A Phase II, Open-label, Single-arm, Multicenter Study to Evaluate Efficacy and Safety of Pembrolizumab Monotherapy in Subjects with Advanced Recurrent Ovarian Cancer

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Primary Objective(s) & Hypothesis(es) In subjects with advanced ROC:1) Objective: To evaluate clinical anti-tumor activity of pembrolizumab monotherapy based on ORR as assessed by CIV per RECIST 1.1 in Cohort A-All Comer group as defined in...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Reproductive neoplasms female malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON47631

Source
ToetsingOnline

Brief title
MK3475-100

Condition

- Reproductive neoplasms female malignant and unspecified

Synonym
Ovarian cancer

Research involving
Human

Sponsors and support

Primary sponsor: Merck Sharp & Dohme (MSD)
Source(s) of monetary or material Support: Industrie

Intervention

Keyword: Ovarian Cancer, Pembrolizumab

Outcome measures

Primary outcome

Primary objective (1) is to evaluate objective response rate (ORR) in the first

180 enrolled subjects who fulfill the eligibility criteria for Cohort A.

Primary objective (2) is to evaluate ORR in subjects who fulfill the

eligibility criteria for Cohort A and with higher expression of program death

ligand protein 1 (PD-L1) in tumor tissue samples.

Primary objective (3) is to evaluate ORR in all enrolled subjects who fulfill

the eligibility criteria for Cohort B.

Primary objective (4) is to evaluate ORR in subjects enrolled into Cohort B who

have tumor tissue PD-L1 expression above the clinical cutpoint established from

the Cohort A training set.

Secondary outcome

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Study description

Background summary

Ovarian cancer is the most lethal gynecologic cancer and the fifth -leading cause of cancer death among women in the United States (US). In the US, the estimated number of new cases and deaths from ovarian cancer in 2014 was 21,980

and 14,270, respectively. Due to lack of tumor-specific signs and symptoms and effective screening tests for early detection, over
70% of ovarian cancer patients are first diagnosed at advanced stages. Based on the US data from 2003 to 2009, at initially diagnosis, 61% had distant metastasis, 18% had regional disease and only 21% had localized disease. The overall 5-year survival rate of ovarian cancer was approximately 44% counting all stages; the 5-year survival rate in patients with distant metastasis was only 27% [3].

Epithelial ovarian cancer (EOC) accounts for >90% of the ovarian cancer and has been recognized as a group of heterogeneous diseases with distinct histopathologic features, genetic alterations and clinical behaviors. Five main EOC subtypes have recently been designated by The International Federation of Gynecology and Obstetrics (FIGO): high - grade serious carcinoma (HGSC, accounts for ~70% EOC), endometrioid carcinoma (EC,
~10% EOC), clear cell carcinoma (CCC, ~10% EOC), mucinous carcinoma (MC, ~3% EOC), low grade serous carcinoma (LGSC, 5% EOC), and those that are unclassifiable [4;
5]. Primary peritoneal carcinoma and fallopian tube carcin oma have typically been managed and studied together with EOC as they share similar clinic-pathologic characteristics with HGSC.

The standard primary treatments for advanced EOC include primary cytoreductive/debulking surgery followed by postoperative front line (i.e., adjuvant) systemic treatment with carboplatin and paclitaxel Q3W IV for 6 cycles. However, weekly paclitaxel has also been frequently used to replace Q3W paclitaxel. In suitable cases, postoperative chemotherapy, usually cisplatin plus paclitaxel, can be delivered via intraperitoneal (IP) route. In cases with bulky diseases that are initially non-operable, neoadjuvant therapy can be given prior to cytoreductive surgery (i.e. interval cytoreductive surgery) then followed by standard platinum/taxane-based chemotherapy [6; 7].

