The effect of extra hydration on kidney function during carboplatin-pemetrexed-pembrolizumab in patients with advanced non-small cell lung cancer.;*Hydration to prevent nephrotoxicity due to pemetrexed (HydraPem Study)*

Published: 25-07-2022
Last updated: 07-02-2025

To investigate the effect of fluid infusion to prevent deterioration of kidney function due to pemetrexed, during treatment with carboplatin, pemetrexed and pembrolizumab in patients with non-squamous NSCLC. The primary objective is to reduce the…

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Respiratory and mediastinal neoplasms malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON52079

Source
ToetsingOnline

Brief title
HydraPem Study

Condition

- Respiratory and mediastinal neoplasms malignant and unspecified
- Renal disorders (excl nephropathies)

Synonym

kidney injury, nephrotoxicity

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: Lilly

Intervention

Keyword: Hydration, Non-squamous non-small cell lung cancer, Premetrexed, Renal failure

Outcome measures

Primary outcome

The main endpoints are a decline in kidney function (AKD) based on: eGFR < 60

mL.min-1 per 1.73m2 for < 3 months, or decrease in eGFR by > 35 or increase in

serum creatinine >50% for <3 months.

Secondary outcome

TIme to occurence of AKD

Rate of decline kidney function (eGFR)

Treatment dose intensity, including number of dose reductions

Study description

Background summary

Platinum-pemetrexed chemotherapy combined with pembrolizumab is standard first-line treatment for patients with non-squamous non-small cell lung cancer (NSCLC) without driver mutation (EGFR mutation or ALK translocation) and programmed death ligand 1 (PD-L1) expression below 50%. Pemetrexed is known to cause renal failure. Pemetrexed is almost exclusively eliminated by the kidney. Renal impairment during pemetrexed maintenance therapy may lead to permanent kidney injury and impair future treating options. Exploring strategies for protection from development of nephrotoxicity is valuable. We hypothesize that hydration during treatment with pemetrexed decreases the risk of developing

renal impairment.

Study objective

To investigate the effect of fluid infusion to prevent deterioration of kidney function due to pemetrexed, during treatment with carboplatin, pemetrexed and pembrolizumab in patients with non-squamous NSCLC. The primary objective is to reduce the incidence of acute kidney disease (AKD) from 30 to 10%. Secondary objective is to prevent the development of chronic kidney disease (CKD).

Study design

This is a randomized controlled multicenter study to investigate the effect of fluid infusion to prevent deterioration of kidney function due to pemetrexed, during treatment with carboplatin, pemetrexed and pembrolizumab. Patients will receive 4 cycles of induction carboplatin (AUC 5), pemetrexed (500mg/m2) and pembrolizumab <65kg: 100mg, from 65kg: 150mg, followed by 4 cycles of pemetrexed (500mg/m2) and pembrolizumab (<65kg: 100mg, from 65kg: 150mg) as maintenance therapy. Pations will be randomized 1:1 to receive carboplatin, pemetrexed and pembrolizumab as standard of care, or with subsequently infusion of 500mL intravenous saline 0.9%. Blood samples for measurement of creatinine in order to estimate renal function, will be drawn at baseline and prior to start of each treatment cycle, which is standard of care.

Intervention

Intravenous infusion of 500mL NatriumChloride 0.9%

Study burden and risks

The intervention in this study is the infusion of 500mL saline 0.9%, subsequently after chemo-immunotherapy infusion. The risk of decompensation cordis due to the extra fluid infusion is small, since patient with cardiac failure are excluded. The risk of blood withdrawals is negligible and part of standard of care. The benefit is the hypothesed reduction of the development of kidney damage.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

Age > 18 years
Patients must be willing and capable of giving written informed consent
Patients with advanced non-squamous cell lung cancer, receiving first line treatment with pemetrexed/pembrolizumab maintenance after carboplatin/pemetrexed/pembrolizumab.
ECOG 0-2
Adequate hematological, renal and liver functions.

Exclusion criteria

• Subject with an active auto-immune disease requiring systemic treatment
• Lung disease requiring systemic steroids in doses of >10 mg prednisolone (or equivalent dose of another steroid)
• Previous allogeneic or organ transplant
• Known heart failure
• Myocardial infarction previous 6 months
• Serious concomitant systemic disorders (for example active infection, unstable cardiovascular disease) which in the opinion of the investigator would compromise the patient's ability to complete the study, or would interfere with

the evaluation of the efficacy and safety of the study treatment

Study design

Design

Study phase:	4
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Diagnostic

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	17-01-2023
Enrollment:	118
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	500mL intravenous saline 0.9%
Generic name:	NaCL
Registration:	Yes - NL intended use

Ethics review

Approved WMO

Date:	25-07-2022
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO

Date:	26-07-2022
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	19-10-2022
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	29-11-2022
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	EUCTR2022-001975-15-NL
CCMO	NL77514.078.22