A Phase 1, Open-label, Dose-escalation and Expansion Study of MEDI1191 Administered Intratumorally as Monotherapy and in Combination with Durvalumab in Subjects with Advanced Solid
Tumors.
Sub-study title: CD8+ Imaging Sub-study Protocol

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Objectives (all are exploratory):• To measure and analyze 89Zr-Df-IAB22M2C uptake cluster of (CD8+ PET signal) at and between baseline and post-treatment in tumor lesions and reference normal tissues, including T-cell rich tissues, using PET imaging...

Ethical review	Approved WMO
Status	Will not start
Health condition type	Miscellaneous and site unspecified neoplasms malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON52188

Source
ToetsingOnline

Brief title
D8510C00001 / ICON # 0597/0115

Condition

- Miscellaneous and site unspecified neoplasms malignant and unspecified

Synonym
cancer, subcutaneous/cutaneous lesions

Research involving
Human

Sponsors and support

Primary sponsor: MedImmune, LLC, a wholly owned subsidiary of AstraZeneca PLC
Source(s) of monetary or material Support: the study sponsor as listed in section B7

Intervention

Keyword: Cancer, CD8+ Imaging Sub-study, Durvalumab, MEDI1191

Outcome measures

Primary outcome

Sub-study, Biomarkers:

• The amount and changes of 89Zr-Df-IAB22M2C uptake (CD8+ PET signal) using PET imaging at baseline and post-treatment in tumor lesions and reference normal tissues, as determined

• The correlation of 89Zr-Df-IAB22M2C uptake (CD8+ PET signal) as determined by SUV-quantitative measures with CD8+ TIL density defined by IHC analysis of biopsied tumor tissue.

• PET imaging signal level and changes from baseline to post-treatment with levels and changes in other exploratory biomarkers beyond CD8+ IHC (eg, TMB, NKp46, CD4+, PD-1, PD-L1 IHC, tumor transcriptomic changes, peripheral blood cytokines, and immune cell changes).

• The amount and changes of 89Zr-Df-IAB22M2C uptake (CD8+ PET signal) using PET

imaging at baseline and posttreatment with individual patient responses (CR, PR, SD and PD, iCR, iPR, iSD, and iPD) and lesion level changes.

Secondary outcome

Sub-study, Biomarkers:

• The amount and changes of 89Zr-Df-IAB22M2C uptake (CD8+ PET signal) using PET imaging at baseline and post-treatment in tumor lesions and reference normal tissues, as determined

• The correlation of 89Zr-Df-IAB22M2C uptake (CD8+ PET signal) as determined by SUV-quantitative measures with CD8+ TIL density defined by IHC analysis of biopsied tumor tissue.

• PET imaging signal level and changes from baseline to post-treatment with levels and changes in other exploratory biomarkers beyond CD8+ IHC (eg, TMB, NKp46, CD4+, PD-1, PD-L1 IHC, tumor transcriptomic changes, peripheral blood cytokines, and immune cell changes).

• The amount and changes of 89Zr-Df-IAB22M2C uptake (CD8+ PET signal) using PET imaging at baseline and post-treatment with individual patient responses (CR, PR, SD and PD, iCR, iPR, iSD, and iPD) and lesion level changes.

Study description

Background summary

Tumor-infiltrating lymphocyte (TIL) densities are linked to prognosis and response to T-cell checkpoint inhibitor therapy across multiple cancer types (Berghoff et al 2016, Fridman et al 2012, Lee et al 2008, Nosho et al 2010). MEDI1191 is a novel messenger ribonucleic acid (mRNA)-based therapy designed for injection directly into tumors. It is composed of a lipid nanoparticle (LNP)-formulated mRNA encoding a linked monomeric bioactive interleukin

