A Phase 4, Multicenter Study to Evaluate Discontinuation and Re-Treatment in Subjects with Tenosynovial Giant Cell Tumor (TGCT) Previously Treated with Pexidartinib

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Main objective: Proportion of subjects who remain treatment-free.Secondary objectives: - Change from Baseline in Patient Reported Outcomes (PROs) (PROMISPF, EQ-5D-5L)- Safety: Total number of subjects in the safety analysis set with any AEcollected...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Soft tissue neoplasms malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON52692

Source
ToetsingOnline

Brief title
PL3397-A-U4003

Condition

- Soft tissue neoplasms malignant and unspecified

Synonym
Pigmented Villonodular Synovitis (PVNS), Tenosynovial giant cell tumor (TGCT)

Research involving
Human

Sponsors and support

Primary sponsor: DAIICHI SANKYO, INC.
Source(s) of monetary or material Support: pharmaceutical industry

Intervention

Keyword: Discontinuation and Re-Treatment, Pexidartinib, Phase 4, Tenosynovial Giant Cell Tumor (TGCT)

Outcome measures

Primary outcome

Proportion of subjects who remain treatment-free at Month 12 and Month 24

Secondary outcome

Change from Baseline in Patient Reported Outcomes (PROs): Mean

change from Baseline* for PROMIS PF and EQ-5D-5L quarterly for the

treatment-free and Re-Treatment periods.

*Note: Baseline is Screening values for Treatment Free Period

Treatment Continuation Cohort. Baseline is reinitiated with subject

entering Re-Treatment period.

Safety: Incidence of AEs/TEAEs and SAEs, ECGs, and laboratory

assessments

Tumor Assessment: Qualitative assessment of the tumor (not applicable

to Treatment-Free period)

Study description

Background summary

Tenosynovial giant cell tumor (TGCT) is a rare, nonmalignant neoplasm of the synovium,

bursae, or tendon sheaths that is driven by overexpression of colony-stimulating factor-1 (CSF-1) often afflicting adults under 40 years of age. Annual TGCT incidence is estimated to be 43 cases per one million individuals, of which approximately 10% are of the diffuse subtype. Surgical resection, when feasible, is the standard treatment for TGCT; however, recurrence of the diffuse subtype is particularly common. Repeated surgeries often result in increasing morbidity and functional limitations of the affected joints. The diffuse disease often has more extensive involvement and a poorer likelihood of a successful cure with surgery, and therefore often may not be amenable to surgical resection due to the risk of morbidity or high risk of recurrence in diffuse disease.Pexidartinib is the first systemic therapy to show a robust tumor response in TGCT with improved patient symptoms and functional outcomes; cholestatic hepatotoxicity has been identified as a risk. Patients with TGCT diagnosed early in their lives face potentially several decades of daily treatment. In the real-world setting, subjects and Investigators are faced with decisions surrounding patients* activities of daily living and treatment with pexidartinib for TGCT.
Further data are necessary to fully understand the safe and effective discontinuation and retreatment with pexidartinib therapy in this patient population.
The purpose of this Phase 4 multicenter study in subjects with TGCT previously treated with pexidartinib are two-fold. At the Screening visit/time of consent, the Investigators and subjects are provided the choice to either continue treatment with pexidartinib or discontinue treatment with the possibility of re-initiating pexidartinib treatment at a later time. Findings from this study will provide important prospective discontinuation and re-treatment data with pexidartinib in previously treated subjects with residual disease.
Ultimately, this study will contribute meaningful information to the body of research on pexidartinib treatment for patients with TGCT and the safe and effective discontinuation and retreatment with pexidartinib therapy.

Study objective

Main objective:

Proportion of subjects who remain treatment-free.

Secondary objectives:

- Change from Baseline in Patient Reported Outcomes (PROs) (PROMIS PF, EQ-5D-5L)
- Safety: Total number of subjects in the safety analysis set with any AE collected between Screening and start of re-treatment or final database lock (whichever occurs first)
- Tumor Assessment: Investigator evaluation of tumor

Study design

This is a Phase 4, multicenter study in subjects with TGCT (PVNS or GCT-TS) who were previously treated with pexidartinib in one of the following studies: PLX108-10 (ENLIVEN), PLX108-01, PL3397-A-A103, and PL3397-A U126. At the Screening visit/time of consent, at the Investigator and subject*s discretion, the subjects are given the choice to either continue treatment with pexidartinib or discontinue treatment with the possibility to reinitiate pexidartinib treatment at a later time.

