Multi-arm, Non-randomized, Open-Label Phase IB Study to Evaluate GSK3052230 in Combination with Paclitaxel and Carboplatin, or Docetaxel or as Single Agent in Subjects with Solid Malignancies and Deregulated FGF Pathway Signaling (FGF117360)

Published: 12-05-2014
Last updated: 20-04-2024

Primary: to characterize the safety and tolerability of GSK3052230 in combination with chemotherapy regimens, to determine the MTD and to assess overall response rate in patients with stage IV or recurrent squamous NSCLC with FGFR1 gene...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Respiratory disorders NEC
Study type	Interventional

Summary

ID

NL-OMON44632

Source
ToetsingOnline

Brief title
FGF117360

Condition

- Respiratory disorders NEC

Synonym
mesothelioma; non-small cell lung cancer; lung cancer

Research involving
Human

Sponsors and support

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

Intervention

Keyword: chemotherapy, GSK3052230, mesothelioma, NSCLC

Outcome measures

Primary outcome

Adverse events, MTD, overall survival.

Secondary outcome

PFS, population PK, Pulmonary Function Test parameters.

Study description

Background summary

Preclinically, the fibroblast growth factor (FGF) pathway plays many roles in the development of cancer, including regulation of cell growth and differentiation, regulation of angiogenesis and participation in tumor-stroma interactions. FGFs can stimulate the proliferation of tumor cells and tumor cell lines. Blockade of FGF signaling can prevent tumor cell growth. FGF signaling is mediated by a family of transmembrane receptor tyrosine kinases encoded by four distinct genes producing FGF
receptor subtypes termed FGFR1-4. FGFR1 is the best characterized of the 4 FGFRs.
GSK3052230 blocks the FGF pathway and may have anti-tumor activity either by inhibiting tumor cell proliferation and/or by inhibition of tumor associated angiogenesis. GSK3052230 has been studied in a Phase 1, open-label, dose-escalation study. No MTD has been established. The 20 mg/kg once weekly dosing schedule was determined to be safe and was declared the *maximum feasible dose*.
Increased expression of FGFRs, FGFR1 gene amplification, or production of FGFs correlates with poor prognosis in a variety of tumor types including NSCLC. A focal amplification of the FGFR1 gene has been detected in approximately 20% of

subjects with squamous NSCLC.
Malignant mesothelioma remains a deadly disease with few effective therapies. The median overall survival ranges from 9-17 months regardless of disease stage. The first-line standard of care remains cisplatin and pemetrexed. There remains no widely approved regimen for recurrent mesothelioma. The poor PFS and OS data underscore the need for more effective therapies in recurrent mesothelioma.
This Phase I study is primarily designed to characterize the safety and tolerability of GSK3052230 in combination with chemotherapy regimens, to determine the MTD and to assess overall response rate in patients with stage IV or recurrent squamous NSCLC with FGFR1 gene amplification and recurrent or unresectable mesothelioma.

New information on18-02-2016:
The enrollment in2 study arms (arms A and B) has been closed. Subjects still on treatment in these arms will continue as planned. The enrollmant for arm C (mesothelioma) will continue as planned. This decision has been taken after review of the available study data sofar.
The decision is not based on safety issues.
Arm A (NSCLC, chemotherapy: paclitaxel + carboplatin (standard)): The preliminary efficacy data in therapy naive subjects with NSCLC indicate a similar treatment effect of chemotherapy with and without GSK3052230. The estimated PFS in this arm is approx. 5* months (versus 4-6 months). 18 subjects have been included in this arm.
In addition the introduction of new immuno-oncological compounds sets new standards in terms of efficacy. The available data from arm A do not seem to compare favourably with these standards.
Arm B (NSCLC, chemotherapy: docetaxel (standard)): The inclusion in arm B is very slow (9 subjects sofar). Dince the last dose escalation cohort t (20 mg/kg) has been completed, it has been decided to close this arm as well..

Study objective

Primary: to characterize the safety and tolerability of GSK3052230 in combination with chemotherapy regimens, to determine the MTD and to assess overall response rate in patients with stage IV or recurrent squamous NSCLC with FGFR1 gene amplification and recurrent or unresectable mesothelioma.
Secondary: PFS, population PK, improvement in Pulmonary Function Tests.

Study design

3-arm, multicenter, non-randomized, parallel-group, uncontrolled, open-label Phase IB study. Dose escalation (see protocol page 33).
Arm A: NSCLC, chemotherapy: paclitaxel + carboplatin (arm closed 18-02-16).
Arm B: NSCLC, chemotherapy: docetaxel (arm closed 18-02-16).
Arm C: mesothelioma, chemotherapy: pemetrexed + cisplatin.

