A Phase II, Randomized, Open-label Platform Trial Utilizing a MastercProtocol to Study Novel Regimens Versus Standard of Care Treatment in NSCLC Participants (study 205801)

Published: 06-12-2018
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Primary:To determine whether experimental regimens provide evidence for improved survival (randomization to death) over standard of care (SoC) therapy in NSCLC patients.Secondary:Milestone survival, measures of antitumor activity, safety and...

Ethical review	Approved WMO
Status	Completed
Health condition type	Respiratory tract neoplasms
Study type	Interventional

Summary

ID

NL-OMON55684

Source
ToetsingOnline

Brief title
study 205801 (ENTREE)

Condition

- Respiratory tract neoplasms

Synonym
non-small cell lung cancer; lung cancer

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Docetaxel, GSK3359609, NSCLC

Outcome measures

Primary outcome

Survival (randomization to death).

Secondary outcome

Milestone survival rate month 12 and 18. Complete or partial response, stable disease, disease progression (CR or PR, SD, PD). Overall response rate (ORR), progression free survival (PFS), Duration of response (DoR). (Serious) adverse events. PK parameters.

Study description

Background summary

Non-small cell lung cancer (NSCLC) in general is considered to be intrinsically resistant to immuno-oncology agents However, as shown by the single-agent response rates of anti-PD-1 inhibitors in NSCLC, a subset of tumors are susceptible to T cell-mediated antitumor effects, suggesting those tumors have some degree of prior T-cell immunity. Since effective anticancer immune response involves stepwise processes, lung cancers may possess or acquire features that enable them to evade immune surveillance, suppress immune reactivity, proliferate, and survive within an inflammatory microenvironment thereby rendering an immune response ineffectual. Therefore, treatment modalities that incorporate combinations with agents targeting different processes within the immune cascade have the potential to reinstate immuno-surveillance; these may include regimens containing chemotherapy that possess advantageous immunological effects to improve clinical efficacy.
Study 205801 is a Phase II platform trial designed to investigate the clinical activity of novel regimens consisting of immuno-oncology agents compared with

standard of care (SoC) regimen in participants with relapsed/refractory advanced non-small cell lung cancer (NSCLC) who have failed a prior platinum-containing regimen and an immuno-oncology agent, such as anti-programmed cell death protein 1 [PD-1] / PD-Ligand 1 [PD-L1] - either in combination or as separate lines.
The study will initially evaluate 2 treatment regimens/arms, but additional regimens/arms may be added via future protocol amendment(s) (see the Study Design on protocol page 13). Each additional treatment arm/regimen will be analyzed relative to the SoC treatment and is considered a sub-study within the overall master protocol.
The study will initially evaluate the efficacy of GSK3359609 (ICOS Agonist) in combination with SoC (docetaxel) compared with SoC alone as the standard subsequent line chemotherapy (sub-study 1) in NSCLC.

Protocolamendment 03:
Addition of three new substudies.
• Sub study 2 - GSK3369609 with Ipilimumab
• Sub study 3 - GSK3369609 with Niraparib
• Sub study 4 - GSK3369609 with Dostarlimab and Cobolimab
The Netherlands will not participate in these substudies.

Protocolamendment 04 contains clarifications of the sub-studies. These are the most important changes that apply to the Netherlands:
• GSK3359609 has been named feladilimab
• Addition of a primary analysis by 75 death events

Study objective

Primary:
To determine whether experimental regimens provide evidence for improved survival (randomization to death) over standard of care (SoC) therapy in NSCLC patients.
Secondary:
Milestone survival, measures of antitumor activity, safety and tolerability, PK parameters of GSK3359609 (ICOS Agonist) given in combination with chemotherapy and/or other immunotherapies.

Study design

Open-label, randomized, multicenter phase II platform trial utilizing a master protocol designed to study novel immunotherapy drug combinations compared with the current SoC, in the treatment of patients with advanced NSCLC.
The study will initially evaluate 2 treatment regimens/arms (sub-study 1), but additional regimens/arms may be added via future protocol amendment(s) (see the Study Design on protocol page 13).
Participants will be stratified by histology (squamous vs. non-squamous) and

line of PD(L)1 therapy (1st vs. 2nd line).
Each additional treatment arm/regimen will be analyzed relative to the SoC treatment and is considered a sub-study within the overall master protocol, as depicted on protocol page 13.
Maximum number of subjects for sub-study 2 and above: 70.

Sub-study 1:
Comparison of IV administered docetaxel ± GSK3359609. Randomization D:D+GSK-1:2. Study duration: 2 years or 35 treatment visits, whichever comes first, or until disease progression or unacceptable toxicity. Docetaxel may be continued until disease progression or unacceptable toxicity. Follow-up for survival (every 12 weeks by phone). 105 subjects.

