AN OPEN-LABEL, MULTICOHORT, PHASE II STUDY OF ATEZOLIZUMAB IN ADVANCED SOLID TUMORS

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON47718

Source
ToetsingOnline

Brief title
MO29518 (Basket)

Condition

- Other condition

Synonym
Advanced solid tumors, cancer

Health condition

gevorderde solide tumoren

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Advanced solid tumors, Atezolizumab, Intravenous, Phase II

Outcome measures

Primary outcome

The primary efficacy objective for this study is as follows:

1. To evaluate non-progression rate (NPR) at 18 weeks in patients with advanced solid tumors treated with Atezolizumab, defined as the percentage of patients with complete response (CR) partial response (PR) or stable disease (SD) as assessed by the Investigator according to Response Evaluation Criteria In Solid Tumors, Version 1.1 (RECIST, v1.1) or according to disease specific criteriat for prostate cancer and malignant pleural mesothelioma

Secondary outcome

EFFICACY OBJECTIVES

The secondary efficacy objectives for this study are as follows:

1. Efficacy: To evaluate NPR at 24 weeks, overall response rate (ORR), best overall response (BOR), clinical benefit rate (CBR), duration of response (DOR), time to tumor progression (TTP) and progression-free survival (PFS), as assessed by the Investigator using RECIST v1.1 and modified RECIST (latter also NPR at 18 weeks) or by disease-specific criteria for prostate cancer and malignant pleural mesothelioma.

Overall survival (OS).

2. Safety: incidence, nature, and severity of adverse events, incidence of anti-atezolizumab antibodies, mean dose and number of cycles of atezolizumab

3. Pharmacokinetics: maximum and minimum serum atezolizumab concentrations

SAFETY OBJECTIVES

The safety objectives for this study are as follows:

1. To evaluate the safety and tolerability of Atezolizumab in patients with advanced solid tumors

2. To characterize the immunogenic potential of Atezolizumab by measuring anti Atezolizumab antibodies and to explore the potential relationship of the immunogenicity response with safety and efficacy

PHARMACOKINETIC OBJECTIVES

The PK objectives for this study are as follows:

1. To characterize the pharmacokinetics of Atezolizumab

EXPLORATORY OBJECTIVES

The exploratory objectives for this study are as follows:

1. To evaluate the relationship between tumor tissue PD-L1 expression and measures of efficacy, including NPR at 18 weeks and 24 weeks, ORR, BOR, CBR, DOR, TTP, PFS and OS.

2.To assess predictive and prognostic exploratory biomarkers in archival and/or

fresh tumor tissue and plasma and their association with disease status and/or

response to study treatment *

3. To evaluate exploratory pharmacodynamic (PD) biomarkers (e.g., T, B and NK

cell enumeration, T cell subpopulations like CD8+ T, effector/memory T cells,

regulatory T cells, changes in expression of CD25 or human leukocyte antigen-DR

[HLA-DR],

interferon [IFN]-gamma production,IL-2 and other exploratory biomarkers) in

tumor tissue and plasma and their association with disease status, and/or

response to study treatment, tumor immunobiology or tumor type

Study description

Background summary

Atezolizumab is a human Ig G1 monoclonal antibody consisting of two heavy chains (448 amino acids) and two light chains (214 amino acids) and is produced in Chinese hamster ovary cells. Atezolizumab was engineered to eliminate Fc-effector function via a single amino acid substitution at position 298 on the heavy chain, which results in a non-glycosylated antibody that has minimal binding to Fc receptors and prevents Fc-effector function at expected concentrations in humans. Atezolizumab targets human PD-L1 and inhibits its interaction with its receptors,PD-1 and B7.1 (CD80, B7-1). Both of these interactions are reported to provide inhibitory signals to T cells. Atezolizumab is being investigated as a potential therapy against solid tumors and hematologic malignancies in humans.

Study objective

The main objective is to evaluate the percentage of patients that do not experience progression during the first 18 weeks of treatment with Atezolizumab in patients affected by advanced solid tumors.