The goal of cytoreductive surgery is to achieve resection of all visible tumors and the goal of postoperative first line chemotherapy are: 1) to help achieving complete remission in those with residual disease, and 2) to prevent disease recurrence for those with complete tumor resection. However, after these primary treatments, only a small proportion of patients will achieve long-term disease-free and survival status. In a meta-analysis performed by du Bois et al [8] on data from three randomized trials following the standard primary treatment with surgery and platinum-taxane based chemotherapy (N = 3126), only 24% of patients were recurrent free after a median follow up time of 53.9 months and the remaining 76% had disease recurred or progressed. The overall 5-year PFS and OS rate was 22.6% and 39.0%, respectively. Based on time to recurrence (TTR) since the last dose of platinum treatment,
22% recurred 0-6 months, 22.5% recurred 6-12 months, and 31.6% recurred >12 months. By
12 months, the 12 months survival rate was 30.6%, 55.1% and 66.1% in the group

with TTR
0-6 months, TTR 6-12 months, and TTR >12 months, respectively; the 24-month survival rate was 13.8%, 24.4% and 34.9% in these three groups, respectively. This data showed an overall poor prognosis for patients with recurrent disease especially in those with a short TTR.

At present, ROC is considered not curable with the available choices of therapies and is an area of highly unmet medical need.

Selection of treatment for ROC should take into consideration several factors including: sensitivity to first line platinum-based therapy, as measured by platinum-free interval (PFI), prior toxicity, comorbidity, age and performance status etc. PFI, which is defined as the period from the cessation of the primary platinum-based chemotherapy to disease recurrence or progression, has been recognized as an important surrogate for prognosis and predicting response to chemotherapy. Based on PFI, ROC can be divided into the following subgroups: platinum-sensitive (PFI >12 months), partiallyplatinum sensitive (PFI of 6-12 months), platinum resistant (PFI >1 to < 6 months), and platinum-refractory (PFI * 4 weeks or progression on treatment) according to the consensus achieved by the GCIG in 2010 [9].

Based on the current National Comprehensive Cancer Network (NCCN) and European Society for Medical Oncology (ESMO) guidelines, patients with platinum-resistant ROC can be treated with either single agent chemotherapy such as gemcitabine, pegylated liposomal doxorubicin (PLD), weekly paclitaxel, topotecan and docetaxel, or bevacizumab in combination with gemcitabine or weekly paclitaxel or topotecan. These single agents had shown similar clinical efficacy with a response rate around 15-20%, median PFS of 3-5 months and median OS of 10-12 months [10; 11]. Bevacizumab plus single agent chemotherapy showed an improved PFS compared to single agent chemotherapy alone (6.7 vs. 3.4 months, HR: 0.48, p <0.001) and an improved response rate (27.3% vs. 11.8%) via a randomized Phase III trial, AURELIA [12]. However, the study didn*t demonstrated overall survival benefit; and based on the Kaplan-Meier curve, less than 20% of subjects in the bevacizumab chemotherapy arm remained progression-free by 12 months, and even less in the single agent chemotherapy arm. Platinum resistant ROC, hence, this is an area with high unmet medical need for novel therapies that can deliver durable clinical benefit.

Partially platinum-sensitive ROC (i.e. PFI > 6-12 months), which used to be classified as part of the platinum-sensitive group, has been considered a challenging group to manage [13; 14]. Even though the recommended treatment for partially platinum -sensitive ROC remains the same as those for platinum-sensitive ROC, i.e., re-treated with a platinum-containing doublet, the partially platinum-sensitive group has significantly reduced clinical benefit compared to those with PFI > 12 months. For example, in a review of 583 ROC patients from six Phase II-III clinical trials by Pujade-Lauraine et. Al.

[15] on the impact of TFI, on clinical response to salvage therapy, patients with TFI of 3-12 months showed an ORR of 35% compared to an ORR of 52% in the group with TFI of 12 -18 months. Median time to progression (TTP) and OS in the group with TFI of 3 -12 months was much shorter (174 days and 393 days, respectively) compared to the group with TFI of 12-18 months (275 days and 657 days, respectively). In the Phase III trial CALYPSO [16] that compared carboplatin plus PLD (CD) versus carboplatin plus paclitaxel (CP), OS was significantly longer in subjects with TFI * 12 months versus subjects with TFI 6-12 months based on multivariate analysis (HR = 0.5; 95% CI 0.43, 0.59; p < 0.001). In the CALYPSO trial, median PFS in the partial platinum- sensitive subpopulation was 9.4 months for the CD arm and 8.8 months for the CP arm; ORR was 39% in the CD arm and 45% in the CP arm . However, when taking a closer look at the Kaplan-Meier PFS curve for partial platinum-sensitive subgroup in this study, less than 20% patients in the CP arm and a little over 20% in the CD arm remained progre ssion-free at 12 months [17].

