A Randomized, Double-blind, Adaptive, Phase II/III Study of GSK3359609 or Placebo in Combination with Pembrolizumab for First-Line Treatment of PD-L1 Positive Recurrent/Metastatic Head and Neck Squamous Cell Carcinoma (study 209229)

Published: 09-12-2019
Last updated: 17-01-2025

Primary: • Compare the efficacy of GSK3359609 in combination with pembrolizumab to pembrolizumab plus placebo in the PD-L1 expression positive (CPS >=1) population and in the PD-L1 expression high (CPS>=20) populationSecondary: • Further...

Ethical review	Approved WMO
Status	Completed
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON52820

Source
ToetsingOnline

Brief title
209229 (INDUCE-3)

Condition

- Other condition

Synonym
Head and neck cancer

Health condition

plaveiselcelcarcinoom van hoofd-halsgebied

Research involving

Human

Sponsors and support

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

Intervention

Keyword: GSK3359609, Head neck cancer, Pembrolizumab, Recurrent / metastatic

Outcome measures

Primary outcome

OS, progression free survival (PSF).

Secondary outcome

PFS, ORR, disease control rate (DCR), duration of response (DOR), OS at 1 and 2

years, adverse events, dose modification, EORTC QLQ-H&N35, time to

deterioration in physical function (PROMIS PF 8c).

Study description

Background summary

Pembrolizumab alone and in combination with 5FU/platinum chemotherapy improved the survival of patients with recurrent or metastatic (R/M) Head and Neck Squamous Cell Carcinoma (HNSCC) as first-line treatment compared with cetuximab and 5FU/platinum chemotherapy. The degree of overall survival (OS) improvement for both monotherapy and combination depended on the programmed cell death receptor 1-ligand 1 (PD-L1) status (CPS), with OS improvement in the total PD-L1 population requiring pembrolizumab in combination with 5FU-platinum regimen. The frequency of all treatment related toxicities and *Grade 3 events were much less with pembrolizumab alone as compared with the cetuximab and 5FU/platinum regimen.

There remains an unmet need due to the limited population of benefit. The aim should be to further improve disease control, and to improve survival across all HNSCC populations.
Combining immunomodulatory agents that target different components of the cancer immunity cycle may be able to overcome the mechanisms of immune suppression which prohibit an effective antitumor immune response.
Thus, targeting both the ICOS and PD-1 axes may translate into enhanced clinical activity and expand the population that benefits with the combination of GSK3359609 (ICOS agonist antibody) and pembrolizumab (PD-1 blocking antibody). This is supported by non-clinical and clinical evidence, e.g. in the INDUCE-1 study the 28% overall response rate (ORR) observed with the combination of GSK3359609 and pembrolizumab was higher than that observed with GSK3359609 monotherapy and higher than that reported for pembrolizumab alone as first-line therapy or subsequent-line therapy in R/M HNSCC.
The purpose of the present study is to evaluate if the addition of GSK3359609 to pembrolizumab improves the efficacy of pembrolizumab in patients with PD-L1 expression positive R/M HNSCC.

protocol amendment 3 (August 2021):
During the interim analysis after 140 subjects in April 2021 it became clear that the addition of GSK3359609 to Pembrolizumab did not result in additional efficacy.
In line with the advice of the IDMC the inclusion of new subjects as well as the treatment with GSK3359609 has been discontinued at once. All subjects were given the opportunity to continue with Pembrolizumab monotherapy up to 35 infusions (=about 2 years) in total.
It has been decided to reduce the burden for the subject as much as possible by drastically reduce the number of study tests:
Visits every 3 weeks (because of Pembrolizumab infusions).
Blood tests on average 7,5 mL per visit in stead of 40 mL
Scans according to the standard of care in the centre
No more questionnaires
No more biopsies.
The ABR form has not been changed with regard to the above. So this form reflects the original study design.
The Dutch centres that did not include any subjects yet at the time of the enrollment stop, have been closed (NKI-AVL, VUmc, UMC Utrecht, UMC Groningen).

Study objective

Primary:
• Compare the efficacy of GSK3359609 in combination with pembrolizumab to pembrolizumab plus placebo in the PD-L1 expression positive (CPS >=1) population and in the PD-L1 expression high (CPS>=20) population
Secondary:
• Further efficacy.
• Safety and tolerability.

• Disease related symptoms and impact on function and health-related quality of life.

Study design

Phase II/III, prospective, randomized, double blind, multi-center trial.
Screening max. 4 weeks. Randomization 1:1 to either pembrolizumab (200 mg IV in 30 min.) plus GSK3359609 (24 mg IV in 30 min.) or pembrolizumab (200 mg IV in 30 min.) plus placebo. Up to 35 cycles of 3 weeks (approx... 2 years). Both infusions on day 1 of each cycle.
A 2-in-1 adaptive phase II/III design is considered, with the option to expand the phase II study seamlessly into phase III study, without changing the eligibility criteria, endpoints or randomization scheme.
374 randomized patients. Should the decision be made to expand the phase II study into phase III study an additional 226 participants will be randomized.

