

Primary sponsor: AVEO pharamaceuticals

Source(s) of monetary or material Support: AVEO pharmaceuticals

Intervention

Keyword: Rollover Protocol Continued Tivozanib

Outcome measures

Primary outcome

Patients will be observed for adverse events and tumor growth.

Secondary outcome

To determine the duration of response and progression-free survival (PFS) of

subjects

who continue on tivozanib.

Study description

Background summary

The formation of new blood vessels, known as angiogenesis, is required to support growth in the
embryo and to allow for repair (e.g., wound healing and remodeling processes in the adult).
Vascular endothelial growth factor (VEGF) plays a critical role during normal embryonic
angiogenesis and also in the pathological angiogenesis that occurs in a number of diseases,
including cancer. Tumors use this vasculature to obtain oxygen and nutrients, both of
which are required to sustain tumor growth. In addition, the new intra-tumoral blood vessels
provide a way for tumor cells to enter the circulation and to metastasize to distant organs.
The various forms of VEGF bind to 3 tyrosine kinase receptors: the vascular endothelial growth
factor receptors, VEGFR-1, VEGFR-2, and VEGFR-3. This binding results in phosphorylation
of the receptors catalyzed by the protein kinase, and the promotion of a signal transduction

cascade. Deregulation of VEGF expression contributes to the development of solid tumors by promoting tumor angiogenesis. Tivozanib inhibits VEGFR-associated tyrosine kinase activity and, as a result, may offer a potential therapy for subjects with cancer by controlling tumor growth.

Study objective

Objectives:
• To allow continued access to tivozanib for subjects who have participated in other tivozanib (monotherapy or combination) protocols, who are tolerating study drug and displaying clinical benefit.
• To assess long-term safety and tolerability in subjects who continue on tivozanib
• To determine the duration of response and progression-free survival (PFS) of subjects who continue on tivozanib

Study design

Open-label, multi-center, multi-national rollover study to allow continued access to tivozanib for subjects who have participated in other tivozanib (monotherapy or combination) protocols. Eligible subjects will continue to receive tivozanib at the same dose and schedule as per the original (parent) protocol. The length of time that a subject must be on the parent protocol before rolling over to this protocol will be dictated by the (original) parent protocol.

Intervention

Patients will receive tivozanib according to the previous guidelines of the study in which they participated.

Study burden and risks

Hypertension has been the primary AE observed in the Phase 1 and 2 monotherapy studies of tivozanib in subjects with solid tumors. Hypertension is a frequent and controllable side-effect of drugs targeting the vascular endothelial growth factor (VEGF) pathway, and has been

observed with varying frequency with several approved agents in clinical use such as
bevacizumab, sunitinib, and sorafenib.

The patients entered in this study had at least stable disease in a previous study and will therefore benefit of continued treatment with tivozanib.

Contacts

Public
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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. The subject must have received tivozanib hydrochloride while enrolled in another protocol, must be tolerating study drug and must currently display clinical benefit. The length of time that a subject must be on the parent protocol before rolling over to this protocol will be dictated by the parent protocol.

a. Subjects who received tivozanib hydrochloride at any time while on parent protocol AV-951-12-205, regardless of sequence, may enroll if they tolerated and displayed clinical benefit while receiving tivozanib hydrochloride.
b. Subjects receiving sorafenib in Study AV-951-09-902 who were tolerating sorafenib and displaying clinical benefit at the time of study termination may initiate tivozanib hydrochloride as a treatment option.
2. If female and of childbearing potential, documentation of negative pregnancy test prior to enrollment (i.e. before the first dose of tivozanib hydrochloride in this protocol).
3. Ability to give written informed consent.

Exclusion criteria

1. Subjects to be excluded > 4 weeks since discontinuation of study drug treatment on a previous AVEO-sponsored clinical trial.
a. For subjects initiating tivozanib hydrochloride (ie receiving sorafenib and demonstrating tolerability and clinical benefit on Study AV-951-09-902 at the time of study termination), > 4 weeks since last dose of sorafenib, unless discussed with Sponsor. •
2. If female, pregnant or lactating.
3. Sexually active male and pre-menopausal female subjects (and their partners) unless they agree to use adequate contraceptive measures, while on study and for 45 days after the last dose of study drug. All fertile male and female subjects (and their partners) must agree to use a highly effective method of contraception. Highly effective birth control includes (a) IUD plus one barrier method; (b) oral, implantable or injectable contraceptive plus one barrier method; or (c) 2 barrier methods. Effective barrier methods are male or female condoms, diaphragms, and spermicides (creams or gels that contain a chemical to kill sperm).
4. Uncontrolled hypertension: systolic blood pressure > 140 mmHg or diastolic blood pressure >90 mmHg documented on 2 consecutive measurements taken at least 24 hours apart.
5. Unhealed wounds (including active peptic ulcers).
6. Serious/active infection or infection requiring parenteral antibiotics.
7. Life-threatening illness or organ system dysfunction compromising safety evaluation.
8. Psychiatric disorder, altered mental status precluding informed consent or necessary testing.
9. Inability to comply with protocol requirements.

Study design

Design

Study phase:	2
Study type:	Interventional

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	15-02-2012
Enrollment:	10
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Geen
Generic name:	Tivozanib Hydrochloride

Ethics review

Approved WMO Date:	29-11-2011
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	13-01-2012
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	08-03-2012
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	04-07-2012
Application type:	Amendment

Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	05-09-2012
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	23-08-2013
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	17-10-2013
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	20-03-2014
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	14-04-2014
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	EUCTR2009-013407-66-NL
CCMO	NL30230.078.11