In a meta-analysis by Hanker et al [18] charterizing impact of second to sixth line of therapy on survival of relapsed ovarian cancer, data of n = 1620 patients from three large randomized phase III trials investigating primary therapy was included. The results showed that median PFS after the first, second, third, fourth and fifth relapse was 10.2 [95% confidence interval (CI) 9.6*10.7], 6.4 (5.9*7.0), 5.6 (4.8*6.2), 4.4 (3.7*4.9) and 4.1 (3.0*5.1) months, respectively. Median OS after the first, second, third, fourth and fifth relapse was 17.6 (95% CI 16.4*18.6), 11.3 (10.4*12.9), 8.9 (7.8*9.9), 6.2 (5.1*7.7) and 5.0 (3.8*10.4) months, respectively. The overall clinical benefit greatly reduced with increased lines of therapy.

In addition to reduced clinical benefit and lack of long-lasting clinical activities from the existing therapies in this group, toxicities from prior or planned platinum doublets further limit the utility of these treatments in this subgroup [13]. Novel therapies with durable clinical efficacy and better safety profile are highly needed for the treatment of partially platinum-sensitive as well as platinum-resistant ROC.

Study objective

Primary Objective(s) & Hypothesis(es)

In subjects with advanced ROC:

1) Objective: To evaluate clinical anti-tumor activity of pembrolizumab monotherapy based on ORR as assessed by CIV per RECIST 1.1 in Cohort A-All Comer group as defined in Section 2.1

2) Objective: To evaluate clinical anti-tumor activity of pembrolizumab monotherapy based on ORR as assessed by CIV per RECIST 1.1 in Cohort A-PD-L1H

subgroup, as defined in Section 2.1, using a PD-L1 expression cutpoint established in the training set.

3) Objective: To evaluate clinical anti-tumor activity of pembrolizumab monotherapy based on ORR as assessed by CIV per RECIST 1.1 in Cohort B -All Comer group as defined in Section 2.1

4) Objective: To evaluate clinical anti-tumor activity of pembrolizumab monotherapy based on ORR as assessed by CIV per RECIST 1.1 in Cohort B PD-L1H subgroup, as defined in Section 2.1, using a PD-L1 expression cutpoint established in the training set from Cohort A

The primary objectives will focus on estimation of ORR, and no formal hypothesis testing is planned.

Secondary Objective(s) & Hypothesis(es)

In subjects with advanced ROC:

1) Objective: To evaluate duration of response (DOR), disease control rate (DCR) and progression-free survival (PFS) as assessed by CIV per RECIST 1.1 in Cohort A-All Comer group, Cohort A-PD-L1H subgroup, Cohort B-All Comer group, Cohort B- PD-L1H subgroup respectively, after treated with pembrolizumab monotherapy. PFS rate at 6, 12 and 18 months will also be evaluated.

2) Objective: To evaluate ORR, DOR, DCR, and PFS as assessed by investigator per RECIST1.1 in Cohort A-All Comer group, Cohort A-PD-L1H subgroup, Cohort B-All Comer group, Cohort B-PD-L1H subgroup, respectively, after treated with pembrolizumab monotherapy

3) Objective: To evaluate ORR, DOR, DCR and PFS as as sessed by CIV and by investigator per RECIST 1.1, in Cohort A-All Comer subgroup with PFI/TFI * 3 * 6 months and the subgroup with PFI/TFI >6 -12 months, respectively, after treated with pembrolizumab monotherapy.

4) Objective: To evaluate OS in Cohort A-All Comer group, Cohort A-PD-L1H subgroup, Cohort A-All Comer subgroup with PFI/TFI * 3 * 6 months and the subgroup with PFI/TFI >6-12 months, Cohort B-All Comer group, Cohort B-PD-L1H subgroup, after treated with pembrolizumab monotherapy.

5) Objective: To evaluate and characterize the tolerability and safety profile of the entire study population and by cohorts and subgroups , respectively, after treated with pembrolizumab monotherapy
6) Objective: To assess population pharmacokinetics (PK) No formal hypotheses

will be tested for secondary objectives.