The secondary objectives are to evaluate the percentage of patients that do not progress during the first 24 weeks of treatment with Atezolizumab, the percentage of patients that achieve a response, the best response achieved, the duration of response and the progression free survival;

these variables will be evaluated according to RECIST criteria v1.1. and according to modified RECIST criteria. Moreover OS will be evaluated as secondary endpoint.

Study design

This will be an open-label, multicenter, multinational, multicohort, phase II study. For each cohort, the study will consist of a Screening Period (Day *35 to *1), a Treatment Period, a Treatment Discontinuation Visit occurring * 30 days after the last dose of study medication and a 24-month Survival Follow-up Period (Figure 1).

Intervention

Atezolizumab IV (fixed dose of 1200 mg) will be administered on Day 1 of 21-day cycles. The initial dose will be delivered over 60 minutes. If the first infusion is well-tolerated, the second and all subsequent infusions may be delivered over 30 minutes. During the initial treatment stage, Atezolizumab treatment may be continued as long as patients are experiencing clinical benefit as assessed by the investigator, i.e., in the absence of unacceptable toxicity or symptomatic deterioration attributed to disease progression after an integrated assessment of radiographic data, biopsy results (if available), and clinical status.

Study burden and risks

For more information, please see the answer on question number E9.

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.Histologically documented advanced (i.e. stages III or IV) solid timors that meet protocol defined cohort specifications, with progressive disease at study entry and at least one line of prior line systemic anticancer therapy or for which there is no alternative therapy known to prolong survival , Measurable disease as defined by RECIST, v1.1. (except for prostate cancer and malignant pleural mesothelioma) and disease-specific criteria for patients with prostate cancer (see Appendix 6) and malignant pleural mesothelioma (see Appendix 7), 3. Estern Cooperative Oncology group (ECOG) Performance Status of 0 or 1, 4. Adequate hematologic and end organ function, defined by labortory results obtained within 3 days prior to the first study treatment., 5.Women who are not postmenopausal (* 12 months of non-therapy-induced amenorrhea) or surgically sterile must have a negative serum pregnancy test result within 14 days prior to initiation of study drug

Exclusion criteria

1. Malignancies other than disease under study within 5 years prior to Cycle 1 Day 1, with the exception of those with a negligible risk of metastasis or death treated with expected curative outcome, 2 .History of treated asymptomatic or symptomatic CNS metastasis or presence of CNS metastases as determined by CT or MRI evaluation during screening and prior radiographic assessments, 3 .Leptomeningeal disease, 4. Any approved anticancer therapy, including chemotherapy, hormonal therapy or radiotherapy, within 3 weeks prior to initiation of study treatment; with certain exception

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):	13-07-2015
Enrollment:	35
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Atezolizumab
Generic name:	Atezolizumab

Ethics review

Approved WMO

Date:	07-04-2015
Application type:	First submission
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)

Approved WMO

Date:	26-06-2015
Application type:	First submission
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)

Approved WMO

Date:	18-09-2015
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)

Approved WMO

Date:	16-10-2015
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)

Approved WMO

Date:	04-11-2015
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)

Approved WMO

Date:	21-01-2016
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)

Approved WMO

Date:	29-01-2016
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)

Approved WMO

Date:	23-09-2016
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)

Approved WMO

Date:	29-09-2016
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)

Approved WMO

Date:	10-11-2016
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van

	Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	03-07-2017
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	13-07-2017
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	09-08-2017
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	11-08-2017
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	25-10-2017
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	21-11-2017
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	14-12-2017
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	28-12-2017

Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	09-04-2018
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	12-04-2018
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	28-05-2018
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	15-06-2018
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	26-11-2018
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	21-12-2018
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	21-02-2019
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)

Approved WMO Date:	11-10-2019
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	28-11-2019
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	02-12-2019
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)

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	EUCTR2015-000269-30-NL
CCMO	NL52894.031.15
Other	Wordt geregistreerd op www.clinicaltrials.gov