Intervention

Treatment with docetaxel monotherapy or docetaxel in combination with GSK3359609.

Study burden and risks

Risk: Adverse events of the study medication. First in human study.
Burden:
• Max. approx. 40 visits. Thereafter survival follow-up (phone call every 12 weeks).
Based on 2 study years:
• Max. 35 infusions GSK3359609, 30 min. per infusion of 250 ml and max. approx. 35 infusions docetaxel 1 hour per infusion of 500 ml.
• Physical examination: 20 times.
• Blood draws: 37 times. 25-60 mL blood per occasion.
• ECG en echocardiography (alternative: MUGA scan): once.
• CT/MRI scan every 6-12 weeks.
• Questionnaires: 3-7 per occasion (PRO-CTCAE, FACT-G item 5, NSCLC-SAQ, QLQ-LC13, PROMIS-PF, QLQ-C30, PGRS/PGIC).
• Tumor biopsy: 0-1.
Optional:
• Blood sample for pharmacogenetics (6 mL).
• Tumor biopsy: 5 times.

Contacts

Public
GlaxoSmithKline

Van Asch van Wijckstraat 55H

Amersfoort 3811 LP
NL
Scientific
GlaxoSmithKline

Van Asch van Wijckstraat 55H
Amersfoort 3811 LP
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

• Male or female, age 18 years and above.
• Histologically or cytologically confirmed diagnosis of NSCLC (squamous or non-squamous).
• Documented disease progression during or after a maximum of 2 lines of systemic treatment for locally/regionally advanced recurrent, Stage IIIb/Stage IV or metastatic disease. For further details: see protocol section 6.1, item 3a-b.
• Measurable disease.
• ECOG performance status 0-1.
• Fresh tumor sample (preferred) or archival tumor tissue obtained at any time from the initial diagnosis to study.
• Not pregnant or postmenopausal females and females of non-reproductive potential or reproductive potential and agrees to follow a required contraceptive method. For further details: see protocol section 6.1, item 9 and appendix 6.
• Male subjects who agree to use one of the required methods of contraception and refrain from sperm donation. For further details: see protocol section 6.1, item 8 and appendix 6.

Exclusion criteria

• Prior treatment with docetaxel, any of the investigational agents tested in this study, systemic approved or investigational treatment within 30 days, prior radiotherapy within 2 weeks. For further details: see protocol section 6.2, item 1.
• Three or more lines of therapy for NSCLC, including patients with BRAF molecular alternations. Patients with known EGFR/ALK/ROS1 molecular alterations are excluded from participation.
• CNS metastases. Exception: see protocol section 6.2, item 4.
• Autoimmune disease (current en history) that has required systemic treatment within the last 2 years. Replacement therapy is not considered a form of systemic treatment. For further details: see protocol section 6.2, item 6-7.
• Live vaccine within 30 days.
• Within the past 6 months: acute diverticulitis, inflammatory bowel disease, intra-abdominal abscess, or gastrointestinal obstruction.
• History or evidence of cardiac and pulmonary abnormalities. For further details: see protocol section 6.2, item 11, 14.
• Within 6 months: uncontrolled symptomatic ascites or pleural or pericardial effusions.
• Active infection requiring systemic therapy, known human immunodeficiency virus infection, positive test for hepatitis B or hepatitis C.

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	03-05-2019

Enrollment:	10
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Feladilimab
Generic name:	Feladilimab
Product type:	Medicine
Brand name:	Taxotere
Generic name:	Docetaxel
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	06-12-2018
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	15-03-2019
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	21-03-2019
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	25-03-2019
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	15-05-2019

Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	05-06-2019
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	21-10-2019
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	22-10-2019
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	17-12-2019
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	31-12-2019
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	01-05-2020
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	04-08-2020
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Approved WMO Date:	27-08-2020
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	29-01-2021
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	02-02-2021
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	15-03-2021
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	22-03-2021
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	03-05-2021
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	04-05-2021
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	09-07-2021
Application type:	Amendment

Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	15-07-2021
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	10-11-2021
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	24-11-2021
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

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	EUCTR2018-001316-29-NL
CCMO	NL68304.100.18
Other	www.gsk-clinicalstudyregister.com; 205801

Study results

Date completed:	15-07-2020
Results posted:	02-06-2022

Summary results
Trial ended prematurely

First publication
16-03-2022

URL result
URL
Type
int
Naam
M2.2 Samenvatting voor de leek
URL

Internal documents
File