Study design

This is a Phase II, open-label, single-arm, two-cohort, multi-center study to evaluate efficacy and safety of pembrolizumab monotherapy 200 mg every 3 weeks (Q3W) in subjects with advanced epithelial ovarian cancer (EOC), fallopian tube cancer, or primary peritoneal cancer (will collectively refer as advanced EOC) who have demonstrated recurrent disease following the primary or interval cytoreductive/debulking surgery and the standard front line platinum* based combination therapy. The study will enroll the following two cohorts of subjects with recurrent ovarian cancer (ROC):

Cohort A will enroll ROC subjects who have received 0 to 2 prior lines for treating ROC (i.e., 1-3 total prior lines counting the front line) and must have a platinum-free interval (PFI) or a treatment-free interval (TFI) of 3 to 12 months based on the last regimen received. Cohort B will enroll ROC subjects who have received 3-5 prior lines for treating ROC (i.e., 4-6 total prior lines counting the front line) and must have a PFI or TFI * 3 months based on the last regimen received. Refer to Section 5.1.for definition of PFI and TFI and detailed inclusion and exclusion criteria for each Cohort. The trial will be conducted in conformance with Good Clinical Practices.

The study has 4 primary objectives. Primary objectives (1) and (2) are designated for Cohort A. Primary objectives (3) and (4) are designated for Cohort B.

Primary objective (1) is to evaluate objective response rate (ORR) in the first 180 enrolled subjects who fulfill the eligibility criteria for Cohort A. This group is designated as Cohort A-All Comer group. Within Cohort A-All Comer group, a minimum of 75 subjects will be enrolled for the subgroup with a PFI or TFI of 3- <6 months and the subgroup with a PFI or TFI of 6 * 12 months. The primary analysis of ORR will be based on the assessment by a central imaging vendor (CIV) per Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1 [1].

Primary objective (2) is to evaluate ORR in subjects who fulfill the eligibility criteria for Cohort A and with higher expression of program death ligand protein 1 (PD-L1) in tumor tissue samples. It is expected that higher PD-L1 expression in tumor tissue will be associated with better clinical responses to pembrolizumab (refer to Section 4 for background and rationale). In order to achieve this primary objective, a PD -L1 expression cutpoint will first be established with a goal to enrich the popula tion for better clinical benefit. The cutpoint will be determined during the planned interim analysis using the clinical efficacy data and PD-L1 expression data from the first 100 enrolled Cohort A subjects. This data set is designated as the *training set* (refer to Section 8.7 on the approach for determining the PD- L1

cutpoint). In order to confirm the association of higher PD-L1 expression with increased clinical activity by pembrolizumab treatment, another 150 subjects who fulfill eligibility criteria for Cohort A will be enrolled, which is designated as the *confirmation set*. Cohort A will therefore, enroll a total of 250 subjects. Based on the established PD-L1 cutpoint from the training set, subjects in the confirmation set will be assigned into the subgroup with PD - L1 expression above or equal to the cutpoint (i.e. , Cohort A PD-L1H) or the subgroup with

PD-L1 expression below the cutpoint (i.e., Cohort A PD-L1L). Enrollment into Cohort A will not be interrupted for interim analysis. However, in order to ensure data integrity, samples from the *confirmation set* will not be assessed for PD-L1 expression until the cutpoint has been established and the assay has been confirmed. Based on the prevalence data regarding higher PD-L1 expression, the total enrollment of Cohort A may be increased to up to 280 to ensure a minimum of 60 subjects from the confirmation set (see below) will have PD-L1 expression above the expected cutpoint.

Approximately 75 subjects will be enrolled in to Cohort B regardless of PD-L1 expression status. Primary objective (3) is to evaluate ORR in all enrolled subjects who fulfill the eligibility criteria for Cohort B. This group is designated as Cohort B-All Comer group. Primary objective (4) is to evaluate ORR in subjects enrolled into Cohort B who have tumor tissue PD-L1 expression above the clinical cutpoint established from the Cohort A training set. The population supporting primary objective (4) is designated as Cohort B PD-L1H group. Tumor tissue samples from Cohort B will not be evaluated until a cutpoint has been established from Cohort A training set.

As part of the inclusion criteria, all subjects must provide a tumor tissue sample collected either from a recent biopsy or prior cytoreductive surgery in order to be enrolled. Part of the tumor tissue sample will be submitted to a designated central laboratory for assessing PD -L1 expression via an immunohistochemistry (IHC) assay. PD-L1 positivity is determined using the combined positive score (CPS) which is defined as the percent PD-L1 positive cells counting tumor cells, immune infiltrating cells and cells from adjacent stroma relative to total tumor cells. Details will be provided in a separate document.

