A phase I, open-label, dose escalation study to investigate the safety, pharmacokinetics, pharmacodynamics and clinical activity of GSK3326595 in subjects with solid tumors and non-Hodgkin*s lymphoma.

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Protein arginine methyltransferases (PRMTs) are a subset of enzymes that methylate arginine residues in various cellular proteins including splicing factors, transcription factors, and histone tails. One of these PRMTs, PRMT5, is aberrantly...

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

Summary

ID

NL-OMON53127

Source
ToetsingOnline

Brief title
GSK3326595 (9018/0006)

Condition

- Other condition

Synonym
solid tumors and non-Hodgkin□s lymphoma

Health condition

solid tumors, non-hodgkin's lymphoma

Research involving
Human

Sponsors and support

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

Intervention

Keyword: GSK3326595, Phase I

Outcome measures

Primary outcome

Part 1 (dose escalation)

Objectives:

* To determine the safety, tolerability, and maximally tolerated dose (MTD) of

orally-administered GSK3326595 in subjects with solid tumors

Part 2 (Dose Expansion)

Objectives:

* To determine clinical activity of GSK3326595 in disease-specific expansion

cohorts

Part 3 (Combination with Pembrolizumab)

* To determine the safety and tolerability of orally-administered GSK3326595,

administered in combination with pembrolizumab, in subjects with solid tumors

Secondary outcome

Part 1 (dose escalation)

Objectives:

* To determine the recommended Phase 2 dose (RP2D) of orally-administered GSK3326595

* To describe the pharmacokinetics of GSK3326595 after single- and repeat-dose administration

* To determine clinical activity of GSK3326595

* To evaluate the preliminary effects of fed versus fasted administration on the pharmacokinetics of GSK3326595

* To evaluate the relative bioavailability of GSK3326595 tablets as compared to capsules

Exploratory:

* To evaluate the relationship between GSK3326595 exposure and safety/efficacy/PD parameters.

* To determine the amount of GSK3326595 excreted in urine

* To characterize the pharmacodynamic profile of GSK3326595 in blood

* To characterize the metabolic profile of GSK3326595 after single and repeat-dosing (in the PK/PD/metabolite expansion cohort(s) only)

* To identify mechanisms of action of GSK3326595 and potential indicators of sensitivity or response to GSK3326595

* To explore the effects of GSK3326595 on tumor metabolism

* To explore the effect of host genetic variation on the response to drugs and disease under study as well as related drug classes and diseases

Part 2 (Dose Expansion)

Objectives:

* To further describe the clinical activity of GSK3326595
* To evaluate the safety and tolerability of GSK3326595 in subjects treated at the RP2D
* To evaluate the relationship between p53 mutational status and clinical response to GSK3326595 in subjects with NHL
* To evaluate the relationship between GSK3326595 exposure and safety/efficacy/PD parameters

Exploratory:

* To evaluate the relationship between p53 mutational status and clinical response to GSK3326595 in subjects with select solid tumors
* To describe the survival and duration of response from (non-ACC tablet cohorts)
* To evaluate disease and treatment related symptoms and impact health-related quality of life
* To identify mechanism(s) of action of GSK3326595 and potential indicators of sensitivity or response to GSK3326595 * To explore the effect of

host genetic variation on the response to drugs and disease under study as well as related drug classes and diseases

Part 3 (Combination with Pembrolizumab)

Objectives:

* To determine the RP2D of orally administered GSK3326595, when administered in combination with pembrolizumab * To describe the clinical activity of GSK3326595 in combination with pembrolizumab in subjects with solid tumors * To describe the pharmacokinetics of GSK3326595 after single and repeat dose administration of GSK3326595, when administered in combination with pembrolizumab

Exploratory:

* To evaluate the relationship between GSK3326595 exposure and safety/efficacy/PD parameters. * To describe the pharmacokinetics and immunogenicity of pembrolizumab after single and repeat dose administration of Pembrolizumab with GSK3326595 *To describe the survival and duration of response from GSK3326595 * To characterize the pharmacodynamic profile of GSK3326595 in blood * To identify mechanism(s) of action of GSK3326595 and potential indicators of sensitivity or response to GSK3326595 * To explore the effect of host genetic variation on the response to drugs and disease under study as well as related drug classes and diseases

Study description

Background summary

Relapsed metastatic solid malignancies (including those under investigation in this study), and virtually all relapsed/refractory hematologic malignancies are incurable diseases which will ultimately prove fatal. In particular, recurrent urinary tract cancer and GBM portend a particularly grim prognosis with an overall survival typically measured in months. At this time, there is no standard of care for these diseases, and as such these patients often consider investigational agents in an attempt to provide some clinical benefit. A wealth of data, including genetics, biochemistry, and cellular biology, implicate PRMT5 in a multitude of human malignancies including those investigated in this study. This study is the first in humans to investigate inhibition of PRMT5 in an attempt to treat and ameliorate malignancy in this population with a high degree of unmet medical need.