(IL)-12p70 protein (IL12B-Gly6Ser-IL12A). The mRNA sequence is optimized to enhance mRNA stability and translation. The mRNA chemistry is designed to improve mRNA translation and reduce non-specific immune activation (100% uridine replacement with 1N-methyl-pseudouridine; (Richner et al 2017, Svitkin et al 2017)). A miR122 binding site in the 3*UTR inhibits mRNA translation in liver hepatocytes in the event of mRNA introduction into the liver (Jain et al 2018). The LNP formulation protects the mRNA from extracellular degradation by RNAses and promotes mRNA cellular uptake and translation (Sabnis et al 2018). Intratumoral (IT) injection of MEDI1191 leads to local production of bioactive IL-12p70 by tumor and myeloid cells. Local IL-12p70 production in tumors enhances innate and adaptive immune cell activation (natural killer cell, T-cell and antigen presenting cell) and interferon gamma production. This leads to cytotoxic T-cell recruitment, activation and tumor cell lysis, and enhanced antitumor immunity. Key translational biomarker profiles are usually established using baseline and on-treatment biopsy samples; however, biopsies may not always be feasible for deep-seated lesions. In addition, this approach restricts the analysis of the biopsied region to a single tumor lesion, which may not be representative of the whole lesion or of other metastatic foci. The ability to quantify cluster of differentiation 8 (CD8+) T-cell densities in vivo, before and after administration of MEDI1191 alone or in concurrent combination with durvalumab, would provide substantial value for clinical translation with broad applications across the cancer immunotherapy clinical development space. A first-in-human study has been conducted with positron emission tomography (PET) based imaging of CD8+ T-cells using a minibody (Mb) directed to the CD8 antigen conjugated with desferrioxamine (Df) and radiolabeled with Zirconium-89 (89Zr) (89Zr-Df-IAB22M2C)
(Pandit-Taskar et al 2020). PET imaging with anti-CD8 labelled Mb has the potential to provide information beyond the standard imaging modalities of computed tomography (CT), magnetic resonance imaging (MRI), and traditional fluorodeoxyglucose-PET imaging. PET imaging of 89Zr-Df-IAB22M2C in vivo can potentially provide a whole-body image to evaluate the distribution of CD8+ T-cells at baseline and treatment-induced pharmacodynamic changes. The approach can also be informative for evaluating pharmacodynamic changes in other lymphoid and non-lymphoid tissues, distinguishing true progression from pseudo progression during the early phases of treatment, and correlating CD8+ T cell distribution with efficacy utilizing accepted efficacy modalities (CT, MRI, etc).

Study objective

Objectives (all are exploratory):
• To measure and analyze 89Zr-Df-IAB22M2C uptake cluster of (CD8+ PET signal) at and between baseline and post-treatment in tumor lesions and reference normal tissues, including T-cell rich tissues, using PET imaging.
• To correlate 89Zr-Df-IAB22M2C uptake (CD8+ PET signal) in biopsied lesion at and between baseline and post-treatment with CD8+ TIL density as assessed by

CD8+ IHC.
• To correlate 89Zr-Df-IAB22M2C uptake (CD8+ PET signal) at and between baseline and post-treatment with molecular and IHC based biomarkers (including but not limited to TMB, NKp46, CD4+, PD-1,and PD-L1) in the tumor and periphery.
• To correlate 89Zr-Df-IAB22M2C uptake (CD8+ PET signal) at and between baseline and post-treatment with RECIST 1.1 and iRECIST clinical outcome.

This sub-study will only be conducted at one site in the Netherlands and will enroll a separate cohort of approximately 14 subjects that will follow a slightly altered treatment plan and schedule of procedures compared to the main study.

A separate analysis from the main study is planned for this sub-study and data collected will be reported in a separate study report.

Study design

This sub-study of protocol Study D8510C00001 will enroll a separate cohort of approximately 14 subjects that will follow a slightly altered treatment plan and schedule of procedures compared to the main study. This substudy will comprise of 2 cohorts and 89Zr-Df-IAB22M2C will be administered twice per cohort. Once at baseline and then again following MEDI1191 alone in Group A, and before and after concurrent MEDI1191 plus durvalumab in Group B. The main protocol should be followed for lesion identification, instruction for injection, management of MEDI1191 related toxicities, inclusion/exclusion criteria, criteria for withdrawal from the study, treatment beyond progression, efficacy evaluation and disease assessment, MEDI1191 preparation, handling and storage, and biopsy procedures and handling of biological specimens. Other descriptions of procedures and assessments not described in the sub-study can be found in the main protocol. MEDI1191 dose will be based on a safe and pharmacodynamically active dose identified from Part 1B of the main study as determined by the Dose Escalation Committee (refer to main protocol Section 3.1.3).

