A Phase III, Randomized, Double-Blind, Placebo-Controlled Clinical Trial of Pembrolizumab (MK-3475) as Monotherapy in the Adjuvant Treatment of Renal Cell Carcinoma Post Nephrectomy (KEYNOTE-564)

Published: 12-12-2018
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This study has been transitioned to CTIS with ID 2022-501251-81-00 check the CTIS register for the current data. To compare disease free and overall survival of RCC patients, after adjuvant treatment with pembrolizumab after surgical renal resection...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Renal and urinary tract neoplasms malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON47954

Source
ToetsingOnline

Brief title
KEYNOTE-564

Condition

- Renal and urinary tract neoplasms malignant and unspecified

Synonym
RCC, renal cell carcinoma

Research involving

Human

Sponsors and support

Primary sponsor: Merck Sharp & Dohme (MSD)
Source(s) of monetary or material Support: MSD/Merck Sharp & Dohme

Intervention

Keyword: Adjuvant, Pembrolizumab, Post Nephrectomy, Renal Cell Carcinoma

Outcome measures

Primary outcome

Disease free survival (DFS)

Secondary outcome

Adverse Events

First local recurrence

DFS / OS in relation to PD-L1 expression

Quality of life, functional (dis)ability, disease related symptoms as reported

by the patient

Study description

Background summary

Renal cell carcinoma (RCC) is a relatively prevalent disease. Worldwide, there are an estimated 209.000 newly diagnosed cases and an estimated 102.000 deaths per year. Amongst others, because of the risk factors (smoking and obesity), the incidence of this type of cancer has been increasing in the past decades. Treatment generally consists of radical surgical resection, but a percentage of these patients will have recurrence. The estimated 5-year survival of subjects with localized RCC is approximately 90%. This percentage decreased to 65% in locally advanced RCC and only 12% in metastatic RCC.
Apart from radical surgical resection, no viable adjuvant treatment options are

currently available, but there are indications that immune therapy could potentially have a positive effect on disease free survival and overall survival (DFS and OS). The therapy is usually well tolerated. The objective of this study is to demonstrate a positive effect of immune therapy on DFS and OS in patients with median-high to high risk on recurrent disease, after renal resection.

Study objective

This study has been transitioned to CTIS with ID 2022-501251-81-00 check the CTIS register for the current data.

To compare disease free and overall survival of RCC patients, after adjuvant treatment with pembrolizumab after surgical renal resection. The objective of the study is to demonstrate that treatment with pembrolizumab, in comparison to placebo, will show a positive effect on DFS and OS.

Study design

This is a double-blind placebo-controlled randomized study. Subjects will be randomized to one of two treatments groups, either placebo or pembrolizumab. Patients will receive up to 17 treatment cycles with the study medication and will be entering long term follow up after treatment conclusion.

Intervention

3-week treatment cycles with pembrolizumab or placebo

Study burden and risks

For this study, patients will be subjected to invasive procedures such as blood collection, IV line insertion, CT-MRI or bone scans, physical exams, possibly confrontational questionnaires, and patients will be asked to visit the hospital regularly. Patients will be administered with pembrolizumab or placebo through an IV line, during three-week cycles, up to a maximum of 17 treatments. Patients receiving pembrolizumab might experience a positive treatment effect, however, this is not certain. For patients receiving placebo, no therapeutic effect is foreseen.
For this group of patients, there are currently no adjuvant treatment options available. Chemotherapy and radiotherapy are not effective in treatment of RCC. Management consists of regular follow up. In the standard of care setting, blood testing and scans are used to monitor the disease. Treatment with the investigational drug and risks of side effects thereof, as well as the questionnaires, are additional in comparison to standard treatment. Pembrolizumab has an acceptable risk profile and is well tolerated. The results of this study will contribute to more knowledge of the treatment of RCC and

will hopefully lead to more options for treatment of this patient group.

Contacts

Public
Merck Sharp & Dohme (MSD)

Waarderweg 39
Haarlem 2031 BN
NL
Scientific
Merck Sharp & Dohme (MSD)

Waarderweg 39
Haarlem 2031 BN
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. Histologically confirmed diagnosis of RCC with clear cell component with or without sarcomatoid features. Diagnosis of RCC with clear cell component is to be made
by the investigator and does not require central histology review.
2. Be >= 18 years of age on day of signing informed consent.
Female Participants:
3. Female participants of childbearing potential must have a negative urine or serum
pregnancy test within 72 hours prior to randomization.

4. 5. Use of acceptable contraception for the duration of the study (from first dose until 120 days after last dose of study medication).
6. Written informed consent/assent for the trial.
7. Intermediate high-risk, high-risk, or M1 NED RCC as defined by protocol.
8. Have received no prior systemic therapy for advanced RCC
9. Have undergone a partial nephroprotective or radical complete nephrectomy incl metastases, with negative surgical margins

Exclusion criteria

1. Has had major surgery, other than nephrectomy and/or resection of pre-existing
metastases for M1 NED participants, within 12 weeks prior to randomization. Note: If participants received major surgery, they must have recovered adequately from
the toxicity and/or complications from the intervention prior to starting study treatment.
2. Has received prior radiotherapy for RCC.
3. Has pre-existing brain or bone metastatic lesions.
4. Has residual thrombus post nephrectomy in the vena renalis or vena cava.
5. Has a diagnosis of immunodeficiency or is receiving chronic systemic steroid therapy or any other form of immunosuppressive therapy within 7 days prior the first dose of study treatment.
6. Has an active autoimmune disease that has required systemic treatment in past 2 years.
7. Has a known additional malignancy that is progressing or required active treatment <=3
years ago. 8. Has a history of (non-infectious) pneumonitis that required steroids or has current pneumonitis.
9. Has an active infection requiring systemic therapy.
10. Has a history of, or is currently on, dialysis
11. Has a known history of human immunodeficiency virus infection.
12. Has a known active hepatitis B or hepatitis C virus
13. Has a known history of active tuberculosis

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:	Recruiting
Start date (anticipated):	05-06-2019
Enrollment:	9
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	KEYTRUDA
Generic name:	pembrolizumab
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	12-12-2018
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	02-01-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	04-04-2019
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO Date:	04-10-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	10-10-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	19-11-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	15-04-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	03-06-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	18-11-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	14-05-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	21-10-2021
Application type:	Amendment

Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	22-04-2022
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
EU-CTR	CTIS2022-501251-81-00
EudraCT	EUCTR2016-004351-75-NL
ClinicalTrials.gov	NCT03142334
CCMO	NL67924.056.18