Study objective

Protein arginine methyltransferases (PRMTs) are a subset of enzymes that methylate arginine residues in various cellular proteins including splicing factors, transcription factors, and histone tails. One of these PRMTs, PRMT5, is aberrantly upregulated in malignant cells compared to wild type, and overexpression of PRMT5 in vitro is sufficient for fibroblast transformation. Clinically, upregulation of PRMT5 confers poor prognosis in a number of tumor types including breast cancer and glioma. In preclinical models, PRMT5 inhibition has been associated with potential benefit in multiple human malignancies. The study drug, GSK3326595, is an inhibitor of PRMT5 that potently inhibits tumor growth in vitro and in vivo in animal models. This first time in human (FTIH), open-label, dose escalation study will assess the safety, pharmacokinetics (PK), pharmacodynamics (PD), and preliminary clinical activity of GSK3326595 in subjects with advanced or recurrent solid tumors, as well as clinical activity in subjects with a subset of solid tumors and non-Hodgkin*s lymphoma (NHL). The study will also assess a tablet formulation of GSK3326595, and clinical activity of GSK3326595 in combination with pembrolizumab in subjects with a subset of solid tumors.

Study design

This is an open-label, repeat-dose, multicenter, three-part study to establish the maximally tolerated dose (MTD)/ recommended phase 2 dose (RP2D) (based on safety and tolerability) and preliminary clinical efficacy of orally-administered GSK3326595, administered as a single agent in subjects with solid tumors and non-Hodgkin*s lymphoma, or administered in combination with pembrolizumab in subjects with select solid tumors.

Part 1 is a dose-escalation phase to identify the MTD/RP2D based on the safety, PK, and PD profiles observed after oral administration of GSK3326595, and to preliminarily identify whether or not there is an effect of fed versus fasted state, and of tablet versus capsule formulation, on the PK of GSK3326595. This Part will be conducted in adult subjects with relapsed and/or refractory solid tumors.

Disease-specific expansion cohorts (Part 2) are planned to further explore clinical activity of GSK3326595 in subjects with select solid tumors and non-Hodgkin*s lymphomas. Based on pre-clinical data, as well as clinical data that emerged during Part 1, enrollment will be limited to subjects with triple-negative breast cancer (TNBC), metastatic transitional cell carcinoma of the urinary system (mTCC), Grade IV anaplastic astrocytoma (glioblastoma multiforme [GBM]), non-Hodgkin*s lymphoma (NHL), adenoid cystic carcinoma (ACC), hormone receptor-positive adenocarcinoma of the breast (ER+BC), human papillomavirus (HPV) positive solid tumors of any histology (including cervical cancer and squamous cell carcinoma of the head and neck [HNSCC]), and p53-wild type non-small cell lung cancer (NSCLC) of any histological subtype; additional cohorts may be added based on emerging pre-clinical data and clinical responses identified during Part 1 or Part 2 of the study. Note: on 18 January 2021, GSK issued a memo to sites to stop recruitment to all ongoing disease-specific expansion cohorts in Part 2, with the exception of the ACC tablet cohort. Subjects consented to the study prior to this date are to continue in the study as planned.

On 22 December 2021, GSK issued a memo to Investigators to pause recruitment into the ACC tablet cohort in Part 2. The rationale was not related to any urgent safety measure, new safety concern, or to a change in the benefit: risk profile of GSK3326595. Subjects consented to the study prior to this date were informed to continue in the study as planned with the intent to follow up with a protocol amendment.

Further to this memo, a decision has been taken to stop recruitment into the Part 2 ACC tablet cohort, and therefore stopping any further recruitment in the study. This decision has been made following a further review of the clinical data collected with GSK3326595 that demonstrated limited signs of monotherapy anti-tumor activity and is not driven by any safety related concerns.

This Protocol Amendment 8 is the follow up of this decision with the primary intent to update study language related to stopping recruitment into the Part 2 ACC tablet cohort, and therefore stopping any further recruitment in the study, updating the end of study definition with final analysis plan (Section 5.5), and clarifying study treatment access for subjects continuing to derive clinical benefit from study drug as per Investigator judgement post final analysis.

