A phase III, multicenter, randomized, placebo-controlled, double-blind study of atezolizumab (anti-PD-L1 antibody) as adjuvant therapy in patients with renal cell carcinoma at high risk of developing metastasis following nephrectomy

Published: 25-01-2017
Last updated: 15-04-2024

Primary objective: To evaluate the efficacy of adjuvanttreatment with atezolizumabSee tabel 3 of the protocol.

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

Summary

ID

NL-OMON55502

Source
ToetsingOnline

Brief title
WO39210 IMmotion010

Condition

- Other condition
- Renal and urinary tract neoplasms malignant and unspecified
- Renal disorders (excl nephropathies)

Synonym
Kidney Cancer, Renal Cell Carcinoma

Health condition

Niercelcarcinoom

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Atezolizumab, High Risk, Nephrectomy, Renal Cell Carcinoma

Outcome measures

Primary outcome

Investigator-assessed DFS, defined as the time from randomization to the

earliest death from any cause or the first documented recurrence event assessed

by IRF, defined as any of the following:

Local recurrence of RCC

New primary RCC

Distant metastasis of RCC

Secondary outcome

• Overall survival defined as the time from randomization to death from any

cause

• Investigator assessed DFS in patients with PD-L1 expression status IC1/2/3

• Independent Review Facility (IRF)-assessed DFS

• IRF assessed DFS in patients with PD-L1 expression status IC1/2/3

• IRF-assessed event-free survival (EFS)

• Disease-specific survival, defined as the time from randomization to death

from RCC

• Distant metastasis-free survival, defined as the time from randomization to

the date of diagnosis of distant (i.e., non-locoregional)

metastases assesed by the investigator or death from any cause

• 3-year IRF-assessed DFS rate, defined as the probability of patients alive

and recurrence free at Year 3 after randomization

• 3-year investigator-assessed DFS rate

Study description

Background summary

Metastatic renal cell carcinoma (RCC) is the most lethal urologic cancer and the sixth leading cause of cancer deaths in developed nations. Worldwide in 2012 there were an estimated 337,860 new diagnoses and approximately 143,369 deaths secondary to RCC.
In the United States in 2016, it is estimated that there will be 62,700 new cases and 14,240 deaths attributable to cancers of the kidney and renal Pelvis. In developed nations, the average age-adjusted incidence of RCC is approximately 12 in 100,000 men and 5 in 100,000 in women. The RCC age-adjusted incidence has been rising for the past 30 years within the United States and most European nations at an annual rate of
approximately 3%. Active and passive smoking, hypertension, genetics, and obesity have been identified as risk factors and may contribute to the rising incidence. In addition, the rising use of medical imaging has led to increased
detection of asymptomatic lesions and an ensuing rise in incidence rates.

See protocol section 1: Background

Study objective

Primary objective:
To evaluate the efficacy of adjuvant
treatment with atezolizumab

See tabel 3 of the protocol.

Study design

This is a Phase III, multicenter, randomized, placebo-controlled, double-blind study designed to evaluate the efficacy and safety of adjuvant treatment with atezolizumab versus placebo in patients with RCC who are at high risk for disease recurrence following resection.

Intervention

Test product Atezolizumab or placebo is administered at a dose of 1200 mg by IV infusion on Day 1 of each 21- day cycle for 16 cycles or 1 year. Extra hospital visits will be performed to follow up recurence of desease.

Study burden and risks

See E9

Contacts

Public
Roche Nederland B.V.

Beneluxlaan 2a
Woerden 3446 GR
NL
Scientific
Roche Nederland B.V.

Beneluxlaan 2a
Woerden 3446 GR
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- Age >= 18 years
- Eastern Cooperative Oncology Group (ECOG) performance status of <= 1
- Able to comply with the study protocol, in the investigator*s judgment
- Pathologically confirmed RCC with a component of either clear cell histology or sarcomatoid histology that has not been previously treated in the adjuvant or neoadjuvant setting. Patient enrolled based on localized disease include those with T2 Grade 4, T3a Grade 3-4, T3b/c any grade, T4 any grade and TxN + any grade are eligible. Patients with pulmonary (treated with sub-lobar or lobar resection), lymph node, or soft-tissue metachronous recurrence of disease occurring greater than 12 months following nephrectomy who undergo complete resection are also eligible. Patients with synchronous adrenal and lung metastases who have undergone complete resection of residual disease witin 12 weeks of nephrectomy are eligible.
- Radical or partial nephrectomy with lymphadenectomy in select patients
- Representative formalin-fixed paraffin-embedded resected tumor specimens in paraffin blocks or at least 15 unstained slides, with an associated pathology report, for central testing and determined to be evaluable for tumor programmed death ligand-1 (PD-L1) expression prior to study enrollment
- Absence of residual disease and absence of metastasis, as confirmed by a negative baseline computed tomography (CT) of the pelvis, abdomen, and chest no more than 4 weeks prior to randomization
- Absence of brain metastasis, as confirmed by a negative CT with contrast or magnetic resonance imaging scan of the brain, no more than 4 weeks prior to randomization for those enrolled based upon a metastasectomy
- Full recovery from nephrectomy or metastasectomy within 12 weeks from randomization following surgery
- Adequate hematologic and end-organ function within 28 days prior to randomization
- For women of childbearing potential: agreement to remain abstinent or use contraceptive methods that result in a failure rate of < 1% per year during the treatment period for at least 5 months after the last dose of study drug and

