A Phase I/II Open-Label, Dose Escalation Study to Investigate the Safety, Pharmacokinetics, Pharmacodynamics, and Clinical Activity of GSK525762 in Subjects with NUT Midline Carcinoma (NMC) and Other Cancers (BET115521)

Published: 19-05-2015
Last updated: 19-04-2024

Primary:To evaluate the clinical activity of GSK525762 in NUT Midline Carcinoma and other solid tumors.Secondary:Effect of treatment with GSK525762 on tumor growth and survival. Pharmacokinetics of GSK525762. Safety.

Ethical review	Approved WMO
Status	Pending
Health condition type	Miscellaneous and site unspecified neoplasms malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON43804

Source
ToetsingOnline

Brief title
BET115521

Condition

- Miscellaneous and site unspecified neoplasms malignant and unspecified

Synonym
NUT Midline Carcinoma and other solid tumors

Research involving
Human

Sponsors and support

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

Intervention

Keyword: BET inhibitor, GSK525762, NUT Midline Carcinoma

Outcome measures

Primary outcome

Adverse events. Overall response rate.

Secondary outcome

PK parameters, cardiac safety parameters, progression free survival, time to

and duration of response, overall survival.

Study description

Background summary

Given the poor prognosis and high unmet medical need of NUT Midline Carcinoma (NMC), as well as in other tumor types such as relapsed/refractory (Non) small cell lung cancer ([N]SCLC), colorectal cancer (CRC), neuroblastoma (NB), castration resistant prostate cancer (CRPC), triple negative breast cancer (TNBC), ER positive breast cancer (ER+BC) and any other MYCN-amplified solid tumor and the exceptional drug-to-target alignment of GSK525762, a combined Phase I/II study (BET115521) is proposed. The BET115521 study comprises
• An accelerated dose titration (Part 1), which will include subjects with NMC and other tumor types that are predicted to be responsive to GSK525762, to determine a maximum tolerated dose (MTD).
The besylate sub-study will be an open-label, randomized, single dose, four period, crossover sub-study to investigate the relative bioavailability of the besylate salt tablet compared to the amorphous free-base tablet. Results of the besylate sub-study will enable the use of the besylate salt tablet formulation later in this study and provide recommendation around the need for fasting status when administering GSK525762. The besylate sub-study will be conducted

at centers in the United States.
• Part 2 is the expansion phase to further explore the efficacy and safety of the MTD in subjects with NMC, SCLC, CRPC, TNBC en ER+BC.
The Netherlands will contribute to Part 2 only. This ABR-form is restricted to information about Part 2.

Study objective

Primary:
To evaluate the clinical activity of GSK525762 in NUT Midline Carcinoma and other solid tumors.
Secondary:
Effect of treatment with GSK525762 on tumor growth and survival.
Pharmacokinetics of GSK525762. Safety.

Study design

Part 2 is the expansion phase to further explore the efficacy and safety of the MTD.
Continuation of treatment until disease progression or unacceptable toxicity.
Approx.150 subjects for part 2.

Intervention

Treatment with GSK525762.

Study burden and risks

Risk: Adverse events of study medication.
Burden:
Twice per week during week 1-2, weekly during week 3-4, every 4 week thereafter.
Physical examination: Nearly every visit.
Blood tests: Every visit. Up to 35 mL per visit.
ECG: Nearly every visit.
Echocardiography: Approx. every 4 weeks.
Holter monitoring 24h: Twice.
Tumor measurements: Every 4-8 weeks.
Tumor biopsy: 2-3 times.
Optional: Pharmacogenetic blood test (6 mL once).

Contacts

Public
GlaxoSmithKline

Huis ter Heideweg 62
Zeist 3705 LZ
NL
Scientific
GlaxoSmithKline

Huis ter Heideweg 62
Zeist 3705 LZ
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

• Males and females, 16 years and above (NL: 18 years and above).
• Diagnosis:
NUT Midline Carcinoma as diagnosed by the Central Laboratory. Subjects may be treatmentnaïve or have had prior therapy.
SCLC, CRPC, TNBC and ER+BC
• Subjects with solid tumors, with the exception of CRPC, must demonstrate measurable disease (NMC: see protocol page 50 for details).
• ECOG Performance Status 0-2 (NMC), 0-1 (other tumor types).
• Females of childbearing potential and males: adequate method of contraception.
• CRPC subjects:
Histologically or cytologically confirmed prostate adenocarcinoma, surgically castrated or continuously medically castrated (for *8 weeks)
Persistent disease with evidence of disease progression following standard therapy(ies). See protocol page 52 for details.
Serum testosterone level <1.7 nmol/l.
PSA level >=2.0 ng/mL.

Exclusion criteria

• Prior and current treatments: see protocol page 53 for details.
• Evidence of severe or uncontrolled systemic diseases. See protocol page 53 for details.
• Cardiac and or ECG abnormalities. See protocol page 54 for details.
• GSK525762 is a benzodiazepine class molecule. Any serious known immediate or delayed hypersensitivity reaction(s) to GSK525762 or idiosyncrasy to drugs chemically related to the investigational drug.
• Hemoptysis > 1 teaspoon in 24 hours within the last 28 days.
• History of major gastrointestinal bleeding within the last 6 months. Any evidence of active gastrointestinal bleeding.
• Pregnancy or breastfeeding.

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-10-2015
Enrollment:	10
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	GSK525762
Generic name:	GSK525762

Ethics review

Approved WMO Date:	19-05-2015
Application type:	First submission
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	02-11-2015
Application type:	First submission
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	03-12-2015
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	19-02-2016
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	02-03-2016
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	10-03-2016
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	26-04-2016
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO	

Date:	11-07-2016
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	15-07-2016
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	06-12-2016
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	16-12-2016
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	29-12-2016
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	26-01-2017
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	26-04-2017
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	28-04-2017
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van

	Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	11-07-2017
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	13-07-2017
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	17-05-2018
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	12-06-2018
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	29-06-2018
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)

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
Other	clinicaltrials.gov; NCT01587703
EudraCT	EUCTR2014-004982-25-NL
CCMO	NL53261.031.15