Part 3 is a dose determination study to evaluate the safety, PK/PD profile, and

clinical activity of orally-administered GSK3326595 at daily doses of 100 mg, 200 mg and 300 mg, in combination with pembrolizumab administered at the approved dose. Enrollment in Part 3 will be limited to subjects with NSCLC, mTCC, melanoma, HNSCC that have failed to respond to treatment with prior programmed cell death protein-1 (PD-1) or programmed death-ligand 1 (PD-L1) directed therapy. In addition squamous cell carcinoma of the cervix patients that have progressed on or after PD-1 or PD-L1 directed therapy OR are PD-1/PD-L1 treatment naïve will be enrolled in Part 3. On 18 January 2021, GSK issued a memo to sites to stop recruitment in Part 3, during recruitment of the 100 mg cohort. Subjects assigned to a 100 mg cohort slot or consented to the study prior to this date are to continue in the study as planned.

Supplementary study conduct information not mandated to be present in this protocol is provided in the accompanying Study Reference Manual (SRM). The SRM will provide the site personnel with administrative and detailed technical information that does not impact subject safety.
Final Last Subject Last visit will be defined as last subject*s treatment discontinuation (including 30-day safety follow up).

The end of this study is defined as the date of the last visit of the last subject undergoing the study.
A final data-cut off (DCO), closure of the study database and final analysis will occur when all subjects have either died, discontinued treatment (including 30-day safety follow up), withdrawn consent, or have consented to continue with treatment as defined in this amendment (Protocol Amendment 8).

When Protocol Amendment 8 is implemented at a site, the collection of data for all enrolled subjects who no longer receive study treatment will stop entirely. Subjects still on treatment at the time of the final DCO date may continue to receive study treatment for as long as they continue to derive clinical benefit from study treatment as assessed by the Investigator and do not meet any protocol-defined study treatment stopping criteria (maximum until the end of availability of study drug which is anticipated to be Q3 2023); subjects may also choose to discontinue study treatment at any time. Subjects in survival follow-up at the time of the final DCO date will be considered to have completed the study.

Subjects who continue study treatment following Protocol Amendment 8 will receive follow-up care in accordance with standard local clinical practice. Assessments will revert to the standard of care at a subject*s particular study site with recommendations for local safety laboratory monitoring of GSK3326595. Only SAEs, AEs leading to treatment discontinuation, overdoses, pregnancies, and pre defined ocular and bone AEs (AESIs) will be reported directly to the Sponsor via a paper process. In addition,
* Ocular assessments will be required and reported via a paper process to the Sponsor only if reporting criteria is met for SAEs, AESIs, or AEs leading to treatment discontinuation.

* Bone (DEXA) assessments will be performed at the discretion of the investigator and reported via a paper process to the Sponsor only if reporting criteria is met for SAEs, AESIs, or AEs leading to treatment discontinuation.

Intervention

See E6

Study burden and risks

This is described in the subject information sheet.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

A subject will be eligible for inclusion in this study only if all of the following criteria apply:
1. Males and females *18 years of age (at the time consent is obtained)
NOTE: For NHL cohort ONLY, subjects must be *75 years of age at the time consent is obtained
2. Capable of giving signed informed consent
3. Able to swallow and retain orally-administered medication
4. Eastern cooperative oncology group (ECOG) performance status (defined in Appendix 3) of 0 to 2
5. Diagnosis of one of the following:
a. Part 1: Histologically- or cytological-confirmed diagnosis of non-resectable or metastatic solid malignancy that has progressed on prior therapy (radiographic documentation of progression is adequate for study participation)
b. Part 2: Histologically- or cytologically-confirmed diagnosis of metastatic or non-resectable disease that has progressed on or after prior therapy (ACC tablet cohort does not require prior therapy for enrollment; for all tumors, radiographic documentation of progression is adequate for study participation):
* TNBC [estrogen receptor negative (ER-), progesterone receptor negative (PR-) and human epidermal growth factor receptor 2 negative (Her2-), as defined by local laboratory standards];
* ER+BC [estrogen receptor positive (ER+) or progesterone receptor positive (PR+), human epidermal growth factor receptor 2 negative (Her2-), as defined by local laboratory standards];
NOTE: Subjects in this cohort must have previously received therapy with a cyclin-dependent kinase (CDK) 4/6 inhibitor or be considered ineligible to receive therapy with these agents
* metastatic or non-resectable transitional cell carcinoma of the bladder, ureter, or renal pelvis;
* recurrent GBM;
NOTE: Subjects with prior low-grade glioma with subsequent imaging demonstrating progression to GBM may be enrolled without confirmatory biopsy on a case-by-case basis after discussion with the medical monitor
* ACC requiring systemic therapy. In order to be eligible for enrolment, ACC subjects must:
o have shown progression by local evaluation of scans, as per RECIST 1.1, within the 13 months prior to enrolment, AND
o have measurable disease, as confirmed by independent central review of baseline scans prior to first dose.
* HPV-positive solid tumor of any primary histology
NOTE: HPV-positive status may be determined locally via any generally accepted test [e.g., HPV DNA OR p16 immunohistochemistry]. A minimum of 10 subjects must be enrolled with cervical cancer;
* non-Hodgkin*s lymphoma that is NOT one of the following subtypes, as determined by local laboratory testing:

