
ClinicalTrials.gov Identifier: NCT04128696

Study of GSK3359609 and Pembrolizumab in Programmed Death Receptor 1-ligand 1 Positive Recurrent or Metastatic Head and Neck Squamous Cell Carcinoma (INDUCE-3)

The safety and scientific validity of this study is the responsibility of the study sponsor and investigators. Listing a study does not mean it has been evaluated by the U.S. Federal Government. Know the risks and potential benefits of clinical studies and talk to your health care provider before participating. Read our disclaimer for details.

Recruitment Status: Recruiting
First Posted: October 16, 2019
Last Update Posted: May 27, 2020

See Contacts and Locations

Sponsor:
GlaxoSmithKline

Collaborator:
Merck Sharp & Dohme Corp.

Information provided by (Responsible Party):
GlaxoSmithKline
Study Description

Brief Summary:
The purpose of study is to evaluate if the addition of GSK3359609 to pembrolizumab as first-line treatment improves the efficacy of pembrolizumab in participants with recurrent or metastatic (R/M) head and neck squamous cell carcinoma/cancer (HNSCC). This is a randomized, double-blind, adaptive Phase II/III study comparing a combination of GSK3359609 inducible T cell co-stimulatory receptor (ICOS) agonist and pembrolizumab to pembrolizumab plus placebo in participants with programmed death receptor 1-ligand 1 (PD-L1) combined positive score (CPS) >=1 R/M HNSCC. Approximately 600 participants will be enrolled in the study and will have a follow-up until death.

<table>
<thead>
<tr>
<th>Condition or disease</th>
<th>Intervention/treatment</th>
<th>Phase</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neoplasms, Head and Neck</td>
<td>Drug: GSK3359609</td>
<td>Phase 3</td>
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<tr>
<td></td>
<td>Drug: Pembrolizumab</td>
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<td>Drug: Placebo</td>
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Study Design

Study Type: Interventional (Clinical Trial)
Estimated Enrollment: 600 participants
Allocation: Randomized
Intervention Model: Parallel Assignment
Intervention Model Description: This will be a randomized, parallel group treatment study with eligible participants receiving GSK3359609 plus pembrolizumab or placebo plus pembrolizumab.
Masking: Double (Participant, Investigator)
Masking Description: This will be a double blind study.
Primary Purpose: Treatment
Official Title: 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

Actual Study Start Date: November 21, 2019
Estimated Primary Completion Date: July 28, 2023
Estimated Study Completion Date: July 28, 2023
Study of GSK3359609 and Pembrolizumab in Programmed Death Recep...

Resource links provided by the National Library of Medicine

Genetics Home Reference related topics:
Head and neck squamous cell carcinoma

Drug Information available for: Pembrolizumab

U.S. FDA Resources

Arms and Interventions

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<thead>
<tr>
<th>Arm</th>
<th>Intervention/treatment</th>
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| Experimental: Participants receiving GSK3359609 and pembrolizumab | Drug: GSK3359609  
GSK3359609 is available as an intravenous infusion.  
Drug: Pembrolizumab  
Pembrolizumab is available as an intravenous infusion. |
| Active Comparator: Participants receiving placebo and pembrolizumab | Drug: Pembrolizumab  
Pembrolizumab is available as an intravenous infusion.  
Drug: Placebo  
Placebo is available as an intravenous infusion. |

Outcome Measures

Primary Outcome Measures:

1. Overall survival (OS) in the PD-L1 expression positive (CPS >=1) population [ Time Frame: Up to 4 years ]

OS is defined as the time from the date of randomization to the date of death due to any cause.
2. OS in the PD-L1 expression high (CPS >=20) population [ Time Frame: Up to 4 years ]
   OS is defined as the time from the date of randomization to the date of death due to any cause.

3. Progression-free survival (PFS) in the PD-L1 CPS >=1 population [ Time Frame: Up to 3 years ]
   PFS is defined as the time from the date of randomization to the date of first documented disease progression or death due to any cause, whichever occurs first.