Intervention

This sub-study will explore CD8+ distribution using PET imaging (Figure 1). The subjects in this sub-study will follow a slightly altered treatment plan and schedule of procedures compared to the main study.

Once a pharmacodynamically active and safe dose has been determined in Part 1B of the main study (concurrent IT MEDI1191 with systemic IV durvalumab in subjects with superficial lesions, which can be visible or palpable cutaneous or subcutaneous lesions) and based on Dose Escalation Committee, the CD8+ PET imaging cohort sub-study will be initiated. 89Zr-Df-IAB22M2C will be administered twice per cohort; at baseline and then again following MEDI1191

alone in Group A, and before and after concurrent MEDI1191 plus durvalumab in Group B. The expected radiation dose of 89Zr-Df-IAB22M2C is 37 MBq (1 mCi) at 1.5 mg API for this study (Section 2.1 and refer to the 89Zr-Df-IAB22M2C Investigator Brochure for more information).

MEDI1191 will be administered IT on Day 1, Day 22, Day 50 and then every 8 weeks (Q8W). A previously injected lesion may be re-injected if all criteria for re-injection are met. In subjects whose lesions no longer meet the criteria for MEDI1191 injection or who have a complete response following at least 1 MEDI1191 injection, MEDI1191 dosing may be omitted. If a lesion subsequently becomes available for injection, then MEDI1191 IT administration can continue at the next scheduled administration (Figure 2). Durvalumab will be administered via IV on Day 22 and repeated every 4 weeks (Q4W). 89Zr-Df-IAB22M2C tracer will be administered at 2 time points during the study. Approximately 14 subjects with malignant melanoma or squamous cell histology will be treated in this sub-study. Refer to the main protocol for criteria for lesion selection (see Section 3.1.5) and MEDI1191 treatment administration (see Section 4.5.1.4). Allocation to treatment arm will be determined by the primary investigator and approved by the Sponsor.

Group A
Subjects in Group A will be administered 37 MBq (1 mCi) of 89Zr-Df-IAB22M2C tracer infusion on Day -5 (± 3 days) followed by the 89Zr-Df-IAB22M2C-PET imaging at 24 hours (± 3 hours) after infusion of 89Zr-Df-IAB22M2C. A mandatory baseline lesion biopsy during screening, preferably following PET imaging on the same day, but no later than 24 hours after, is required for the MEDI1191 injected lesion. In addition, and if clinically feasible, a biopsy of a non-injected lesion should also be taken at baseline following PET imaging. During treatment, Group A subjects will receive the second 89Zr-Df-AB22M2C tracer infusion on Day 14 (± 3 days) followed by PET imaging within 24 hours (± 3 hours). A mandatory lesion biopsy taken no later than 24 hours after the PET imaging post-treatment (Day 15) is required for the MEDI1191 injected lesion. A biopsy of the non-injected lesion should be taken post-treatment following PET imaging, if clinically feasible.

Group B
Subjects in Group B will be administered 37 MBq (1 mCi) of 89Zr-Df-IAB22M2C tracer infusion on Day 14 (± 3 days) followed by PET imaging within 24 hours (± 3 hours). A
mandatory lesion biopsy taken no later than 24 hours after the PET imaging is required for the MEDI1191 injected lesion. In addition, and if clinically feasible, a biopsy of a non-injected lesion should also be taken following PET imaging. The second 89Zr-Df-IAB22M2C tracer infusion will occur during treatment on Day 35 (± 3 days) followed by PET imaging within 24 hours (± 3 hours). A mandatory lesion biopsy taken no later than 24 hours after the PET imaging post-treatment is required for the MEDI1191 injected lesion. A biopsy of a noninjected lesion should be taken post-treatment following PET imaging,

if clinically feasible. The timing of the on-treatment biopsies may be changed based on emerging data. The Principal Investigator has the option, in certain subjects, to administer the tracer infusion followed by PET imaging and biopsy at all three time points (baseline, Day 14, and Day 35) after discussion and approval by the Sponsor.