GSK3052230 will be administered as a 30-minute intravenous (i.v.) infusion once a week (Day 1, Day 8, Day 15) of each 21-day cycle. Chemotherapy will be administered i.v. on Day 1 of each 21-day cycle. Paclitaxel/carboplatin will be limited to 4 to 6 cycles. Docetaxel and pemetrexed/cisplatin until disease progression.
Approx.70 (range 38-120) patients.

Intervention

Treatment with GSK3052230.

Study burden and risks

Risk: Adverse events of study medication combined with chemotherapy.
Burden: Visits cycle 1 4x, cycle 2 and thereafter 3x, final visit approx. 30 days after last administration of study medication.
I.v. infusion with GSK3052230 every week.
Chemotherapy conform standard.
Pre-screening for NSCLC patients for FGFR1 mutation (archived tumor material, if necessary fresh tumor tissue). Mandatory.
Research tumor tissue in patients with a mesothelioma (archived tumor material, if necessary fresh tumor tissue). Mandatory.
Physical examination 1x/cycle.
Eye examination every 4th cycle.
Blood tests: During First 6 weeks 65-100 ml per visit and thereafter approx. 45 ml per visit. During screening and final visit approx. 15 ml.
Pregnancy test: start and end of study.
Urine tests every 4th cycle.
ECG: cycle 1 2x, thereafter every 4th cycle.
Tumor measurements conform standard.
Pulmonary function test every odd cycle.
Questionnaire on symptoms every cycle.
Optional: pharmacogenetic blood test (6 ml once).

Contacts

Public
GlaxoSmithKline

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Scientific
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

• Histologically or cytologically confirmed diagnosis:
Arms A and B: Stage IV or recurrent metastatic squamous NSCLC with FGFR1 gene amplification.
Arm A: No prior therapy for Stage IV or recurrent metastatic disease.
Arm B: Documented tumor progression or intolerability after receiving only one prior line of platinum containing combination chemotherapy for Stage IV or recurrent metastatic disease.
Arm C: recurrent after local therapy or unresectable mesothelioma with measurable lesions. No prior systemic therapy for mesothelioma.
See protocol page 28 for further details..
• Availability of archival tumor tissue or fresh biopsy is required.
Arms A and B, Prospective screening for FGFR1 gene amplification.
• Measurable disease.
• Male or female at least18 years.
• Women of childbearing potential must agree to use effective contraception. See protocol page 29 for details.
• Men with a female partner of childbearing potential must have either had a prior vasectomy or agree to use effective contraception. See protocol page 29 for details.
• ECOG Performance Status of 0-1 for Arm A and 0-2 for Arms B and C.

Exclusion criteria

• For Arms A, B, C: Treatment with any FGFR inhibitor.
For Arm B: Treatment with any anti-cancer therapy during the preceding 4 weeks or within 4

half-lives of the therapy.
• Any biological therapy within 6 weeks of the first dose of GSK3052230.
• Uncontrolled infection, major surgery or trauma within 28 days, any non-healing wound, fracture, or ulcer.
• Any prohibited medication(s) as described on protocol page 78-79.
• Conditions likely to increase the potential for abdominal perforation or fistula formation. See protocol page 30 for details.
• Symptomatic leptomeningeal or brain metastases or spinal cord compression. See protocol page 30 for details.
• Hemoptysis (>* teaspoon of red blood) 2 weeks prior to the first dose of GSK3052230.
• Pregnant, lactating females.

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	11-09-2014
Enrollment:	7
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Carboplatin
Generic name:	carboplatine
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Cisplatin
Generic name:	cisplatine
Registration:	Yes - NL outside intended use

Product type:	Medicine
Brand name:	GSK3052230
Generic name:	GSK3052230
Product type:	Medicine
Brand name:	Taxol
Generic name:	paclitaxel
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Taxotere
Generic name:	docetaxel
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	12-05-2014
Application type:	First submission
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	27-08-2014
Application type:	First submission
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	30-01-2015
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	02-02-2015
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	13-04-2015

Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	21-09-2015
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	30-09-2015
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	03-02-2016
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	12-02-2016
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:	05-04-2016
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	12-05-2016
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)

Approved WMO Date:	20-05-2016
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	06-06-2016
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	16-06-2016
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	03-10-2016
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	06-10-2016
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	13-10-2016
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	05-12-2016
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	15-12-2016
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, NCT01868022
EudraCT	EUCTR2013-000354-21-NL
CCMO	NL48044.031.14