A Phase III, Open Label, Randomised, 3 Arm, Multi Centre Study of Savolitinib plus Durvalumab versus Sunitinib and Durvalumab Monotherapy in Participants with MET Driven, Unresectable and Locally Advanced or Metastatic Papillary Renal Cell Carcinoma (PRCC)

Published: 30-06-2021
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This study has been transitioned to CTIS with ID 2022-503105-38-00 check the CTIS register for the current data. The purpose of this study is to assess whether a new combination treatment (Savolitinib and Durvalumab) is better than standard...

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

Summary

ID

NL-OMON54072

Source
ToetsingOnline

Brief title
SAMETA

Condition

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

Synonym

Renal tumour

Research involving
Human

Sponsors and support

Primary sponsor: Astra Zeneca
Source(s) of monetary or material Support: AstraZeneca AB

Intervention

Keyword: Durvalumab, MET Driven, Savolitinib, Sunitinib

Outcome measures

Primary outcome

Primary Endpoint:

- Progression-Free Survival

More details see protocol v1.0 par 9.5.2.1

Secondary outcome

Secondary Endpoints:

- Overall Survival

- Objective Response Rate

- Duration of Response

- Disease Control Rate

- Time from Randomisation to Second Progression or Death (PFS2)

- Clinical Outcome Assessments

More details see protocol v1.0 par 9.5.2.2

Study description

Background summary

Papillary RCC is the most common subtype of nccRCC, accounting for 10% to 15% of renal malignancies. Few studies have evaluated a specific treatment for PRCC as the primary histologic tumour type. In practice, treatment of PRCC is based on data from studies conducted in ccRCC, and international clinical guidelines recommend a clinical study as one of the preferred options for treatment of advanced/metastatic PRCC patients. Therefore, effective treatment for patients with PRCC represents an unmet medical need. Abnormalities of MET are not only a differentiating characteristic of PRCC, but may be a potential therapeutic target. The MET pathway may also be involved in immunomodulation. Non-clinical and clinical data suggest that there is a potential synergistic anti-tumour effect of a MET inhibitor in combination with an immune checkpoint inhibitor. The SAMETA study aims to evaluate the efficacy and safety of the savolitinib plus durvalumab combination compared with sunitinib in first-line participants with unresectable and locally advanced or metastatic PRCC that is MET driven without co-occurring FH mutations. The study will also investigate the contribution of durvalumab to the savolitinib plus durvalumab combination.

Study objective

This study has been transitioned to CTIS with ID 2022-503105-38-00 check the CTIS register for the current data.

The purpose of this study is to assess whether a new combination treatment (Savolitinib and Durvalumab) is better than standard treatment sunitinib in MET-driven PRCC. The study will also assess the contribution of one part of the combination (Durvalumab) into the overall treatment efficacy.

Study design

This is a Phase III, randomised, open label, 3 arm, multi-centre, international study assessing the efficacy and safety of savolitinib plus durvalumab compared with sunitinib in participants with MET-driven (without co-occurring FH mutations), unresectable and locally advanced or metastatic PRCC, who have not received any prior systemic anti-cancer therapy in the metastatic setting. The study will also investigate the contribution of durvalumab to the savolitinib plus durvalumab combination.

See also protocol v1.0. - par 1.2, figure 1 Study Design

Intervention

The treatments options include
1) treatment with 2 investigational drugs, savolitinib and durvalumab in combination;
2) treatment with 1 investigational drug, durvalumab, alone; and
3) treatment with sunitinib which is a standard treatment for PRCC.

See also protocol v1.0 par 6. Study Intervention

Study burden and risks

Overall the benefit/risk assessment supports the further investigation of savolitinib plus durvalumab versus sunitinib in participants with MET-driven, unresectable and locally advanced or metastatic PRCC based upon: the non*clinical and clinical safety profile of savolitinib and durvalumab as monotherapies, the preliminary clinical safety profile of savolitinib in combination with durvalumab from the CALYPSO study, the risk minimisation and AE management plans, the study design, the limited life expectancy due to malignant disease, the lack of effective alternative treatments, the strength of the scientific hypothesis under evaluation based on efficacy data of savolitinib monotherapy from Phase II and III studies (SAVOIR) in PRCC, the anti-tumour activities of other IO monotherapies in PRCC, non-clinical data showing potential synergistic anti-tumour activities of MET inhibition and anti-PD-L1, and emerging clinical efficacy signals from CALYPSO study.

See protocol v1.0 par 2.3.3

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

• Histologically confirmed unresectable and locally advanced or metastatic PRCC
• PRCC must be centrally confirmed as MET-driven using a sponsor-designated central laboratory validated NGS assay
• No prior systemic anti-cancer treatment in the metastatic setting; no prior exposure to MET inhibitors, Durvalumab or Sunitinib in any setting
• Karnofsky Score > 70
• At least one lesion, not previously irradiated, that can be accurately measured at baseline
• Adequate organ and bone marrow function
• Life expectancy >=12weeks at Day 1

Exclusion criteria

• History of serious liver disease, with or without, normal LFTs, such as cirrhosis or Wilson*s disease
• Spinal cord compression or brain metastases, unless asymptomatic and stable on treatment for at least 14 days prior to study intervention
• Active or prior cardiac disease (within past 6 months) or clinically significant ECG abnormalities and/or factors/medications that may affect QT and/or QTc intervals
• Active infection including HIV, TB, HBV and HCV
• Active or prior documented autoimmune or inflammatory disorders
• Receipt of live attenuated vaccine within 30 days prior to the first dose of study intervention

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	21-12-2021
Enrollment:	14
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	IMFINZI
Generic name:	Durvalumab
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	n/a
Generic name:	Savolitinib
Product type:	Medicine
Brand name:	Sutent
Generic name:	Sunitinib
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	30-06-2021
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	14-10-2021
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	08-02-2022
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	03-03-2022
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	10-03-2022
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	06-04-2022
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	10-09-2022
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	21-09-2022
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	11-02-2023
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO	

Date:	23-03-2023
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	24-07-2023
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	15-12-2023
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	05-02-2024
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	CTIS2022-503105-38-00
EudraCT	EUCTR2021-000336-55-NL
CCMO	NL77678.091.21