Group A and B
Evaluable subjects are those who have received investigational product and 89Zr-Df-IAB22M2C, completed the two PET imaging evaluations, and had the two related
biopsies. For the purposes of this sub-study, subjects who drop out before the second PET imaging scan or who have inadequate baseline and on-treatment tumor samples are considered non-evaluable and may be replaced, however, they may continue with the sub-study. Subjects who are not able to be dosed with MEDI1191 (Day 1 for Group A) or with MEDI1191 and durvalumab (Day 22 for Group B) are also considered non-evaluable and may be replaced, however, they may continue with the sub-study.

Study burden and risks

Please refer to section *What side effects could you experience?* and section *What are the pros and cons if you take part in the study?* in the *Subject Information For Participation In Medical Research Form* for an overview of the risks and side effects.

Preclinical data, both in vivo and in vitro (see the 89Zr-Df-IAB22M2C IB) have demonstrated that 89Zr-Df-IAB22M2C had no measurable effect on proliferation, T-cell activation or cytokine release. Potential risks of 89Zr-Df-IAB22M2C include site infusion reactions of redness, itching and pain, allergic reaction (including anaphylaxis), renal failure, hepatic failure, arthritis, and/or hypotension. Insertion of IV catheters for infusions and blood draws may cause minor pain, bruising and/or infection at the infusion site. The safety monitoring practices employed in the main protocol (see Sections 3.1.7 and 5.3) should be followed to guide subject safety for this sub-study. The ability to quantify CD8+ T-cell densities in vivo, before and after administration of MEDI1191 alone or in combination with durvalumab, would substantially benefit clinical translation with broad applications across the cancer immunotherapy clinical development space.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

Please note that due to removing inclusion/ exclusion criteria not relevant for the protocol conducted in The Netherlands, the numbers deviate from those in the Main Protocol.

Subjects must meet all of the following criteria:
1. Subjects >= 18 years of age.
2. Have given written informed consent prior to any study prior to performing any protocol related procedures, including screening evaluations.
3. Eastern Cooperative Oncology Group (ECOG) performance status of 0 to 1.
4. Have at least 1 measurable lesion, other than the planned injected lesion(s), using standard techniques by RECIST v1.1. Injected tumor lesion(s) must be deemed clinically feasible for injection by the investigator.
a. A previously irradiated lesion, or a lesion subjected to other loco-regional therapy, can be considered a target lesion only if the lesion has clearly progressed during or after most recent therapy, and is well defined, measurable per RECIST v1.1.
b. Subjects undergoing fresh tumor biopsies must have additional non-target lesions that can be biopsied at acceptable risk as judged by the investigator or if no other lesion is deemed suitable for biopsy, then a RECIST v1.1 target

