PERICLES (PEnile cancer Radio- and Immunotherapy CLinical Exploration Study) - a Phase 2 study of atezolizumab with or without radiotherapy in penile cancer

Published: 20-06-2018
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The primary objective is efficacy of atezolizumab in advanced penile cancer patients measured by progression-free survival.

Ethical review	Approved WMO
Status	Completed
Health condition type	Reproductive neoplasms male malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON52808

Source
ToetsingOnline

Brief title
PERICLES study

Condition

- Reproductive neoplasms male malignant and unspecified
- Penile and scrotal disorders (excl infections and inflammations)

Synonym
Penile cancer

Research involving
Human

Sponsors and support

Primary sponsor: Antoni van Leeuwenhoek Ziekenhuis
Source(s) of monetary or material Support: Farmaceutische industrie,Hoffmann-La Roche

Intervention

Keyword: Atezolizumab, Immunotherapy, Penile cancer, Radiotherapy

Outcome measures

Primary outcome

Progression-free survival (PFS) at 1 year after initiation of treatment. A PFS event is defined as RECIST 1.1 progressive disease (appearance of new lesions or progression of existing target/nontarget lesions) or death from any cause.

Secondary outcome

- Overall Survival (OS) rate at 2 years in the full study population

- Feasibility of combining immunotherapy with radiotherapy as measured by number of patients who complete the combined modality treatment (Arm A). Completion is defined as having received at least 90% of planned radiation doses.

- Locoregional Recurrence-free survival in patients treated with the combination of radiotherapy and atezolizumab (arm A)

- Response rate for patients with measurable disease

- Median PFS (as measured by RECIST 1.1) and OS for the full study cohort (Arm A+B)

- 2-year PFS (as measured by RECIST 1.1) and OS for PD-L1-positive patients in the full study cohort (Arm A+B)

- Toxicity by CTCAE-NCI V4 in the combined modality arm

Study description

Background summary

Patients with advanced penile cancer have a poor prognosis (21% 2-year overall survival from moment of diagnosis) and high morbidity due to progressive locoregional disease. Translational studies show high rates of infiltrating immune cells and PD-L1 positvity, suggesting that immunotherapy may be beneficial in this disease. Atezolizumab, targeting PD-L1, is active in several cancer types and is generally well-tolerated. This study will investigate whether atezolizumab can be combined with radiotherapy to control locoregional lymph node disease. Furthermore, the activity of atezolizumab in advanced penile cancer patients will be investigated.

Study objective

The primary objective is efficacy of atezolizumab in advanced penile cancer patients measured by progression-free survival.

Study design

This is a single-center, nonrandomized, Phase IB study with 2 treatment arms.

Intervention

All patients will receive atezolizumab, 1200 mg, every 3 weeks, by IV infusion. Patients in group A will additionally receive 33 fractions of 1.5 or 1.8 Gy irradiation on locoregional affected lymph nodes, concurrently with atezolizumab treatment.

Study burden and risks

Patients will be treated every 3 weeks with atezolizumab for one year or until loss of clinical benefit. Atezolizumab is generally well tolerated although immune-related toxicity does occur. Toxicity of combining atezolizumab with a long course of radiotherapy is unknown and may result in increased toxicity. It is unknown whether atezolizumab will induce responses in patients with advanced penile cancer.

*In exceptional cases, in consultation with the principal investigator and after careful consideration of the pros and cons with the subject, an

additional 1 year of treatment may be administered. This will only happen in the case of clinical benefit and good tolerance and therefore does not change the consideration in terms of risk/burden*.

