THE ADDED VALUE OF 166HO TRANS-ARTERIAL RADIOEMBOLIZATION TO SYSTEMIC THERAPY IN LIVER METASTATIC BREAST CANCER PATIENTS

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We aim to introduce 166Ho radioembolization combined with systemic chemotherapy and investigate its safety and feasibility.

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

Summary

ID

NL-OMON51771

Source
ToetsingOnline

Brief title
HoLiBreast

Condition

- Hepatobiliary neoplasms malignant and unspecified
- Metastases

Synonym
liver metastatic breast cancer; metastasis in the liver from breast cancer

Research involving
Human

Sponsors and support

Primary sponsor: Antoni van Leeuwenhoek Ziekenhuis

Source(s) of monetary or material Support: Terumo,Terumo Europe

Intervention

Keyword: Brachytherapy, Breast neoplasms, Intra-arterial injection, Neoplasm metastasis

Outcome measures

Primary outcome

We expect that this treatment strategy of TARE and systemic chemotherapy is feasible if 85% of the included patients safely received the combination therapy. Safety is defined as the percentage of the 90 day post-radioembolization toxicity (CTCAE/SIR grade 3 or higher) which leads to discontinuation of the current systemic chemotherapy.

Secondary outcome

We will collect data that might be associated with lesion- and patient-based response, overall toxicity and quality of life. These data can be used to improved future study protocols.

Study description

Background summary

Liver metastases occur in approximately 50% of the metastatic breast cancer patients and are an independent negative prognostic factor for OS. Most LMBC patients have extended systemic disease and will therefore receive systemic therapy. Challenges of chemotherapy remain the toxicity levels and resistance which necessitate a switch or a break of chemotherapeutical. When patients become resistant to systemic therapy and have liver metastasis, they may benefit from an intra-arterial therapy, such as TARE. The available literature for TARE in LMBC patients is however more limited with mainly retrospective or small prospective series. Nevertheless, these reports show promising results with a pooled response rate of 49% (range 9-100%) and a pooled median survival of 9.2 months (range 6.1-35.4 months). The longest OS after TARE to date was reached in the study that combined 90Y TARE with systemic therapy in 83% of the

patients. Yet, two out of the four serious adverse events occurred in the patients that concurrently received pembrolizumab and carboplatin. Therefore, safety of the combination of TARE and systemic therapy should be evaluated first before moving into an efficacy trial. The current available evidence for TARE in LMBC patients is mainly built with 90Y microspheres. 166Ho microspheres have recently become available in the European market as the third type of microspheres for radioembolization. 166Ho has specific imaging and treatment benefits over 90Y TARE which can potentially enhance the results of this treatment in unresectable liver metastases. To date, only small numbers of LMBC patients are treated with 166Ho radioembolization.
We hypothesize that the addition of 166Ho TARE to systemic chemotherapy can enhance the response rate of liver metastatic breast cancer patients after failed initial systemic chemotherapy with an acceptable toxicity level.

Study objective

We aim to introduce 166Ho radioembolization combined with systemic chemotherapy and investigate its safety and feasibility.

Study design

Multicenter clinical pilot study.

Intervention

Patients start with their newly selected chemotherapy. If no extra-hepatic tumour progression is seen after their chemotherapy evaluation of the newly selected therapy, she can be screened for inclusion. A blood sample is taken and a liver MRI, and a mapping angiography will be performed to evaluate if she is suitable for radioembolization. If she is suitable for TARE and meets the inclusion criteria she can be included. The radioembolization will be performed within two weeks after the mapping angiography. Chemotherapy needs to be stopped 2-5 weeks prior to TARE and can be continued after two weeks at earliest.

Study burden and risks

We expect that the addition of 166Ho TARE to systemic chemotherapy can enhance the response rate a of liver metastatic breast cancer patients and eventually improve survival in this patient population. It is expected that the combined use of systemic chemotherapy and TARE has an increased but acceptable toxicity over the use of systemic chemotherapy alone. With our strict inclusion criteria we try to select a group of patients that is less prone for toxicity. The toxicity will be an endpoint of this study. Patients need to visit the hospital 6 times extra for this study and have to fill in three Quality of life forms. Two extra blood samples will be taken and two MRI's of the liver will be

performed. The screenings investigations and the actual treatment are included in these 6 extra hospital visits. These procedures are minimal invasive and will be performed at most under local anesthesia.

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

• Women >18 years
• Patients with hormone positive and HER2 negative liver dominant metastatic breast cancer
• No extra-hepatic disease progression at the evaluation of at least second line systemic chemotherapy
• Suitable for TARE evaluated after the mapping angiography
• Measurable target tumors in the liver according to RECIST 1.1

• Liver tumor burden <50 %
• ECOG performance score 0 to 1
• Laboratory parameters: neutrophils >1000/µL; thrombocyte count >1000000 µL; eGFR >45/mL/min/1.73 m2; albumin > 3.0 g/dl, bilirubin < 1.5x ULN (unless Gilbert syndrome); aminotransferase (ALAT/ASAT) <3.0 ULN
• Able to read Dutch

Exclusion criteria

• Life expectancy <=3 months
• Patient eligible for other curative local liver therapy (ea. surgery, ablation)
• Brain, pleural, peritoneal or extensive visceral metastases
• Other life-threatening disease (i.e. Dialysis, unresolved diarrhea, serious unresolved infections (HIV, HBV, HCV etc.))
• Contraindication for angiography or MRI
• Significant toxicities due to prior cancer therapy that have not resolved before the initiation of the study, if the investigator determines that the continuing complication will compromise the safe treatment of the patient
• Prior or planned embolic intra-arterial liver directed therapy (TACE, TAE, TARE)
• Prior or planned external or internal radiation therapy of the liver
• Cirrhosis or portal hypertension
• Main portal vein thrombosis
• Intervention for, or compromise of, the Ampulla of Vater
• Ascites (except minor focal ascites)
• Baseline use of analgesics for abdominal pain
• Pregnancy (Women at childbearing potential need at least one form of birth control) or breastfeeding
• Flow to extra hepatic vessels not correctable by reposition or embolization
• Estimated dose to the lungs greater than 30 Gy in a single administration or 50 Gy cumulatively
• Target tumoral absorbed dose of < 90Gy or an absorbed dose to the normal liver parenchyma of >50Gy.

Study design

Design

Study type: Interventional
Masking: Open (masking not used)

Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	19-10-2023
Enrollment:	7
Type:	Actual

Medical products/devices used

Generic name:	166Ho microspheres
Registration:	Yes - CE intended use

Ethics review

Approved WMO Date:	06-12-2022
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	11-12-2024
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
CCMO	NL81493.041.22