**Secondary Outcome Measures**:  
1. PFS per immune-based RECIST (iRECIST) in the PD-L1 CPS >=1 population  
   [ Time Frame: Up to 3 years ]
   PFS per iRECIST is defined as the time from the date of randomization to the date of first documented disease progression confirmed consecutively per iRECIST.

2. PFS per RECIST v1.1 in the PD-L1 CPS >=20 population [ Time Frame: Up to 3 years ]
   PFS per RECIST v1.1 is defined as the time from the date of randomization to the date of first documented disease progression per RECIST v1.1.

3. PFS per iRECIST (iPFS) in the PD-L1 CPS >=20 population [ Time Frame: Up to 3 years ]
   PFS per iRECIST is defined as the time from the date of randomization to the date of first documented disease progression confirmed consecutively per iRECIST.

4. Milestone OS rate at 12 months in the PD-L1 CPS >=1 population [ Time Frame: Up to 12 months ]
   Milestone OS rate at 12 months will be evaluated from the survival curves.

5. Milestone OS rate at 24 months in the PD-L1 CPS >=1 population [ Time Frame: Up to 24 months ]
   Milestone OS rate at 24 months will be evaluated from the survival curves.

6. Milestone OS rate at 12 months in the PD-L1 CPS >=20 population [ Time Frame: Up to 12 months ]
   Milestone OS rate at 12 months will be evaluated from the survival curves.
7. Milestone OS rate at 24 months in the PD-L1 CPS >=20 population [Time Frame: Up to 24 months]
   Milestone OS rate at 24 months will be evaluated from the survival curves.

8. Overall response rate (ORR) per RECIST v1.1 in the PD-L1 CPS >=1 population
   [Time Frame: Up to 3 years]
   ORR is defined as the proportion of the participants who have a complete response (CR) or partial response (PR) as the best overall response per RECIST v1.1.

9. ORR per RECIST v1.1 in the PD-L1 CPS >=20 population [Time Frame: Up to 3 years]
   ORR is defined as the proportion of the participants who have a CR or PR as the best overall response per RECIST v1.1.

10. Disease control rate (DCR) per RECIST v1.1 in the PD-L1 CPS >=1 population
    [Time Frame: Up to 3 years]
    DCR is defined as the percentage of participants with a best overall response of CR or PR at any time plus stable disease (SD) meeting the minimum time of 15 weeks per RECIST v1.1.

11. DCR per RECIST v1.1 in the PD-L1 CPS >=20 population [Time Frame: Up to 3 years]
    DCR is defined as the percentage of participants with a best overall response of CR or PR at any time plus SD meeting the minimum time of 15 weeks per RECIST v1.1.

12. Duration of response (DoR) per RECIST v1.1 in the PD-L1 CPS >=1 population
    [Time Frame: Up to 3 years]
    DoR is defined as the time from first documented evidence of CR or PR until first documented disease progression per RECIST v1.1, whichever occurs first, among participants who demonstrated CR or PR as the best overall response per RECIST v1.1.

13. DoR per RECIST v1.1 in the PD-L1 CPS >=20 population [Time Frame: Up to 3 years]
    DoR is defined as the time from first documented evidence of CR or PR until first documented disease progression per RECIST v1.1, whichever occurs first, among participants who demonstrated CR or PR as the best overall response per RECIST v1.1.

14. Number of participants with any adverse events (AEs) and serious adverse events (SAEs)
    [Time Frame: Up to 4 years]
    Number of participants with any adverse events (AEs) and serious adverse events (SAEs)
per ICH definitions.

15. Number of participants with adverse events of special interest (AESI) [Time Frame: Up to 4 years]

AESI are defined as events of potential immunologic etiology, including immune-related AEs (irAEs).

16. Number of participants with dose modifications [Time Frame: Up to 4 years]

Number of participants with dose modifications (i.e. interruptions, discontinuations) will be reported.