lesion used for biopsy must be >= 2 cm in longest diameter.
5. Adequate bone marrow, renal, and hepatic function
a. Hematological (criteria listed cannot be met with recent blood transfusions or require ongoing growth factor support within 2 weeks of starting study treatment):
i. Absolute neutrophil count >= 1.5 × 109/L (1,500/mm3).
ii. Platelet count >= 100 × 109/L (100,000/mm3).
iii. Hemoglobin >= 9.0 g/dL within first 2 weeks prior to first dose.
b. Renal: calculated creatinine clearance (CrCL) (Cockcroft-Gault formula will be used to calculate CrCL) or 24-hour urine CrCl > 50 mL/min.
c. Hepatic:
i. TBL <= 1.5 × ULN; for subjects with documented/suspected Gilbert's syndrome or liver metastases, bilirubin <= 3 × ULN.
ii. AST and ALT <= 3 × ULN if no demonstrable liver metastasis; <= 5 x ULN in the presence of liver metastases.
iii. Albumin > 3 g/dL.
iv. International normalized ratio (INR) and activated partial thromboplastin time (aPTT) < 1.5 × ULN.
6. Prior to the first dose of MEDI1191, subjects with central nervous system (CNS) metastases must have been treated and must be asymptomatic and meet the following:
a. No concurrent treatment, inclusive of but not limited to surgery, radiation, and/or corticosteroids.
b. Subjects must be clinically stable with no CNS symptoms following CNS treatment for a period of at least 28 days prior to first dose of MEDI1191.
c. At least 7 days since last dose of corticosteroids first dose of MEDI1191.
NOTE: Subjects with clinical symptoms or cord compression or with leptomeningeal disease are excluded from the study.
7. Cessation of immunosuppressive medications including systemic corticosteroids at doses exceeding 12 mg/day prednisone or equivalent, methotrexate, azathioprine, ustekinumab (Stelara®), and tumor necrosis factor (TNF) α/IL 6 blockers for at least 7 days prior to the first dose of MEDI1191 (corticosteroids at doses of 12 mg/day prednisone equivalent or lower, inhaled, intranasal, intraarticular, and topical steroids are permitted).
8. The imaging and the results of imaging done up to 6 months prior to screening (ie, >= 1 additional time point before baseline assessment) are to be made available to the sponsor for evaluation of the kinetics of tumor progression if allowed by country.
9. Subjects with cutaneous or subcutaneous tumor lesions are defined as visible or palpable non-visceral lesions for Part 1A, 1B, and Part 2 expansion cohorts. This definition includes lesions involving superficial muscle tissue and lesions involving the fascia overlying these muscles (eg, breast mass, supraclavicular lymph nodes etc.).
a. Subjects with cutaneous/subcutaneous lesions must have lesions:
i. Non-visceral, measurable lesions by CT scan, MRI or calipers, and must have a minimum of 1 lesion that is easily accessible for injection.
ii. Measure >= 1.5 cm in the smallest diameter.

iii. Be located in an anatomic location where MEDI1191 can be safely administered, ie, not in close proximity to critical structures eg, carotid artery, jugular vein, or other major blood vessels, nerve bundle, trachea or other major airway tract.
10. For Part 1A and 1B, subjects must be willing to consent and undergo pre-treatment biopsy of the lesion selected for MEDI1191 injection and if clinically feasible, also, of a lesion not selected for injection. Subjects enrolled in the pharmacodynamic expansion cohort for Parts 1A and 1B, must be willing to consent and undergo pre-treatment tumor biopsy of an injected (mandatory), and non-injected lesion (if clinically feasible).
11. Subjects in Parts 1A and 1B must be willing to undergo an on treatment biopsy of previously injected and if clinically feasible un-injected lesions.

Part 1:
12. Histologic or cytologic confirmation of advanced solid tumor, including NSCLC, squamous cell carcinoma of the head and neck, urothelial carcinoma, or other tumors known to be responsive to checkpoint inhibitors, with the exception of ocular melanoma and hepatocellular carcinoma.
13. Subjects must have received and have progressed on or be refractory to at least 1 line of standard systemic therapy in the recurrent/metastatic setting. Additionally, subjects must meet the following qualifications:
a. Parts 1A and 1B (IT injection of cutaneous or subcutaneous lesions): Must have at least 1 site that is located in subcutaneous (eg, axillary) or cutaneous or supraclavicular area and easily accessible for injection. At least 1 other lesion must meet definition of target lesion per RECIST v1.1.