Intervention

1. Subjects who choose to continue treatment with pexidartinib will be enrolled in the Treatment Continuation Cohort.
The assessments from the subject*s *End-of-Treatment visit* (i.e., the visit on which they received their last dose of study treatment) from their prior study (eg, tumor assessments, PRO measures, and safety parameters) will serve as the Baseline measurements for PL3397-A-U4003 study. These subjects will remain on their current dosage of pexidartinib and undergo clinical assessments at 3-month intervals for the duration of the study.
2. Subjects who choose to discontinue pexidartinib treatment will be enrolled into the Treatment-Free period of the Treatment-Free/Re-Treatment Cohort. The assessments from the subject*s End-of-Treatment visit from their prior study (eg, tumor assessments, PRO measures, and safety parameters) will serve as the Baseline measurements for PL3397-A-U4003 study. Subjects will discontinue pexidartinib treatment and undergo clinical assessments at 3-month intervals during the Treatment-Free period. Re-treatment with pexidartinib will be based on the discretion of the subject and Investigator. Tumor assessment, subjective and/or functional measures, and

safety will be considered in the
decision-making process. The rationale for discontinuing and restarting pexidartinib re-treatment will be recorded
accordingly.
Subjects in the Treatment-Free/Re-Treatment Cohort who enter the Re-Treatment period will be administered
pexidartinib at the dose at which they completed the prior study. Dosing is required on an empty stomach (at least
1 hour before or 2 hours after a meal or snack), at approximately the same times of the day, and approximately 12 hours
apart. During the Re-Treatment period, Investigators will ensure weekly liver monitoring tests for the first 8 weeks
(2 months), then every 2 weeks for 1 month, then once every 3 months or more frequently as directed by the
Investigator.

Study burden and risks

In this study the subjects are given the choice to either continue treatment with pexidartinib or discontinue treatment with the possibility to reinitiate pexidartinib treatment at a later time.
Participartion in this study might entail more testing than the subject would usually have. (i.e. blood draws, MRI's).
This study will contribute meaningful information to the body of research on pexidartinib treatment for patients with TGCT and the safe and effective discontinuation and retreatment with pexidartinib therapy.

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

Subjects must meet all of the following criteria to be eligible for enrollment into the study:
1. Currently enrolled and have not been discontinued from pexidartinib treatment in one of the following studies: Study PLX108-10 (ENLIVEN), Study PLX108-01, Study PL3397-A-A103, or Study PL3397-A-U126.
2. Willing and able to complete the PROMIS (Physical Function Scale) and EQ-5D-5L (European Quality of Life) throughout the study.
3. Willing and able to provide written informed consent form (ICF) prior to any study-related procedures and to comply with all study requirements.
4. Females of reproductive potential must have a negative urine pregnancy test at Screening/Baseline (to be confirmed by a serum pregnancy test taken on the End-of-Treatment visit of their prior study) and should be advised to use an effective, non-hormonal method of contraception during treatment with pexidartinib and for 1 month after the last dose. Males with female partners of reproductive potentialshould be advised to use an effective method of contraception during treatment with pexidartinib and for 1 month after the last dose. Female partners of male patients should concurrently use effective contraceptive methods (hormonal or non-hormonal).
Note: A female is considered of reproductive potential following menarche and until becoming postmenopausal (no menstrual period for a minimum of 12 months) unless permanently sterile (undergone a hysterectomy, bilateral salpingectomy or bilateral oophorectomy) with a confirmed by follicle stimulating hormone (FSH) test level >40 mIU/mL.
5. Male subjects must not freeze or donate sperm starting at Screening and throughout the study period, and for at least 5 half-lives or 1 month after the final study drug administration, whichever is longer.
Female subjects must not donate, or retrieve for their own use, ova from

the time of Screening and throughout the study treatment period, and for at least 1 month or 5 half-lives after the final study drug administration, whichever is longer.

Exclusion criteria

Subjects who meet any of the following criteria are NOT eligible for enrollment into the study
1. Subject has a clinically significant abnormality identified by the Investigator at Screening on physical examination, laboratory tests, or electrocardiogram which, in the judgement of the Investigator, would preclude the subject's safe completion of the study.
2. Exposure to another investigational drug or current participation in other therapeutic investigational procedures, besides pexidartinib studies, within 1 month prior to start of study treatment. Any known contraindication to treatment with, including hypersensitivity to, the study drug(s) or excipients in pexidartinib.

Study design

Design

Study phase:	4
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	12-01-2021
Enrollment:	1
Type:	Actual

Medical products/devices used

Product type:	Medicine

Brand name:	Turalio
Generic name:	Pexidartinib

Ethics review

Approved WMO Date:	17-06-2020
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	09-09-2020
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	15-10-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	02-06-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	03-06-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	14-06-2022
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	EUCTR2020-000192-20-NL
CCMO	NL74094.056.20