o Burkitt*s lymphoma or other high-grade lymphoma
o Double- or triple-hit large B-cell lymphoma
NOTE: Any questions regarding eligibility of subtypes should be directed to the medical monitor
* OR NSCLC, of any histologic sub-type; with local mutational analysis demonstrating wild-type status of TP53 (i.e., p53 wild-type NSCLC)
NOTE: Subjects in the cohort must have previously received treatment with an anti-PD1 and/or PD-L1 therapy or be considered ineligible to receive therapy with these agents
NOTE: Subjects whose tumors harbor actionable mutations (e.g., EGFR mutations or ALK rearrangements) must have received prior therapy with targeted agents prior to enrollment.
c. Part 3: Histologically- or cytologically-confirmed diagnosis of metastatic or non-resectable NSCLC (of any histologic sub-type), mTCC, HNSCC, or melanoma that failed to respond to prior treatment with PD-1 or PD-L1 targeted therapy and recurrent/metastatic cervical squamous cell carcinoma that have progressed on or after PD-1 or PD-L1 directed therapy or are PD-1/PD-L1 treatment naïve.
NOTE: NSCLC, mTCC, HNSCC or Melanoma Subjects must have had SD (with subsequent documented progression as per iRECIST) or PD as best response to prior PD-1 or PD L1 targeted therapy to be eligible for enrollment.
6. Prior therapy
* ACC tablet cohort: subjects must be systemic therapy-naïve. Prior surgery and/or radiation is permitted
* NHL cohort: subjects may have received up to 4 prior lines of systemic therapy for disease
* Tumors with actionable mutations (e.g., BRAF V600E in melanoma; EGFR mutations or ALK rearrangements in NSCLC) must have received prior therapy with targeted agents prior to enrollment
* Apart from ACC tablet cohort, subjects must have received at least one line of prior systemic therapy (or have a disease for which no approved therapy exists), AND have no standard-of-care therapy that would be expected to achieve a durable clinical response, OR refuse standard therapy, OR are not candidates for standard therapy.
7. Evaluable disease
a. During Part 1, evaluable disease is required; measurable disease per RECIST v1.1 is recommended but not required
b. Subjects enrolled in Part 2 and Part 3 must demonstrate measurable disease per the disease-specific criteria described in Appendix 4.
8. PK/PD/biomarker/metabolite expansion cohort(s) only (Section 4.2.5): Subjects must consent to pre- and post-dose tumor biopsies and additional sample collection procedures as specified in the Time and Events Table (Section 8.1).
9. Food effect and relative bioavailability sub-study only (Section 4.2.6): Subjects must consent to additional procedures as specified in the Time and Events Table (Table 13).
10. Part 3 only: Subjects must consent to additional procedures (including paired biopsies) as specified in the Time and Events Table (Table 15)

11. All prior treatment-related toxicities must be NCI-CTCAE v4 * Grade 1 (except alopecia [permissible at any Grade] and peripheral neuropathy [which must be * Grade 2]) at the time of treatment allocation.
NOTE: Subjects with treatment-related toxicities that are unlikely to resolve in the opinion of the treating physician may be enrolled on a case-by-case basis after discussion with the medical monitor
12. Adequate organ function, as defined in Table 7.
13. Reproductive criteria:
a. A male subject with female partner of child bearing potential must agree to use one of the methods of contraception specified in Section 7.3.2 for the duration specified in that section.
b. A female subject is eligible to participate if she is not pregnant (as confirmed by a negative serum human chorionic gonadotrophin [hCG] test), not nursing, and at least one of the following conditions applies:
Reproductive potential: subject must agree to follow one of the options and the duration specified in Section 7.3.1.
* Non-reproductive potential defined as:
Pre-menopausal females with one of the following:
Documented tubal ligation
Documented hysteroscopic tubal occlusion procedure with follow-up confirmation of bilateral tubal occlusion
Hysterectomy
Documented Bilateral Oophorectomy
Postmenopausal defined as 12 months of spontaneous amenorrhea with an appropriate clinical profile or females over 60 years of age. Females on hormone replacement therapy (HRT) and whose menopausal status is in doubt will be required to use one of the highly effective contraception methods if they wish to continue their HRT during the study. Otherwise, they must discontinue HRT to allow confirmation of post-menopausal status prior to study enrollment.