17. Time to deterioration in pain in the PD-L1 CPS >=1 population [Time Frame: Up to 4 years]

The time to deterioration in pain will be measured by structured patients questionnaire.

18. Time to deterioration in pain in the PD-L1 CPS >=20 population [Time Frame: Up to 4 years]

Time to deterioration in pain is defined as the time from the date of randomization to the date of first definitive meaningful deterioration in score measured by structured patients questionnaire.

19. Time to deterioration in physical function in the PD-L1 CPS >=1 population [Time Frame: Up to 4 years]

The time to deterioration in physical function will be measured by the participant-reported outcomes measurement.

20. Time to deterioration in physical function in the PD-L1 CPS >=20 population [Time Frame: Up to 4 years]

Time to deterioration in physical function is defined as the time from the date of randomization to the date of first definitive meaningful deterioration in score measured by structured patients questionnaire.
Choosing to participate in a study is an important personal decision. Talk with your doctor and family members or friends about deciding to join a study. To learn more about this study, you or your doctor may contact the study research staff using the contacts provided below. For general information, Learn About Clinical Studies.

Ages Eligible for Study: 18 Years and older (Adult, Older Adult)
Sexes Eligible for Study: All
Accepts Healthy Volunteers: No

Criteria

Inclusion Criteria:

- Capable of giving signed informed consent
- Male or female, age ≥18 years
- Histological or cytological documentation of Head and Neck Squamous Cell Carcinoma (HNSCC) that is 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 (except for systemic therapy given as part of multimodal treatment for locally advanced disease)
- Measurable disease per RECIST version 1.1 guidelines
- ECOG Performance PS score of 0 or 1
- Adequate organ function
- Life expectancy of at least 12 weeks
- Female participants: must not be pregnant, not breastfeeding, and at least one of the following conditions apply:
  1. Not a woman of childbearing potential (WOCBP)
  2. A WOCBP who agrees to use a method of birth control from 30 days prior to randomization and for at least 120 days after the last dose of study treatment.
- Male participants with female partners of child-bearing potential: must agree to use a highly effective contraception while receiving study treatment and for at least 120 days after the last dose of study treatment and refrain from donating sperm during this period.
- Provide tumor tissue from excisional or core biopsy (fine needle aspirates and bone biopsies are not acceptable) acquired within 2 years prior to randomization for PD-L1 immunohistochemistry.
(IHC) testing by central laboratory.

- Have PD-L1 IHC CPS 1 status by central laboratory testing
- Have results from testing of Human Papilloma Virus (HPV) status for oropharyngeal cancer

Exclusion Criteria:

- Prior therapy with an anti-PD-1/L1/L2 and/or anti-ICOS directed agent
- Systemic approved or investigational anticancer therapy within 30 days or 5 half-lives of the drug, whichever is shorter.
- Major surgery 28 days prior to randomization.
- Toxicity from previous anticancer treatment that includes toxicity related to prior treatment that has not resolved to Grade 1 (except alopecia, hearing loss, endocrinopathy managed with replacement therapy, and peripheral neuropathy which must be Grade 2)
- Received transfusion of blood products or administration of colony stimulating factors within 14 days prior to randomization
- Central nervous system (CNS) metastases, with the following exception: Participants with asymptomatic CNS metastases who are clinically stable and have no requirement for steroids for at least 14 days prior to randomization
- Invasive malignancy or history of invasive malignancy other than disease under study within the last 3 years, except as noted below:
  a. Any other invasive malignancy for which the participant was definitively treated, has been disease-free for 3 years and in the opinion of the principal investigator and GSK Medical Monitor will not affect the evaluation of the effects of the study treatment on the currently targeted malignancy, may be included in this clinical study
- Autoimmune disease or syndrome that required systemic treatment within the past 2 years
- Has a diagnosis of immunodeficiency or is receiving systemic steroids (≥10 mg oral prednisone per day or equivalent) or other immunosuppressive agents within 7 days prior to randomization
- Receipt of any live vaccine within 30 days prior randomization
- Prior allogeneic/autologous bone marrow or solid organ transplantation
- Has current pneumonitis or history of non-infectious pneumonitis that required steroids or other immunosuppressive agents
- Recent history (within the past 6 months) of uncontrolled symptomatic ascites, pleural or pericardial effusions
- Recent history (within the past 6 months) of gastrointestinal obstruction that required surgery, acute diverticulitis, inflammatory bowel disease, or intra-abdominal abscess
- Recent history of allergen desensitization therapy within 4 weeks of randomization
- History or evidence of cardiac abnormalities within the 6 months prior to randomization.
- Cirrhosis or current unstable liver or biliary disease per investigator assessment defined by the presence of ascites, encephalopathy, coagulopathy, hypoalbuminemia, esophageal or gastric varices, or persistent jaundice.
- Active infection requiring systemic therapy
- Known HIV infection, or positive test for hepatitis B active infection (presence of hepatitis B surface antigen), or hepatitis C active infection
- History of severe hypersensitivity to monoclonal antibodies or any ingredient used in the study treatment formulations
- Known history of active tuberculosis
- Any serious and/or unstable pre-existing medical (aside from malignancy), psychiatric disorder, or other condition that could interfere with participant's safety, obtaining informed consent, or compliance to the study procedures in the opinion of the investigator
- Is currently participating in (unless in follow-up phase and 4 weeks have elapsed from last dose of prior investigational agent), or has participated in a study of an investigational agent or has used an investigational device within 4 weeks prior to date of randomization

Information from the National Library of Medicine

To learn more about this study, you or your doctor may contact the study research staff using the contact information provided by the sponsor.

Please refer to this study by its ClinicalTrials.gov identifier (NCT number):

NCT04128696
GlaxoSmithKline

Merck Sharp & Dohme Corp.

Investigators

Study Director: GSK Clinical Trials GlaxoSmithKline

More Information

Responsible Party: GlaxoSmithKline

ClinicalTrials.gov Identifier: NCT04128696 History of Changes

Other Study ID Numbers: 209229

First Posted: October 16, 2019 Key Record Dates

Last Update Posted: May 27, 2020

Last Verified: May 2020

Individual Participant Data (IPD) Sharing Statement:

Plan to Share IPD: Yes

Plan Description: IPD for this study will be made available via the Clinical Study Data Request site.

Supporting Materials:

- Study Protocol
- Statistical Analysis Plan (SAP)
- Informed Consent Form (ICF)
- Clinical Study Report (CSR)

Time Frame: IPD will be made available within 6 months of publishing the results of the primary endpoints of the study.

Access Criteria: Access is provided after a research proposal is submitted and has received approval from the Independent Review Panel and after a data sharing agreement is in place. Access is provided for an initial period of 12 months, but an extension can be granted, when justified, for up to another 12 months.

URL: http://clinicalstudydatarequest.com

Studies a U.S. FDA-regulated Drug Product: Yes

Studies a U.S. FDA-regulated Device Product: No

Keywords provided by GlaxoSmithKline:

- GSK3359609
- Pembrolizumab
- Programmed death receptor 1-ligand 1
- Inducible T cell co-stimulatory receptor
- Keynote-A01
- Head & neck
Head and neck squamous cell carcinoma/cancer

Additional relevant MeSH terms:
- Carcinoma
- Carcinoma, Squamous Cell
- Squamous Cell Carcinoma of Head and Neck
- Head and Neck Neoplasms
- Neoplasms, Glandular and Epithelial
- Neoplasms by Histologic Type
- Neoplasms
- Neoplasms, Squamous Cell
- Neoplasms by Site
- Pembrolizumab
- Antineoplastic Agents, Immunological
- Antineoplastic Agents