A PHASE II, MULTICENTER, RANDOMIZED, DOUBLE-BLIND STUDY OF RO7247669 COMBINED WITH NAB-PACLITAXEL COMPARED WITH PEMBROLIZUMAB COMBINED WITH NAB-PACLITAXEL IN PARTICIPANTS WITH PREVIOUSLY UNTREATED, PD-L1*POSITIVE, LOCALLY-ADVANCED UNRESECTABLE OR METASTATIC TRIPLE-NEGATIVE BREAST CANCER

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Primary Objective: This study will evaluate the efficacy, safety, and pharmacokinetics of RO7247669 plus nab-paclitaxel compared with pembrolizumab plus nab-paclitaxel in patients with previously untreated, locally advanced, unresectable or...

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

Summary

ID

NL-OMON53202

Source
ToetsingOnline

Brief title
CO44194

Condition

- Other condition
- Breast neoplasms malignant and unspecified (incl nipple)

Synonym
Breast cancer, TNBC

Health condition

TNBC

Research involving
Human

Sponsors and support

Primary sponsor: Roche Nederland B.V.
Source(s) of monetary or material Support: Sponsor

Intervention

Keyword: PD-L1 positive, Pembrolizumab, RO7247669, Triple Negative Breast Cancer

Outcome measures

Primary outcome

PFS, defined as the time from randomization to the first occurrence of disease progression, as determined by the investigator according to RECIST v1.1, or death from any cause (whichever occurs first).

Secondary outcome

• ORR, defined as the proportion of participants with a CR or a PR on two consecutive occasions >= 4 weeks apart, as determined by the investigator according to RECIST v1.1

• DOR, defined as the time from the first occurrence of a confirmed objective response to the first occurrence of disease progression, as determined by the investigator according to RECIST v1.1, or death from any cause, whichever

occurs first

• OS, defined as the time from randomization to death from any cause

• PFS rate at 12 months, defined as the proportion of participants who have not experienced disease progression or death from any cause at 12 months after randomization, as determined by the investigator, according to RECIST v1.1

• OS rate at 12 months, defined as the proportion of participants who have not experienced death from any cause at 12 months after randomization

• Incidence and severity of adverse events, with severity determined according to NCI CTCAE v5.0

• Change from baseline in targeted clinical laboratory test results

• Change from baseline in targeted vital signs

• PK profiles and parameters derived for RO7247669 including but not limited to, when appropriate and when data allow, the parameters listed below:

- Maximum concentration

- Time of maximum concentration

- Clearance

- Volume of distribution at steady state

- Area under the concentration-time curve

- Half*life

• Incidence and titer of RO7247669 ADA during the study relative to the prevalence of ADA at baseline and impact of ADAs on exposure, activity and

safety

Study description

Background summary

Breast cancer is the most frequently diagnosed cancer among women, and the leading cause of cancer-related deaths in women worldwide.
TNBC is characterized immunohistologically by the lack of expression of hormonal estrogen receptor (ER) and progesterone receptor (PgR), and lack of overexpression and/or amplification of the human epidermal growth factor receptor 2 (HER2)/neuraminidase (NEU) gene . Patients with metastatic TNBC have relatively poorer outcomes (shorter duration of progression-free survival [PFS] and overall survival [OS]) compared with patients with other breast cancer subtypes.
The treatment approach for this disease in the first-line (1L) setting is chemotherapy, in combination with an anti-programmed death-1 (PD-1)/PD-L1 inhibitor for patients with PD-L1*positive TNBC.
Despite the advances lately, OS in the 1L metastatic setting remains modest at less than 3 years. Therefore, there remains an urgency to improve upon chemotherapy in combination with PD*1/PD*L1*targeting agents in 1L PD-L1 positive advanced TNBC. Combinations targeting novel immune checkpoints are attractive because they aim to take advantage of distinct mechanisms that could improve the success of immunotherapy in TNBC and potentially expand the proportion of patients whose tumors respond to immunotherapy

Study objective

Primary Objective: This study will evaluate the efficacy, safety, and pharmacokinetics of RO7247669 plus nab-paclitaxel compared with pembrolizumab plus nab-paclitaxel in patients with previously untreated, locally advanced, unresectable or metastatic PD-L1-positive TNBC.

Secondary objective:
- To evaluate the efficacy of RO7247669 plus nab-paclitaxel compared with pembrolizumab plus nab-paclitaxel in the FAS

- To evaluate the efficacy of RO7247669 plus nab-paclitaxel compared with pembrolizumab plus nab-paclitaxel in SP263-positive analysis set and 22C3-positive analysis set and SP142-positive analysis set
- To evaluate the safety of RO7247669 plus nab-paclitaxel compared with pembrolizumab plus nab-paclitaxel in the SAS
- To characterize the RO7247669 PK profile
- To evaluate the immunogenicity to RO7247669

The exploratory objectives are described in protocol section 3

Study design

This is a Phase II, randomized, double-blind, global, multicenter study designed to evaluate the efficacy, safety, and pharmacokinetics of RO7247669 in combination with nab-paclitaxel compared with pembrolizumab plus nab-paclitaxel in patients with previously untreated, locally advanced, unresectable or metastatic (Stage IV) PD*L1-positive TNBC.

Intervention

RO7247669 plus nab-paclitaxel compared with pembrolizumab plus nab-paclitaxel

Study burden and risks

The general burden for the patient consists of (a.o.) the withdrawal of blood samples, possible collection of tumor sample,
administration of investigational products which may lead to various adverse events. These are described in the Investigators'
Brochure of RO7247669 and Pembrolizumab and Nab-Paclitaxel.

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

• Signed Informed Consent Form
• Age >= 18 years at the time of signing Informed Consent Form
• Metastatic or locally advanced unresectable, histologically documented TNBC (absence of HER2-over-expression, ER, and PgR expression by local assessment)
• Measurable disease per RECIST v1.1
• If metastatic disease (Stage IV), measurable disease outside of the bone
• Previously irradiated lesions can be considered as measurable disease only if disease progression has been unequivocally documented at that same lesion since radiation
• No prior systemic therapy for metastatic or locally advanced unresectable TNBC
• Tumor PD-L1 expression as documented through central testing of a representative tumor tissue specimen.
• Eastern Cooperative Oncology Group (ECOG) Performance Status of 0 or 1 (see Appendix 9)

More inclusion criteria are stated in protocol section 5.1

Exclusion criteria

• Pregnancy or breastfeeding, or intention of becoming pregnant during the study or within 4 months after the final dose of RO7247669 or pembrolizumab, and 6 months after the final dose of nab-paclitaxel.
• Poor venous access
• Glomerular filtration rate (GFR) < 30 mL/min/1.73 m2 as calculated through use of the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation
• History of malignancy within 5 years prior to consent, except for the cancer under investigation in this study and malignancies with a negligible risk of metastasis or death (e.g., 5-year OS rate > 90%)
• Symptomatic, untreated, or actively progressing central nervous system (CNS) metastases

More exclusion criteria are stated in the protocol section 5.2

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	02-10-2023
Enrollment:	2
Type:	Anticipated

Medical products/devices used

Generic name:	Device 1: PD-L1 22C3 IHC Assay; TE-IHC-85 Device 2: PD-L1 (SP142) IHC assay; TE-IHC-198 Device 3: PD
Registration:	Yes - CE outside intended use

Ethics review

Approved WMO

Date:	22-08-2023
Application type:	First submission
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
Other	2022-502457-34-00
CCMO	NL84956.000.23