Intervention

Treatment with pembrolizumab plus GSK3359609 or pembrolizumab plus placebo.

Study burden and risks

Risk: Adverse effects of study treatment.
Burden:
Treatment:
Pembrolizumab 200 mg IV Q3W (100 mL in 30 min.). Max. 35 infusions.
GSK3359609 24 mg IV Q3W (100 mL in 30 min.). Max. 35 infusions.
Physical examination: every visit (=37 times).
Blood tests: every visit, 40 mL per occasion.
Pregnancy test (if relevant) monthly.
ECG and echocardiogram or MUGA-scan: once.
CT/MRI scan: HN, chest, abdomen every 6 weeks for the first year and every 12 weeks thereafter.
Tumor biopsy: 0-1 (screening).
Questionnaires: EORTC IL50; EORTC IL51; BPI-I3 PROMIS PF 8c; EQ-5D-3L; PGIS; FACT GP5: PGIC: first year every 6 weeks, thereafter every 12 weeks.
Optional tumor biopsy: 0-2 during and at the end of treatment.

Contacts

Public
GlaxoSmithKline

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Scientific
GlaxoSmithKline

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Amersfoort 3811 LP
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

• Age >=18 years.
• Histological or cytological documentation of HNSCC that was diagnosed as recurrent or metastatic and considered incurable by local therapies.
• Primary tumor location of the oral cavity, oropharynx, hypopharynx or larynx.
• No prior systemic therapy administered in the recurrent or metastatic setting. See protocol chapter 5.1, item 5 for exceptions.
• Measurable disease.
• ECOG 0 or 1.
• Adequate organ function. See protocol chapter 5.1, item 8 for details.
• Life expectancy at least 12 weeks.
• Contraception for females and males as stated in chapter 5.1 items 10-11 of the protocol.
• Tumor tissue at screening as defined in chapter 5.1 item 12 of the protocol.
• PD-L1 IHC CPS >=1 status. See also chapter 5.1 item 13 of the protocol.
• Have results from testing of HPV status for oropharyngeal cancer

Exclusion criteria

• Prior therapy with an anti-PD-1/L1/L2 and/or anti-ICOS directed agent.
• Systemic anticancer therapy within 30 days or 5 half-lives of the drug, whichever is shorter.
• High risk of bleeding. See protocol chapter 5.2, item 3 for details.
• Active tumor bleeding.
• Grade 3/4 hypercalcemia.
• Transfusion of blood products or administration of CSF within 14 days prior to randomization. See protocol chapter 5.2, item 8 for details.
• CNS metastases. See protocol chapter 5.2, item 9 for details.
• Autoimmune disease or syndrome that required systemic treatment within the past 2 years. See protocol chapter 5.2, item 11 for details.
• Immunodeficiency or systemic steroids (>=10 mg oral prednisone per day or equivalent) or other immunosuppressive agents within 7 days prior to randomization. See protocol chapter 5.2, item 12 for details.
• Live vaccine within 30 days prior randomization.
• Prior allogeneic/autologous bone marrow or solid organ transplantation.
• Pneumonitis or history of non-infectious pneumonitis that required steroids or other immunosuppressive agents. See protocol chapter 5.2, item 15 for details.
• Gastrointestinal problems in the past 6 months. See protocol chapter 5.2, item 17 for details.
• Allergen desensitization therapy within 4 weeks of randomization.
• Cardiac abnormalities within the 6 months prior to randomization. See protocol chapter 5.2, item 19 for details.
• Cirrhosis or current unstable liver or biliary disease. See protocol chapter 5.2, item 20 for details.
• Pregnant, breastfeeding, or planning to become pregnant or father children during the study treatment or within 120 days after the last dose of study treatment.

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)

Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	26-06-2020
Enrollment:	25
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	GSK3359609
Generic name:	Feladilimab
Product type:	Medicine
Brand name:	Keytruda
Generic name:	Pembrolizumab
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	09-12-2019
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	12-05-2020
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	22-05-2020
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Approved WMO Date:	17-08-2020
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	19-08-2020
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	22-12-2020
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	24-12-2020
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	03-03-2021
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	06-03-2021
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	11-05-2021
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	23-05-2021
Application type:	Amendment

Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	08-08-2021
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	20-08-2021
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	12-11-2021
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)
Approved WMO Date:	14-09-2022
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	20-09-2022
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	16-02-2023
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO	

Date:	21-02-2023
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	EUCTR2019-002263-99-NL
CCMO	NL71453.100.19
Other	www.gsk-clinicalstudyregister.com, 209229

Study results

Date completed:	26-05-2023
Results posted:	25-04-2024

First publication
18-02-2022