A randomized, blinded, placebo-controlled, phase II trial of LEE011 in patients with relapsed, refractory, incurable teratoma with recent progression

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PrimaryTo assess the efficacy of LEE011 compared to placebo in patients with relapsed/refractory teratoma with recent progressionSecondaryTo assess other measures of efficacy of LEE011 compared with placebo To assess safety and tolerability of...

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

Summary

ID

NL-OMON41774

Source
ToetsingOnline

Brief title
LEE011 versus placebo in relapsed, incurable teratoma

Condition

- Miscellaneous and site unspecified neoplasms benign

Synonym
organoid tumor, Teratoma

Research involving
Human

Sponsors and support

Primary sponsor: Novartis
Source(s) of monetary or material Support: Novartis Pharma BV

Intervention

Keyword: LEE011, placebo, Teratoma

Outcome measures

Primary outcome

Progression Free Survival (PFS) as per RECIST v1.1

Secondary outcome

Best Overall Response (BOR),

Overall response rate (ORR)

Disease Control Rate (DCR) at 4 months as per RECIST v1.1,

Overall Survival (OS), and OS rate at 12 months.

Incidence and severity of adverse events, serious adverse events, changes in

laboratory values, electrocardiograms, and vital signs to assess the safety as

per CTCAE v.4.03.

Dose interruptions and changes will be used to assess the tolerability.

Study description

Background summary

Teratomas consist of cell types derived from one or more of the germ layers and arise most commonly in the gonads or midline structures Teratoma classification is dichotomized into benign and malignant. Benign teratomas are distinguished as mature or immature based on the proportion of differentiated tissue observed. Malignant teratomas include mature/immature teratomas that

have metastasized or contain non-germinal malignant patterns (malignant transformation) Teratomas may also arise within other germ cell tumor (GCT) types, most commonly non-seminomatous germ cell tumors (NSGCT).

Malignant teratoma is rare in both the pediatric and adult populations with an incidence of 0.14/100,000 women-years . The frequency is higher in males. Malignant transformation (MT) of teratomatous elements arises in 3-6% of testicular NSGCT and progressive localized growth of teratoma. The US incidence of testicular GCT is 5.7/100,000 males, The incidence of testicular cancer is similar in Western Europe and Australia

Unlike NSGCTs which are sensitive to cytotoxic chemotherapy, teratomas are highly chemo-resistant and optimally treated by complete surgical resection. More than 80% of cases of GTS are successfully managed by surgical resection. Evidence of teratoma with malignant transformation at initial presentation of NSGCT may also be successfully managed with intensive chemotherapy and extensive resection. However, no standard therapy exists for progressive, unresectable teratoma Given the known deregulation of the RB tumor suppressor pathway in GCTs and that nearly all malignant teratomas stain positively for nuclear pRB, treatment of non-resectable malignant teratoma with a CDK 4/6 inhibitor such as LEE011 is a rational approach.

Study objective

Primary
To assess the efficacy of LEE011 compared to placebo in patients with relapsed/refractory teratoma with recent progression

Secondary
To assess other measures of efficacy of LEE011 compared with placebo
To assess safety and tolerability of LEE011 compared with placebo

Study design

multi-center, randomized, double blind, placebo controlled phase II study randomized at a 2:1 ratio to LEE011 or placebo

Intervention

600mg LEE011 Capsule for oral use Daily (21 days followed by one week break)
Placebo Capsule for oral use Daily (21 days followed by one
week break)

Study burden and risks

Risks: toxicities due to the study drug: LEE011

Burden: cycles of 28 days, with 2 visites per cycle.
Blooddraws as specified in section J, inclusive PK sampling
ECGs
MUGA scan and CT scan (see section J)
optional Tumor biopsies

Contacts

Public
Novartis

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Scientific
Novartis

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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. Age > 15 years old at time of informed consent.
2. Diagnosis of teratoma for which no additional standard surgical or medical therapy exists.
3. Availability of an archival or newly obtained tumor sample accompanying pathology report.
* Patients without a tumor sample may be permitted to participate after discussion between Novartis and the investigator.

4. Patients must have completed at least 1 prior line of chemotherapy for germ cell tumor.
5. Radiographic progression, defined by RECIST v.1.1, after the last cancer treatment and within 12 weeks prior to enrollment, compared with scans within 1 year of enrollment.
6. Measurable or evaluable extra-cranial disease as defined by RECIST v.1.1.
7. Patients must have ECOG performance status of 0-1.
8. Written informed consent/assent before any study-specific screening procedures.

Exclusion criteria

1. CNS disease unless radiation therapy and/or surgery has been completed and serial evaluation by CT (with contrast enhancement) or MRI over a minimum of 2 months demonstrates stable disease.
2. Malignant germ cell tumors other than that being treated in this study
3. Concurrent malignancy other than teratoma within 3 years of randomization
4. Prior treatment with any CDK4/6 inhibitor therapy
5. Any concurrent severe and/or uncontrolled medical condition that, in the investigator*s judgment serves as a contraindication to patient participation
6. Patients who have not recovered to * CTCAE grade 1 from the acute toxic effects of all prior chemotherapy, immunotherapy, or radiotherapy.

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	10-08-2015
Enrollment:	6

Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	LEE011
Generic name:	Ribociclib

Ethics review

Approved WMO Date:	10-02-2015
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	06-05-2015
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	07-08-2015
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	07-09-2015
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	03-12-2015
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	22-12-2015
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	10-02-2017

Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	07-08-2017
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	24-11-2017
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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	EUCTR2014-000428-12-NL
ClinicalTrials.gov	NCT02300987
CCMO	NL50782.042.14