A Phase 1 Pharmacology Study of the Dual MDMX/MDM2 Inhibitor, ALRN-6924, in Healthy Volunteers.

Published: 29-07-2020
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PrimaryTo determine the pharmacologically optimal dose of ALRN-6924 to induce transient cell cycle arrest in human bone marrow and other tissues.SecondaryTo characterize relative to ALRN-6924 administration the time to onset, the magnitude, and the...

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

Summary

ID

NL-OMON52916

Source
ToetsingOnline

Brief title
CS0351-200052 Aileron

Condition

- Other condition

Synonym
to induce cell cycle arrest in human bone marrow

Health condition

Chemoprotection effects

Research involving
Human

Sponsors and support

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

Intervention

Keyword: human bone marrow, pharmacological effects, safety, tolerability

Outcome measures

Primary outcome

Optimal cell cycle arrest defined as the lowest proportion of S-phase cells in the presence of the lowest rate of apoptosis in bone marrow cells using flow cytometry, or optimal cell cycle arrest defined as >2-fold induction of p21 over baseline in bone marrow cells using immuno-histochemistry (IHC)

Secondary outcome

Time to onset of cell cycle arrest in the bone marrow following administration of a single dose of ALRN-6924.

Percent reduction in S-phase cells in the bone marrow following administration of a single dose of ALRN-6924.

Duration of cell cycle arrest in the bone marrow following administration of a single dose of ALRN-6924.

Pharmacodynamic response (time to onset of cell cycle arrest, percent reduction in S-phase cells, and duration of cell cycle arrest) in the bone marrow following slow bolus injection compared to IV infusion of a single dose of ALRN-6924.

Determination of ALRN-6924 repeated dosing schedule for inducing and maintaining prolonged (0h-72h) cell cycle arrest in the bone marrow.

PK parameters (eg, AUC, Cmax, tmax, t1/2) of ALRN-6924.

Proportion of subjects with NCI CTCAE Grade 1/2 TEAEs.

Study description

Background summary

ALRN-6924 is being developed by Aileron Therapeutics, Inc. (Aileron) as a potential treatment for the supportive care of patients with TP53-mutant tumors, but an intact p53 pathway in their non-malignant tissues.

Study objective

Primary
To determine the pharmacologically optimal dose of ALRN-6924 to induce transient cell cycle arrest in human bone marrow and other tissues.
Secondary
To characterize relative to ALRN-6924 administration the time to onset, the magnitude, and the duration of cell cycle arrest in human bone marrow
To characterize the pharmacodynamic characteristics of IV infusion vs slow bolus injection of ALRN-6924
To evaluate schedules of repeated ALRN-6924 administration that will result in prolonged (0h-72h) cell cycle arrest in human bone marrow
To evaluate the pharmacokinetic (PK) profile of ALRN-6924 following IV infusion and slow bolus injection
Safety and tolerability of single and repeat doses of ALRN-6924 in healthy volunteers

Study design

This is a Phase 1, open-label, single center clinical trial for evaluation of ALRN-6924 pharmacological effects on human bone marrow in healthy volunteers. The study will be conducted in 2 parts.

Intervention

ALRN-6924 or 250 mL of 0.9% NaCl solution.

Study burden and risks

Since the study is being executed in healthy volunteers, there are no anticipated benefits of the IMP. Please see the IB for further

information.

Contacts

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Aileron Therapeutics Inc.

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

Is healthy, defined as being free from clinically significant (and clinically relevant per Principal Investigator) illness or disease as determined by their medical history, medical assessment, physical examination, clinical laboratory tests, and 12-lead ECG obtained during Screening and predose on Day 1.
Is male or female, aged 18-65 years, inclusive, at the time of informed consent (except for cohorts of subjects undergoing scalp biopsy who will be females aged 18-60 years).
Has a BMI ranging between 18.0 and 30.0 kg/m2, inclusive, at Screening.
Has negative urine drug and cotinine screen results at Screening and predose on

Day 1.

Exclusion criteria

Has resting systolic blood pressure <=90 or >=140 mmHg and a resting diastolic blood pressure <=51 or >=90 mmHg at Screening.
Has resting pulse <=50 or >=100 bpm at Screening.
Has QTc intervals corrected for heart rate via the Fridericia method (QTcF) >450 msec (males) and >480 msec (females) at Screening.
Is pregnant or a nursing female.

Study design

Design

Study type:	Interventional
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	24-11-2020
Enrollment:	105
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Nap
Generic name:	Nap

Ethics review

Approved WMO Date:	29-07-2020
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	12-08-2020
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	03-05-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	04-05-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	14-10-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	09-11-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	04-03-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO	

Date:	09-03-2022
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	EUCTR2020-003178-34-NL
CCMO	NL74659.056.20

Study results

Results posted: 01-11-2023

Summary results
Trial ended prematurely

First publication
13-04-2023