Exclusion criteria

A subject will not be eligible for inclusion in this study if any of the following criteria apply:
1. Malignancy attributed to prior solid organ transplant
2. Leptomeningeal disease, spinal cord compression, or brain metastases that require immediate CNS-specific treatment in the opinion of the Investigator (e.g., for symptomatic disease).
NOTE: Subjects who require local therapy for CNS metastases may be considered for eligibility once local therapy is completed and acute treatment-related toxicities have resolved
NOTE: Subjects with untreated lesions should be followed with intracranial imaging (e.g., MRI) at each disease assessment, as detailed in Section 8.1.
NOTE: This criterion does not apply to subjects with GBM. In Part 1, subjects with GBM may enroll provided that they are on a stable to decreasing dose of

corticosteroids for at least 14 days prior to the first dose of GSK3326595. In Part 2, subjects with GBM may enroll irrespective of steroid dose.
3. Recent prior therapy, defined as follows:
* Any non-monoclonal anti-cancer therapy within 14 days or 5 half-lives, whichever is longer, prior to the first dose of GSK3326595. Any nitrosoureas or mitomycin C within 42 days prior to the first dose of GSK3326595. Prior therapy with biologic agents (including monoclonal antibodies) is permitted so long as 28 days have elapsed since therapy and all therapy-related AEs have resolved to
* Grade 1, with the exception of those listed in Section 4.2.4.2. Note that subjects with immunotherapy-related endocrinopathies, currently managed with replacement therapy, will be allowed on study.
* Any radiotherapy within 14 days or major surgery within 28 days prior to the first dose of GSK3326595. For subjects in the GBM cohort, subjects must have completed radiation therapy at least 28 days prior to the first dose of GSK3326595.
* Anti-androgen therapies for prostate cancer, such as bicalutamide, must be stopped 4 weeks prior to enrollment. Second-line hormone therapies such as enzalutamide or abiraterone should be stopped 2 weeks prior to enrollment. Subjects with prostate cancer should remain on luteinizing hormone releasing hormone (LHRH) agonists or antagonists. Subjects with prostate cancer may also remain on low-dose prednisone or prednisolone (up to 10 mg/day) and still be eligible for this study.
4. Part 3 only: History of any of the following:
* Recent history (within the past 2 years) of autoimmune disease or syndrome that required systemic treatment
Note: Replacement therapies which include hormone replacement (e.g., thyroid hormone) or physiological doses of corticosteroids for treatment of endocrinopathies (e.g., adrenal insufficiency) are not considered systemic treatments.
* A diagnosis of immunodeficiency or administration of systemic steroids (*10 mg oral prednisone or equivalent) or other immunosuppressive agents within 7 days prior to randomization
Note: Physiologic doses of corticosteroids for treatment of endocrinopathies or steroids with minimal systemic absorption, including topical, inhaled, or intranasal corticosteroids may be continued if the participant is on a stable dose. Steroids as premedication for hypersensitivity reactions (e.g., computed tomography [CT] scan premedication) are permitted.
* Receipt of any live vaccine within 30 days prior randomization
* Prior allogeneic/autologous bone marrow or solid organ transplantation
* Current pneumonitis or history of non-infectious pneumonitis that required steroids or other immunosuppressive agents
Note: post-radiation changes in the lung related to prior radiotherapy and/or asymptomatic radiation-induced pneumonitis not requiring treatment (Grade 1) may be permitted if agreed upon by the investigator and Medical Monitor.
* Recent history of allergen desensitization therapy within 4 weeks of randomization
* History of severe hypersensitivity to monoclonal antibodies

