A Phase 1/2 Study of the Safety, Tolerability, Pharmacokinetics and Preliminary Efficacy of Relatlimab Plus Nivolumab in Pediatric and Young Adult Participants with Recurrent or Refractory Classical Hodgkin Lymphoma and Non-Hodgkin Lymphoma

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This study has been transitioned to CTIS with ID 2023-503715-14-00 check the CTIS register for the current data. Part A: To characterize the safety, tolerability, and define the MTD or RP2D for the combination of relatlimab + nivolumab in pediatric…

Ethical review	Approved WMO
Status	Pending
Health condition type	Lymphomas Hodgkin's disease
Study type	Interventional

Summary

ID

NL-OMON53587

Source
ToetsingOnline

Brief title
RELATIVITY-069

Condition

- Lymphomas Hodgkin's disease

Synonym
Hodgkin Lymphoma and Non-Hodgkin Lymphoma

Research involving
Human

Sponsors and support

Primary sponsor: Bristol-Myers Squibb
Source(s) of monetary or material Support: Industry

Intervention

Keyword: Hodgkin lymphoma, Pediatric, Phase 1/2, Relatlimab + nivolumab

Outcome measures

Primary outcome

1/Part A- Dose-limiting toxicities (DLTs), Maximum Tolerated Dose/Recommended Phase 2 Dose; (MTD/RP2D), and incidences of Adverse Events (AEs), Serious Adverse Events (SAEs), AEs leading to discontinuation, deaths and laboratory abnormalities

2/Part A- maximum observed serum concentration (Cmax), trough observed concentration (Ctrough), time to maximum concentration (Tmax), and area under the curve within a dosing interval (AUC(TAU)) for relatlimab

3/Part B- Complete Metabolic Response (CMR) rate

Secondary outcome

1/Part B: Incidences of AEs, SAEs, AEs leading to discontinuation, deaths, and laboratory abnormalities

2/Part B: Overall Response Rate (ORR)

Study description

Background summary

Participants with recurrent/relapsed or refractory cHL and NHL have limited treatment options. There is currently no consensus or identified best salvage regimen in pediatric and adolescent patients with recurrent/relapsed or refractory (R/R) cHL. There is little consistency in therapeutic approaches, and there is no formal recommendation on the best approach for this poor prognostic subgroup; new treatment options are needed.

Study objective

This study has been transitioned to CTIS with ID 2023-503715-14-00 check the CTIS register for the current data.

Part A: To characterize the safety, tolerability, and define the MTD or RP2D for the combination of relatlimab + nivolumab in pediatric participants less than 18 years of age with R/R cHL and NHL.

Part A: To characterize the PK of relatlimab for the combination of relatlimab + nivolumab in pediatric participants less than 18 years of age with R/R cHL and NHL.

Part B: To assess the preliminary efficacy of relatlimab + nivolumab based on the RP2D from part A in participants less than or equal to 30 years old with cHL (Cohort 1).

Study design

CA224069 is an open-label, Phase 1/2 clinical trial of relatlimab + nivolumab in children, adolescents, and young adults with R/R cHL and NHL. Part A will encompass safety and dose determination of relatlimab + nivolumab. Part B will be composed of an expansion cohort of cHL (Cohort 1) and an exploratory assessment in NHL (Cohort 2).

Participants will continue treatment until progressive metabolic disease (PMD), death, unacceptable toxicity, symptomatic deterioration, the Investigator*s decision to discontinue treatment, the participant*s decision to discontinue treatment or withdraw consent, for a maximum of 2 years of study treatment, the participant is lost to follow-up, or study

termination by the Sponsor.