agreement to refrain from donating eggs during this same period

Exclusion criteria

-Bilateral synchronous tumors with inheritable forms of RCC including von Hippel-Lindau
- Any approved anti-cancer therapy, including chemotherapy or hormonal therapy, within 3 weeks prior to initiation of study treatment
- Treatment with any other investigational agent or participation in another clinical study with therapeutic intent within 28 days or five half-lives of the investigational agent, whichever is longer, prior to enrollment
- Central nervous system metastases or leptomeningeal disease
- Malignancies other than RCC within 5 years prior to Cycle (C) 1, Day (D) 1. Patients with malignancies of a negligible risk of metastasis or death (e.g., risk of metastasis or death < 5% at 5 years) are eligible provided they meet all of the following criteria: Malignancy treated with expected curative intent (e.g., adequately treated carcinoma in situ of the cervix, basal or squamous cell skin cancer, or ductal carcinoma in situ of the breast treated surgically with curative intent). No evidence of recurrence or metastasis by follow-up imaging and any disease-specific tumor markers
- Life expectancy of < 24 weeks
- Pregnancy or lactation, or intending to become pregnant during the study
- Serum albumin < 2.5 g/dL
- History of severe allergic, anaphylactic, or other hypersensitivity reactions to chimeric or humanized antibodies or fusion proteins
- Known hypersensitivity or allergy to biopharmaceuticals produced in Chinese hamster ovary cells or any component of the atezolizumab formulation
- History of autoimmune diseases. Patients with a history of autoimmune-related hypothyroidism and Type 1 diabetes mellitus on a stable dose of hormone or insulin replacement may be eligible for this study. Patients with well controlled, limited autoimmune skin conditions may be eligible.
- Patients with prior allogeneic stem cell or solid organ transplantation
- History of idiopathic pulmonary fibrosis, drug-induced pneumonitis, organizing pneumonia, or evidence of active pneumonitis on screening chest CT scan
- Significant cardiovascular disease, such as New York Heart Association cardiac disease (Class III or greater), myocardial infarction within 3 months prior to initiation of study treatment, unstable arrhythmias, or unstable angina
- Patients with a known left ventricular ejection fraction <40%.
- Positive test for human immunodeficiency virus
- Patients with active hepatitis B and hepatitis C
- Active tuberculosis
- Severe infections within 4 weeks prior to initiation of study treatment.
- Receipt of therapeutic oral or intravenous antibiotics within 2 weeks prior to initiation of study treatment

- Major surgical procedure within 4 weeks prior to initiation of study treatment or anticipation of need for a major surgical procedure during the course of the study other than for diagnosis
- Administration of a live, attenuated vaccine within 4 weeks before C1D1
- Any other diseases, metabolic dysfunction, physical examination finding, or clinical laboratory finding giving reasonable suspicion of a disease or condition that contraindicates the use of an investigational drug or that may affect the interpretation of the results or render the patient at high risk from treatment complications
- Prior treatment with CD137 agonists, anti-CTLA-4, anti-PD*1, or anti*PD-L1 therapeutic antibody or pathway-targeting agents

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	09-10-2017
Enrollment:	12
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Tecentriq
Generic name:	Atezolizumab
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	25-01-2017
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	15-03-2017
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	23-04-2017
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	10-05-2017
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	07-06-2017
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	03-07-2017
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	13-07-2017
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO	

Date:	19-10-2017
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	26-10-2017
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	06-12-2017
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	07-03-2018
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	20-03-2018
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	09-04-2018
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	12-04-2018
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	26-04-2018
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek

	(Assen)
Approved WMO Date:	01-05-2018
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	24-06-2018
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	07-01-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	21-01-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	21-02-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	11-10-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	23-03-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	24-04-2020

Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	27-10-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	20-03-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	25-10-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	18-01-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	30-08-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	10-11-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	02-12-2022
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	EUCTR2016-001881-27-NL
CCMO	NL60191.056.17

Study results