5. History of a second malignancy, excluding non-melanoma skin cell cancer, within the last three years. Subjects with second malignancies that were indolent, in situ or definitively treated may be enrolled even if less than three years have elapsed since treatment. Consult the GSK Medical Monitor if there are questions whether second malignancies meet the requirements specified above.
6. Current use of a prohibited medication or planned use of any forbidden medications during treatment with GSK3326595 (see Section 7.1.2 for the list of medications).
7. Evidence of severe or uncontrolled systemic diseases (e.g., unstable or uncompensated respiratory, hepatic, renal, cardiac disease, or clinically significant bleeding episodes). Any serious and/or unstable pre-existing medical (aside from malignancy), psychiatric disorder, or other conditions that could interfere with subject*s safety, obtaining informed consent or compliance to the study procedures, in the opinion of the Investigator.
8. Any clinically significant gastrointestinal (GI) abnormalities that may alter absorption such as malabsorption syndrome or major resection of the stomach and/or bowels.
9. History of known human immunodeficiency virus (HIV) infection or positive HIV test result at screening. NOTE: HIV * Patients may be eligible if they fullfill all of the requirements below: Have started on antiviral therapy for at least 4 weeks prior to start of study drug treatment, Not be taking HIV related therapy (antivirals, antibiotics) that is on the prohibited list per protocol, Have a CD4 count *350 cells/uL, Have a HIV viral load <400 copies/ml.
10. Presence of hepatitis B surface antigen (HBsAg) or positive hepatitis C antibody test result at screening.
NOTE: Subjects with chronic hepatitis B virus (HBV) infection, who meet the criteria for anti HBV therapy may be eligible if subject is on a supportive antiviral therapy prior to initiation of cancer therapy.
NOTE: Subjects with positive Hepatitis C antibody due to prior resolved disease can be enrolled only if a confirmatory negative Hepatitis C RNA polymerase chain reaction (PCR) is obtained. Also Hep B - Patients may be eligible if they have both: completed curative therapy, have a HCV viral load limit.
11. Any of the following cardiac abnormalities:
* Recent history (within 6 months of first dose of study drug) of acute coronary syndromes (including myocardial infarction and unstable angina), coronary angioplasty, or stenting
* Presence of a cardiac pacemaker
* Baseline Corrected QT (Fridericia*s formula) interval (QTcF) *450 msec
* Uncontrolled arrhythmias. Subjects with rate-controlled atrial fibrillation for > 1 month prior to first dose of study drugs may be eligible.
* Class II, III or IV heart failure as defined by the New York Heart Association (NYHA) functional classification system.
12. History of sensitivity to any of the study medications, or components thereof or a history of drug or other allergy that, in the opinion of the investigator or Medical Monitor, contraindicates their participation.

13. History of optic nerve neuropathy or neuritis.

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	01-02-2017
Enrollment:	39
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	GSK3326595
Generic name:	GSK3326595
Product type:	Medicine
Brand name:	Keytruda
Generic name:	Pembrolizumab
Registration:	Yes - NL intended use

Ethics review

Approved WMO

Date:	17-05-2016
Application type:	First submission
Review commission:	METC NedMec

Approved WMO

Date:	12-10-2016
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	04-01-2017
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	13-01-2017
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	09-08-2017
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	11-08-2017
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	21-11-2017
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	23-11-2017
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	16-03-2018
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	30-03-2018
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO	

Date: 04-06-2018

Application type: Amendment

Review commission: METC NedMec

Not approved

Date: 14-06-2018

Application type: Amendment

Review commission: METC NedMec

Approved WMO

Date: 15-06-2018

Application type: Amendment

Review commission: METC NedMec

Approved WMO

Date: 27-08-2018

Application type: Amendment

Review commission: METC NedMec

Approved WMO

Date: 03-10-2018

Application type: Amendment

Review commission: METC NedMec

Approved WMO

Date: 21-12-2018

Application type: Amendment

Review commission: METC NedMec

Approved WMO

Date: 11-01-2019

Application type: Amendment

Review commission: METC NedMec

Approved WMO

Date: 12-07-2019

Application type: Amendment

Review commission: METC NedMec

Approved WMO

Date: 22-07-2019

Application type: Amendment

Review commission: METC NedMec

Approved WMO

Date:	15-10-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	29-10-2019
Application type:	Amendment
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Approved WMO Date:	20-01-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	23-01-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	11-06-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	15-06-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	16-12-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	30-12-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	07-06-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO	

Date:	22-06-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	02-08-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	12-08-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	11-05-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	24-05-2022
Application type:	Amendment
Review commission:	METC NedMec

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	EUCTR2016-000278-39-NL
CCMO	NL57508.031.16