Intervention

Flat-dosing (AF) cohort will include: participants >= 12 years old who weigh >= 40 kg:
• D = Relatlimab 160 mg + nivolumab 480 mg intravenous (IV) Q4W (A1F); if the starting dose
is found to be not tolerated, then the relatlimab dose will be decreased as follows:
• D-1 = Relatlimab 80 mg + nivolumab 480 mg IV Q4W (A2F).
Age/weight-based dosing (AW) cohort will include: participants >= 12 years old and with a
weightwho weigh < 40 kg and/or participants < 12 years old irrespective of weight:
• D = Relatlimab 2 mg/kg (max 160 mg) + nivolumab 6 mg/kg (max 480 mg) Q4W (A1W); if
the starting dose is found to be not tolerated, then the relatlimab dose will be decreased as
follows:
• D-1 = Relatlimab 1 mg/kg (max 80 mg) with nivolumab 6 mg/kg (max 480 mg) Q4W (A2W).

Study burden and risks

The study contains a screening phase, treatment phase and a follow-up phase.

We anticipate a 2 year treatment phase for patients with a 3 year follow up period.

Visits can last 5-6 hours.
The subject will have to undergo several examinations, tests and/or procedures before, during and after his/her treatment. Please referto the procedure table in the ICF and Schedule of Assessment of the protocol for more information.

In addition, questions are asked about the medical history, demographics and eligibilty questions
Subjects will also be tested for HIV and hepatitis. Female patients will be tested for pregnancy .
The anticipated total duration of the study is approximately 5 years.

Possible side effects that are already known are described in the Investigator's Brochure and the patient informed consent form.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)
Children (2-11 years)

Inclusion criteria

- Male and female participants less than 18 years of age (Part A), and less than or equal to
30 years of age (Part B) with R/R cHL (Cohort 1) and NHL (Cohort 2).
- Participants with pathologically confirmed high-risk R/R cHL, after non-response to or failure
of first-line standard therapy prior to a definitive therapy (eg. HDCT/ASCT).
- high-risk for cHL is defined by early relapse, extranodal disease or B symptoms at relapse,
extensive disease where radiation therapy was contraindicated at relapse, and/or relapse in

a prior radiation field.
- Participants with pathologically confirmed R/R NHL after failure or non-response to first-line therapy, including but not limited to primary mediastinal B-cell lymphoma, diffuse large B-cell lymphoma (DLBCL), mediastinal gray zone lymphoma (MGZL), anaplastic large cell lymphoma (ALCL), or peripheral T-cell lymphoma (PTCL).
- high-risk for NHL is defined as applicable (eg, in young adults) by a second-line therapy age-adjusted International Prognostic Index score of >= 2 factors.
- The participant*s current disease state must be R/R to standard therapy.
- Participants must have measurable PET positive disease in both cHL and NHL cohorts.

Exclusion criteria

- Aggressive B-cell lymphomas subtypes including Burkitt lymphoma (BL), lymphoblastic lymphoma, and NK/T-cell lymphoma/leukemia.
- Primary CNS lymphoma of the brain or spinal cord, and secondary CNS lymphoma (ie, from systemic non-Hodgkin lymphoma) involving the brain, spinal cord, or with leptomeningeal seeding.
- Prior treatment with an anti-cytotoxic T-lymphocyte-associated protein 4 antibody, or any other antibody or drug specifically targeting T-cell co-stimulation or checkpoint pathways, with the exception of anti-PD(L)-1 targeted therapies.
- Prior treatment with LAG-3-targeted agents.
- Participants with prior autologous stem cell transplantation (HDCT/ASCT).
- Participants with a history of allogeneic bone marrow transplantation.
- Participants with clinically significant systemic illnesses unrelated to the cancer as judged by the investigators, which would compromise the participant*s ability to tolerate the study treatment.
- Participants with autoimmune disease.
- Participants who are pregnant or breastfeeding.

Study design

Design

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	28-04-2023
Enrollment:	2
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Nivolumab
Generic name:	Nivolumab
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Relatlimab
Generic name:	Relatlimab

Ethics review

Approved WMO Date:	14-02-2023
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	22-05-2023
Application type:	First submission
Review commission:	METC NedMec
Approved WMO	

Date:	26-05-2023
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	14-06-2023
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
EU-CTR	CTIS2023-503715-14-00
EudraCT	EUCTR2021-000493-29-NL
ClinicalTrials.gov	NCT05255601
CCMO	NL82628.041.23