All Parts (Reproductive Criteria):
14. Females of childbearing potential who are sexually active with a nonsterilized male partner must use at least one highly effective method of contraception (see Appendix A for definition of females of childbearing potential and for a description of highly effective methods of contraception) from screening, and must agree to continue using such precautions for 3 months after the final dose of investigational product. It is strongly recommended for the male partner of a female subject to also use male condom plus spermicide throughout this period. Cessation of contraception after this point should be discussed with a responsible physician. Periodic abstinence, the rhythm method, and the withdrawal method are not acceptable methods of contraception.
a. Females of childbearing potential are defined as those who are not surgically sterile (ie, surgical sterilization includes bilateral tubal ligation, bilateral oophorectomy, or hysterectomy) or postmenopausal (defined as 12 months with no menses without an alternative medical cause).
b. A highly effective method of contraception is defined as one that results in a low failure rate (ie, less than 1% per year) when used consistently and correctly.
c. Should a woman become pregnant or suspect she is pregnant while she or her partner is participating in this study, she must inform her treating physician immediately.

d. Female subjects must refrain from egg cell donation and breastfeeding while on study and for 6 months after the final dose of investigational product.
15. Nonsterilized male subjects who are sexually active with a female partner of childbearing potential must use a male condom with spermicide from Day 1 through 6 months after receipt of the final dose of investigational product. It is strongly recommended for the female partner of a male subject to also use a highly effective method of contraception throughout this period as described in Appendix A. In addition, male subjects must refrain from sperm donation while on treatment and for 6 months after the final dose of investigational product.
16. Subjects must have malignant melanoma or squamous cell histology tumors to be eligible.

Exclusion criteria

Please note that due to removing inclusion/ exclusion criteria not relevant for the protocol conducted in The Netherlands, the numbers deviate from those in the Main Protocol.

Any of the following would exclude the subject from participation in the study:
1. Prior IL-12 either alone or as part of a treatment regimen.
2. Concurrent enrollment in another clinical study within 30 days prior to treatment administration, unless it is an observational (non interventional) clinical study or the follow-up period of an interventional study.
3. Receipt of live attenuated vaccines within 30 days prior to the first dose of study treatment. Subjects who receive study treatment should not receive live or live attenuated vaccine during the study and 30 days after the last dose of investigational products.
4. Known allergy or hypersensitivity to any component of MEDI1191 or durvalumab formulations.
5. Active or prior documented autoimmune disorders within the past 5 years prior to the first scheduled dose of study treatment. The following are exceptions to this criterion:
a. Subjects with vitiligo or alopecia.
b. Subjects with hypothyroidism (eg, following Hashimoto syndrome) stable on hormone replacement.
c. Any chronic skin condition that does not require systemic therapy.
d. Subjects with celiac disease controlled by diet alone.
6. History of primary immunodeficiency, other immune-deficiency states (eg, myelodysplastic disorders, marrow failure states, human immunodeficiency virus infection [even if viral load is undetectable], history of solid organ transplant, bone marrow allograft), or active tuberculosis (in settings where there is clinical or radiographic evidence of tuberculosis, active disease must be excluded prior to enrollment in line with local practice).
7. History of coagulopathy resulting in uncontrolled bleeding, eg, hemophilia, von Willebrand's disease. History of other bleeding disorders or a Grade >= 3

