A PHASE III, OPEN-LABEL, MULTICENTER, RANDOMIZED STUDY OF ATEZOLIZUMAB (ANTI-PD-L1 ANTIBODY) VERSUS OBSERVATION AS ADJUVANT THERAPY IN PATIENTS WITH PD-L1-SELECTED, HIGH RISK MUSCLE INVASIVE UROTHELIAL CARCINOMA AFTER SURGICAL RESECTION

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

Summary

ID

NL-OMON46906

Source
ToetsingOnline

Brief title
IMvigor 010 (WO29636)

Condition

- Other condition

Synonym
high risk muscle invasive urothelial cancer, Urothelial Cancer

Health condition

Hoog risico, spier geinvaseerde urotheelkanker.

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Atezolizumab, Intravenous, Surgical resection, Urothelial Carcinoma

Outcome measures

Primary outcome

Efficacy Outcome Measures

The primary efficacy outcome measure for this study is as follows:

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

of first occurrence of a DFS event, defined as any of the following:

Local (pelvic) recurrence of UC

Upper urinary tract or urethral recurrence of UC

Distant metastasis of UC

Death from any cause

Secondary outcome

The secondary efficacy outcome measures for this study are as follows:

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

• DSS, defined as the time from randomization to the date of death from UC per

investigator assessment of cause of death

• DMFS, defined as the time from randomization to the date of diagnosis of

distant (i.e., non-locoregional) metastases or death from any cause

For Safety Outcome Measures. Pharmacokinetic Outcome Measures, Patient-Reported

Outcome Measures and Exploratory Outcome Measures see paragraph 3.4.2, 3.4.3,

3.4.4 and 3.4.5 of the protocol

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.

Study objective

Efficacy Objectives
The primary efficacy objective for this study is as follows:
• To evaluate the efficacy of adjuvant atezolizumab treatment in patients with PD- L1*selected muscle invasive urothelial cancer, as measured by disease-free survival (DFS)
The secondary efficacy objectives for this study are as follows:
• To evaluate the efficacy of adjuvant atezolizumab treatment, as measured by overall survival (OS)
• To evaluate the efficacy of adjuvant atezolizumabtreatment, as measured by disease-specific survival (DSS)
• To evaluate the efficacy of adjuvant atezolizumabtreatment, as measured by distant metastasis-free survival (DMFS)

For the other objectives of the study please see paragraph 2. of the protocol.

Study design

Study WO29636 is a global Phase III, open-label, randomized, controlled trial designed to evaluate the efficacy and safety of adjuvant treatment withatezolizumab compared with observation in patients with PD-L1-selected urothelial cancrcinoma who are at high risk for recurrence following surgical resection.

Patients who have received prior neoadjuvant chemotherapy are eligible, but must have tumor staging of ypT2*4a or ypN+ at pathological examination of the cystectomy specimen. Patients who have not received prior neoadjuvant chemotherapy must be ineligible for or declined treatment with cisplatin-based adjuvant chemotherapy and have tumor staging of pT3*4a or pN+. Cystectomy tumor specimens from patients meeting eligibility criteria will be evaluated for PD-L1 expression by IHC.
.
Patients will be randomized to one of the following arms in a 1:1 ratio:
• Arm A (experimental arm): atezolizumab1200 mg q3w
• Arm B (control arm): Observation

For more information, see page 24 and 25 in the protocol.

Intervention

The dose level of atezolizumab to be tested in this study is 1200 mg (equivalent to an average body weight*based dose of 15 mg/kg) administered by IV infusion every 3 weeks (21 [± 3] days) for 16 cycles or 1 year (whichever occurs first).

Study burden and risks

The subject may get side effects from the drugs or procedures used in this study. Side effects can range from mild to severe and can vary from person to person. In some cases, side effects can be severe, long persisting or never disappear. There is also a very small risk of death.

SIDE EFFECTS RELATED ATEZOLIZUMAB TREATMENT

The subject may experience the side effects described below. It is also possible that side effects occur, which are not yet known at this time. As with any experimental drug, atezolizumab may cause unknown and potentially serious or life-threatening side effects.
The following adverse reactions are believed to be related to atezolizumab:
• Inflammation of the thyroid and adrenal glands (hypothyroidism, hyperthyroidism, or adrenal insufficiency)
• Hepatitis (inflammation of the liver)
• Pneumonitis (inflammation of the lungs)

• skin reactions (rash, itching, dry skin, redness and changes in skin pigmentation)
• Flu-like illness (symptoms include fever, fatigue, asthenia [lack of energy], chills, myalgia [muscle pain], arthralgia [joint pain] and headache).
• Reactions associated with infusion (adverse events occurred during infusion or within 1 day of infusion and include fever, chills, dyspnea and flushing).
• Colitis (inflammation of the intestines).
• Meningitis (inflammation of the membrane around the spinal cord and brain).
• Neuropathies (damage to the nerves).

The adverse reactions observed when atezolizumab is administered solely, are described in the protocol as well as the risks of other study procedures.

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

• Histologically confirmed muscle-invasive UC (also termed TCC) of the bladder or upper urinary tract (i.e., renal pelvis or ureters)
Patients with mixed histologies are required to have a dominant transitional cell pattern.
• TNM classification (UICC/AJCC 7th edition) at pathological examination of surgical resection specimen as follows:
For patients treated with prior neoadjuvant chemotherapy: tumor stage of ypT2 -4a or ypN+ (ypT2-4 or ypN+ for patients with UTUC)
For patients who have not received prior neoadjuvant chemotherapy: tumor stage of pT3*4a or pN+ (pT3-4 or pN+ for patients with UTUC)
• Surgical resection of muscle-invasive UC of the bladder, or UTUC

Exclusion criteria

• Treatment with any other investigational agent or participation in another clinical trial with therapeutic intent within 28 days or five half-lives of the drug, whichever is longer, prior to enrollment
• Any approved anti-cancer therapy, including chemotherapy, or hormonal therapy within 3 weeks prior to initiation of study treatment
• Adjuvant chemotherapy or radiation therapy for UC following surgical resection
Patients who have received primary chemoradiation for bladder preservation before cystectomy are eligible and will be treated as the same as patients who have received prior neoadjuvant chemotherapy.
Postsurgical intrapelvic/intravesical chemotherapy or BCG is not allowed for patients with UTUC.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	21-06-2016
Enrollment:	20
Type:	Actual

Medical products/devices used

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

Ethics review

Approved WMO Date:	03-07-2015
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	03-11-2015
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	12-01-2016
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	29-01-2016
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	12-02-2016
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO	

Date:	19-02-2016
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	16-08-2016
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	14-09-2016
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	21-10-2016
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	10-11-2016
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	12-01-2017
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	13-01-2017
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	28-04-2017
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	30-05-2017
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO	

Date:	27-06-2017
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	29-06-2017
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	25-07-2017
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	09-08-2017
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	19-10-2017
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	09-11-2017
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	17-11-2017
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	02-03-2018
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	09-04-2018
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO	

Date:	12-04-2018
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	28-05-2018
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	14-06-2018
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	15-11-2018
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	29-11-2018
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	17-12-2018
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	11-01-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	21-02-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	15-03-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO	

Date:	27-09-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	11-10-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	11-03-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	12-03-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	15-05-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	11-06-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	27-10-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	29-10-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	07-10-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO	

Date:	14-10-2021
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
EudraCT	EUCTR2014-005603-25-NL
ClinicalTrials.gov	NCT02450331
CCMO	NL53644.031.15

Study results