Clinical cutoff for interim analysis will be at least 4 months after the 100th Cohort A subject has been enrolled to allow adequate clinical follow up. For each designated study population (i.e., Cohort A-All Comer, Cohort A PD-L1H, or Cohort B), the clinical cutoff for the final analysis of the primary endpoint ORR will be at least 8 months after the last subject for each population has been enrolled. The final clinical cutoff for the study (i.e. , study completion) will be 3 years after the last subject is enrolled for final overall survival (OS) analysis. Refer to Sections 3.2 and 3.3 for details

regarding secondary and exploratory study objectives, and Figure 1 in Section 2.2 for illustration of the overall study design.

Intervention

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Study burden and risks

The patient will visit the doctor every three weeks. The first visit a tumor biopsy will take place (if necessary). Each visit, a physical examination will be performed, and blood samples will be taken.

The patient may experience physical and or psychological discomfort with some of the procedures performed during a visit, such as blood sampling, the IV line, ECG, CT scan, MRI and tumor biopsy.

The main side effect reported with the use of MK3475 are fatigue, itching, rash, frequent or excessive bowel movements, joint pain and nausea.

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

1. Be willing and able to provide written informed consent for the trial. The subject may also provide consent for Future Biomedical Research. However, the subject may participate in the main trial without participating in Future Biomedical Research.
2. Be > or <= 18 years of age on day of signing informed consent.
3. Have histologically confirmed epithelial ovarian cancer, fallopian tube cancer or primary peritoneal cancer
4. Have received a front line platinum-based regimen (administered via either IV or IP route) per local SOC or treatment guideline following the primary or interval debulking surgery with documented disease recurrence.
Note: Maintenance treatment following the front line treatment is permitted and counted together as part of the front line treatment.
5. Have fulfilled the following additional requirements regarding prior treatments for recurrent ovarian cancer (ROC) depending on the cohort subject is to be enrolled. Each subject must have documented evidence of clinical response or disease stabilization to the last regimen received.
Cohort A: Have received 0 to 2 additional prior lines for treating ROC (or 1-3 total prior lines counting the front line) and must have a platinum-free interval (PFI) of > or <= 3 to 12 months if the last regimen received is a platinum-based, or a treatment-free interval (TFI) of > or <= 3 to 12 months if the last regimen received is a non-platinum-based.
Cohort B: Have received 3 to 5 additional prior lines for treating ROC (or 4-6 total prior lines counting the front line) and must have a PFI of > or <=3 months if the last regimen received is a platinum-based, or a TFI of > or <= 3 months if the last regimen received is a non-platinum-based.
Note: PFI is defined as the time elapsed between the last dose of platinum and the documented evidence of disease progression per RECIST 1.1. TFI is defined as the time elapsed between the last dose of the regimen received and the documented evidence of disease progression per RECIST 1.1.
6. Have measurable disease at baseline based on RECIST 1.1 as determined by the central imaging vendor.
Note: Tumor lesions situated in a previously irradiated area are considered measurable if progression has been demonstrated in such lesions.
7. Have an ECOG performance status of 0 or 1
8. Have a life expectancy of > or <=16 weeks.
9. Have provided a tumor tissue sample either collected from prior cytoreductive surgery or fresh newly obtained tumor tissue at screening.

Formalin-fixed paraffin-embedded (FFPE) block specimens are preferred to slides. Additional samples may be requested if tumor tissue provided is not adequate for quality and/or quantity as assessed by the central laboratory.
Note 1: Tumor tissue samples from recent biopsy are much preferred as it represents the current disease status and is much more informative for understanding the correlation between clinical activity and tumor microenvironment.
If available, paired tumor tissue samples from prior cytoreductive surgery and recent biopsy are strongly encouraged in order to understand the changes in tumor microenvironment during the course of the treatments.
Note 2: For archival tumor tissue samples, block specimens are much preferred than slides. If submitting unstained cut slides, freshly cut slides should be submitted to the testing laboratory within 14 days from when the slides are cut. See Section 4.2.3.3 in protocol for an explanation.
10. Have demonstrated adequate organ function as defined in Table 1 of the protocol. All screening labs should be performed within 10 days of treatment initiation.
11. Female subjects of childbearing potential (see Section 5.7.1) must be willing to use an adequate method of contraception as outlined in Section 5.7.1
* Contraception, for the course of the study through 120 days after the last dose of study medication. Note: Abstinence is acceptable if this is the usual lifestyle and preferred contraception for the subject.
12. Female subjects of childbearing potential must have a negative urine or serum pregnancy test within 72 hours prior to receiving the first dose of study medication. If the urine test is positive or cannot be confirmed as negative, a serum pregnancy test will be required.