bleeding event within 3 months prior to first dose of investigational products.
8. Require continuous anticoagulation or antiplatelet therapy (except for <= 100 mg acetylsalicylic acid [ASA]) which cannot be interrupted for more than 7 days for IT delivery of MEDI1191.
9. Any concurrent chemotherapy, radiotherapy, immunotherapy, biologic or hormonal therapy for cancer. NOTE: Concurrent use of hormones for noncancer-related conditions (eg, insulin for diabetes and hormone replacement therapy for post-menopausal symptoms) or specific cancer-related conditions (ie, LHRH-based hormonal therapy for prostate cancer with documented progression) is acceptable. Local treatment of isolated lesions for palliative intent is acceptable (eg, by local surgery or radiotherapy)
10. Receipt of any conventional or investigational anticancer therapy within 21 days or palliative radiotherapy within 7 days prior to the first dose of study treatment. For subjects who have received prior immunotherapy, the following additional exclusion criteria apply:
a. Received only one dose of prior immunotherapy agent alone or as part of a combination regimen within 21 days.
b. Experienced a toxicity that led to permanent discontinuation of prior immunotherapy
c. All AEs while receiving prior immunotherapy did not resolve to <= Grade 1 or baseline prior to screening for this study.
d. Experienced a >= Grade 3 AE (including pneumonitis) or neurologic, ocular, or cardiac AE of any grade while receiving prior immunotherapy (NOTE: Subjects with an endocrine AE of any grade are permitted to enroll if they are stably maintained on appropriate replacement therapy and are asymptomatic).
e. Required the use of additional immunosuppression other than corticosteroids for the management of an AE, or experienced recurrence of an AE if re challenged, or is currently requiring a maintenance dose of > 12 mg prednisone or equivalent per day.
11. Any toxicity from prior therapy that has not completely resolved to <= Grade 1 or baseline at the time of consent. NOTE: Subjects with treatment-related Grade 2 toxicities that are deemed stable or irreversible and not reasonably expected to be exacerbated by any of the investigational products (eg, sensory neuropathy, hearing loss) may be enrolled.
12. Current or prior use of immunosuppressive medication within 14 days prior to the first dose of MEDI1191. The following are exceptions to this criterion:
a. Intranasal, topical, inhaled corticosteroids or local steroid injections (eg, intraarticular injection).
b. Systemic corticosteroids at physiologic doses not to exceed 12 mg/day of prednisone or equivalent.
c. Steroids as premedication for hypersensitivity reactions (eg, CT scan premedication).
13. Have moderate or severe cardiovascular disease:
a. Presence of acute coronary syndrome including myocardial infarction or unstable angina pectoris, other arterial thrombotic event including cerebrovascular accident or transient ischemic attack within 6 months prior to study entry.

b. New York Heart Association Class 3 or 4 congestive heart failure, or uncontrolled hypertension (> 160 mmHg systolic and/or > 100 mmHg diastolic, despite antihypertensive medication).
14. Any condition that, in the opinion of the investigator or sponsor, would interfere with evaluation of the investigational product or interpretation of subject safety or study results.
15. Uncontrolled intercurrent illness, including but not limited to, ongoing or active bacterial, fungal or viral infections, interstitial lung disease, serious gastrointestinal conditions associated with diarrhea, or psychiatric illness/social situations that would limit compliance with study requirements, substantially increase risk of incurring AEs or compromise the ability of subject to give written informed consent.
16. Untreated, active hepatitis B or C as defined by seropositivity for hepatitis B or C surface antigen (HBsAg, HCsAg) or positive hepatitis B core (HBc) antibody.
a. Subjects with chronic hepatitis B, confirmed by the presence of anti-HBc, or hepatitis C, confirmed by the presence of detectable hepatitis C virus (HCV) RNA or anti-HCV antibody, receiving antiviral therapy are allowed to enroll if disease has been controlled for at least 1 month prior to screening.
i. Controlled hepatitis B is defined as serum hepatitis B virus DNA < 2000 IU/mL by polymerase chain reaction (PCR).
ii. Controlled hepatitis C is defined as undetectable hepatitis C RNA by PCR either spontaneously or in response to a successful prior course of anti-hepatitis C therapy.
17. Major surgery (as defined by the investigator) within 4 weeks prior to first dose of MEDI1191 or still recovering from prior surgery. NOTE: Minor procedures (eg, placement of venous access devices, core needle biopsy) are allowed if completed at least 24 hours prior to the first dose of MEDI1191.
18. Subjects with untreated active major depression with suicidal ideation and/or plan.
19. Female subjects who are pregnant, lactating, or intend to become pregnant during their participation in this study.

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	14
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Durvalumab
Generic name:	Durvalumab
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	MEDI1191
Generic name:	MEDI1191

Ethics review

Approved WMO Date:	01-11-2021
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	23-05-2022
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

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	EUCTR2020-005784-31-NL
ClinicalTrials.gov	NCTnumber:NCT03946800
CCMO	NL78127.000.21

Study results

Summary results
Trial never started