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

- Age >= 18 years at time of study entry., - Advanced histologically documented, squamous cell carcinoma of the penis or distal urethra. Advanced disease is defined as:, -Distant metastases, OR, -LRAPC, defined as a large or inoperable primary tumor (T4), palpable nodes >3cm in diameter or fixed nodes, suspicion of extra-nodal extension or pelvic node involvement (N2/N3), Arm A: Locoregional disease (with or without distant metastases), likely to derive benefit from locoregional radiotherapy and not previously treated with

radiotherapy., Arm B: Benefit of locoregional radiotherapy unlikely OR previously treated with irradiation. , Adequate normal organ and marrow function as defined below: , -Haemoglobin >= 5.6/mmol/L, -White blood cell count (WBC) >= 2 x 109/L (> 1500 per mm3), -Absolute neutrophil count (ANC) >= 1.5 x 109/L (> 1500 per mm3), -Platelet count >= 100 x 109/L (>100,000 per mm3), -Serum bilirubin <= 1.5 x institutional upper limit of normal (ULN). This will not apply to subjects with confirmed Gilbert*s syndrome, who will be allowed in consultation with a study physician., -AST/ALT <= 2.5 x institutional ULN unless liver metastases are present, in which case it must be <= 5x ULN., -Serum creatinine clearance >30 mL/min by calculation with the Cockcroft-Gault formula (Cockcroft and Gault 1976) or by 24-hour urine collection measurement.

Exclusion criteria

1. Involvement in the planning and/or conduct of the study (applies to both Roche staff and/or staff at the study site). Previous enrolment in the present study., 2. Participation in another clinical study with an investigational product during the last 4 weeks, 3. Any previous treatment with a PD1 or PD-L1 inhibitor, 4. History of another primary malignancy except for:, •Malignancy treated with curative intent and with no known active disease >=2 years before the first dose of study drug, •Low potential risk of 3-year cancer-specific death (estimated<5%), including adequately treated non-melanoma skin cancer without evidence of disease, adequately treated carcinoma in situ without evidence of disease, or localized prostate cancer treated with curative intent and absence of prostate-specific antigen (PSA) relapse or incidental prostate cancer (Gleason score <= 7 and PSA < 10 ng/mL) undergoing active surveillance., 5. Treatment with the last dose of any systemic anti-cancer therapy <= 21 days prior to the first dose of study drug. Local treatment of isolated lesions for palliative intent is acceptable (eg, local surgery or radiotherapy). , 6. Current or prior use of immunosuppressive medication within 14 days before the first dose of study drug, with the exceptions of intranasal and inhaled corticosteroids or systemic corticosteroids at systemic doses below <= 10 mg/day of prednisone, or an equivalent corticosteroid., 7. History of primary immunodeficiency, allogeneic organ transplant or autoimmune disease, including, but not limited to, myasthenia gravis, myositis, autoimmune hepatitis, systemic lupus erythematosus, rheumatoid arthritis, inflammatory bowel disease, vascular thrombosis associated with antiphospholipid syndrome, Wegener*s granulomatosis, Sjögren*s syndrome, Guillain-Barré syndrome, multiple sclerosis, vasculitis, or glomerulonephritis.* Patients with a history of autoimmune-related hypothyroidism on a stable dose of thyroid replacement hormone will not be excluded from this study. Patients with controlled diabetes mellitus type 1 on a stable dose of insulin regimen may be eligible for this study. , 8. Uncontrolled intercurrent illness including, but not limited to, ongoing or active infection (including acute or

chronic hepatitis B, hepatitis C or human immunodeficiency virus (HIV), symptomatic congestive heart failure, unstable angina pectoris, cardiac arrhythmia, active peptic ulcer disease or gastritis, active bleeding diatheses or psychiatric illness/social situations that would limit compliance with study requirements or compromise the ability of the subject to give written informed consent, 9. Known active tuberculosis, 10. Any condition that, in the opinion of the investigator, would interfere with evaluation of study treatment or interpretation of patient safety or study results, 11. Brain metastases or leptomeningeal disease. Inclusion of patients with brain metastases is allowed if patients have been adequately treated and no signs of progression on brain imaging >=*28 days after completion of treatment (including surgery, radiotherapy or treatment with systemic corticosteroids). , 12. Subjects with uncontrolled seizures.

Study design

Design

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

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	18-10-2018
Enrollment:	32
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:	20-06-2018
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	05-09-2018
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	19-10-2018
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	25-10-2018
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	15-11-2018
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	25-01-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	15-02-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	30-10-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	12-02-2021

Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	18-02-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	18-02-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	24-02-2022
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	EUCTR2018-000603-17-NL
CCMO	NL65067.031.18