Exclusion criteria

1. Is currently participating in or has participated in a clinical study and received an investigational agent or used an investigational device within 4 weeks prior to the first dose of study treatment.
Note: Subjects who have entered the follow-up phase of an investigational study may participate as long as it has been 4 weeks since the last dose of the previous investigational agent or device.
2. Has an active autoimmune disease that has required systemic treatment in the past 2 years (i.e. use of disease modifying agents, corticosteroids or immunosuppressive drugs). Replacement therapy (e.g., thyroxine, insulin, or physiologic corticosteroid replacement therapy for adrenal or pituitary insufficiency, etc.) is not considered a form of systemic treatment.
3. Has a diagnosis of immunodeficiency or is receiving systemic steroid therapy or any other form of immunosuppressive therapy within 7 days prior to the planned first dose of the study. The use of physiologic doses of corticosteroids may be approved after consultation with the Sponsor.
4. Has had prior anti-cancer monoclonal antibody (mAb), chemotherapy, targeted

small molecule therapy, or radiation therapy within 4 weeks prior to the planned first dose of the study
5. Has not recovered from adverse events to < or = Grade 1 or prior treatment level due to a previously administered agent.
Note: Subjects with < or = Grade 2 neuropathy or alopecia of any grade are an exception to this criterion and may qualify for the study.
Note: If subject received major surgery, they must have recovered adequately from the toxicity and/or complications from the intervention prior to starting therapy.
6. Has EOC with mucinous histology subtype. Or has a known additional malignancy that progressed or required active treatment within the last 5 years. Exceptions include basal cell carcinoma of the skin, squamous cell carcinoma of the skin that has undergone potentially curative therapy or in situ cervical cancer.
7. Has known active central nervous system (CNS) metastases and/or carcinomatous meningitis. Subjects with previously treated brain metastases may participate provided they have stable brain metastases.
8. Has known history of, or any evidence of active, non-infectious pneumonitis.
9. Has an active infection requiring systemic therapy.
10. Has symptoms of bowel obstruction in the past three months
11. Has a history or current evidence of any condition, therapy, or laboratory abnormality that might confound the results of the trial, interfere with the subject*s participation for the full duration of the trial, or is not in the best interest of the subject to participate, in the opinion of the treating investigator.
12. Has known psychiatric or substance abuse disorders that would interfere with cooperation with the requirements of the trial.
13. Is pregnant or breastfeeding, or expecting to conceive children within the projected duration of the trial, starting with the screening visit through 120 days after the last dose of trial treatment.
14. Has received prior therapy with an anti-PD-1, anti-PD-L1, anti-PD-L2 agent or with an agent directed to another co-inhibitory T-cell receptor (e.g. CTLA-4, OX-40, CD137) or has participated in prior pembrolizumab trials.
15. Has a known history of Human Immunodeficiency Virus (HIV) (HIV 1/2 antibodies).
16. Has known active Hepatitis B (e.g., HBsAg reactive) or Hepatitis C (e.g., HCV RNA [qualitative] is detected).
17. Has received a live vaccine within 30 days of the planned first dose of the study.
Note: Seasonal influenza vaccines for injection are generally inactivated flu vaccines and are allowed; however intranasal influenza vaccines (e.g., Flu-Mist®) are live attenuated vaccines, and are not allowed.

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	03-05-2016
Enrollment:	23
Type:	Actual

Medical products/devices used

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

Ethics review

Approved WMO

Date:	11-02-2016
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO

Date:	29-03-2016
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO Date:	21-11-2016
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	27-03-2017
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	26-06-2017
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	29-06-2017
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	18-10-2017
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	19-01-2018
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	02-08-2018
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	26-08-2019
Application type:	Amendment

Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	31-10-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	07-11-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	23-04-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	05-11-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

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	EUCTR2015-003338-29-NL
CCMO	NL56470.056.16

Study results

Results posted: 05-09-2019

First publication
05-09-2019