Trial Description

Title

Safety and Efficacy of Ho-166-Radioembolisation by SPECT- and MR-Image guidance optimized substrate application - a comparative Study to Y-90-Radioembolisation

Trial Acronym

HOLOGRAMM I

URL of the trial

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Brief Summary in Lay Language

The study is a comparison of efficacy and safety in clinical application of two approved radioembolisates (so-called phase 4 trial). Treatment will be performed in patients with liver metastases from colorectal carcinoma (or mamma carcinoma) by Holmium-166 (Ho-166) labeled microspheres (QuiremSpheres) or alternatively Yttrium-90 (Y-90) labeled microspheres (Y-90-SIR-Spheres). Patients will be treated in concordance to clinically standard procedure of the different radioembolisation procedures. The assignment to the treatment arms (QuiremSpheres vs. Y-90-SIR-Spheres) is performed by a random process (randomization). The duration of the study, including treatment and follow-up, is one year after finishing radioembolisation procedure. Imaging commonly performed in treatment (6w, and 3, 6, 9, 12 months post therapy) is supplemented by questionnaires regarding quality of live.

Brief Summary in Scientific Language

The study is a comparison of efficacy and safety of radioembolisation (RE) in clinical application in patients with hepatic metastases from colorectal carcinoma (or mamma carcinoma) for two approved radioembolisates (so-called phase 4 trial). The radioembolisates are Y-90-SIR-Spheres (Arm A) and die Ho-166-QuiremSpheres (Arm B). Both substances are approved for treatment of liver metastases. The intended use in the study is in concordance to the individual approval. The study includes radioembolisation and follow-up. Follow-up procedure includes image-based evaluation with contrast-enhanced MRI plus laboratory-chemical examination for a time frame of 12 months. In parallel, quality of life is evaluated by standardized questionnaires.

Organizational Data

- DRKS-ID: **DRKS00014139**
- Date of Registration in DRKS: **2018/03/01**
- Date of Registration in Partner Registry or other Primary Registry: **[---]***
- Investigator Sponsored/Initiated Trial (IST/IIT): **yes**

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Investigator Sponsored/Initiated Trial (IST/IIT): **yes**

- Ethics Approval/Approval of the Ethics Committee: **Approved**
- (leading) Ethics Committee Nr.: **07/18 , Ethikkommission der Medizinischen Fakultät der Otto-von-Guericke-Universität Magdeburg**

Secondary IDs

- Universal Trial Number (UTN): **U1111-1209-8693**

Health condition or Problem studied

- ICD10: **C18 - Malignant neoplasm of colon**
- ICD10: **C50 - Malignant neoplasm of breast**

Interventions/Observational Groups

- Arm 1: **Patients with hepatic metastases from colorectal carcinoma or mamma carcinoma and indication for Radioembolisation (RE) with Y-90-microspheres (Y-90-SIR-Spheres)**

  In this arm treatment is performed using Y-90-Microspheres. Screening is part of clinical routine (data from clinical routine ≤ 45 days before randomization). Patients are assigned to a study arm by randomization (first RE has to be performed ≤ 20 days after randomization).

  Treatment is performed using a single time point setup (single liver lobe) or sequentially at dual time points (both liver lobes, sequentially 2. RE 4-6 weeks after 1.RE).

  Quality-of-live questionnaire is assessed prior to 1. RE (Baseline Assessment). Y-90-PET/CT is performed 1-2 days after RE to document intrahepatic distribution of the radioembolisate.

  Within Follow-Up additionally data were observed:

  (1.) Blood tests, (2.) contrast media enhanced liver MRI und (3.) Quality-of-Life

  (1.) Blood tests: 1-2 days after RE and 4-6 weeks, 3 months, 6 months, 9 months und 12 months after RE.

  (2.) Contrast media enhanced liver MRI: 1-2 days after RE (incl. DWI) and 4-6 weeks, 3 months, 6 months, 9 months und 12 months after RE.

(3.) Quality-of-Life questionnaire: 6-9 days after RE and 4-6 weeks, 3 months, 6 months, 9 months und 12 months after RE.

In a sequentially setup (bilobar treatment): Items (1.) - (3.) are repeated 4-6 weeks after the 2. RE. Additionally, blood tests were performed before 2. RE.

All data were observed until hepatic progression. Furthermore, over all survival is monitored.

- Arm 2: **Patients with hepatic metastases from colorectal carcinoma or mamma carcinoma and indication for radioembolisation with Ho-166-microspheres (QuiremSpheres)**

  In this arm treatment is performed using Ho-166-Microspheres. Screening is part of clinical routine (data from clinical routine ≤ 45 days before randomization). Patients are assigned to a study arm by randomization (first RE has to be performed ≤ 20 days after randomization).

  Treatment is performed using a single time point setup (single liver lobe) or sequentially at dual time points (both liver lobes, sequentially 2. RE 4-6 weeks after 1.RE).

  Quality-of-live questionnaire is assessed prior to 1. RE (Baseline Assessment). SPECT-CT is performed 1-2 days after RE to document intrahepatic distribution of the radioembolisate.

  Within Follow-Up additionally data were observed:

  (1.) Blood tests, (2.) contrast media enhanced liver MRI und (3.) Quality-of-Life

  (1.) Blood tests: 1-2 days after RE and 4-6 weeks, 3 months, 6 months, 9 months und 12 months after RE.

  (2.) Contrast media enhanced liver MRI: 1-2 days after RE (incl. DWI and T2*) and 4-6 weeks (incl. T2*), 3 months (incl. T2*), 6 months(incl. T2*), 9 months und 12 months after RE.

  (3.) Quality-of-Life questionnaire: 6-9 days after RE and 4-6 weeks, 3 months, 6 months, 9 months und 12 months after RE.

  In a sequentially setup (bilobar treatment): Items (1.) - (3.) are repeated 4-6 weeks after the 2. RE. Additionally, blood tests were performed before 2. RE.

  All data were observed until hepatic progression. Furthermore, over all survival is monitored.

Characteristics

- Study Type: **Interventional**
- Study Type Non-Interventional: **[---]***

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- Allocation: **Randomized controlled trial**
- Blinding: **[---]***
- Who is blinded: **[---]***
- Control: **Active control (effective treament of control group)**
- Purpose: **Treatment**
- Assignment: **Parallel**
- Phase: **IV**
- Off-label use (Zulassungsüberschreitende Anwendung eines Arzneimittels): **N/A**

Primary Outcome

Efficacy and safety of radioembolisation with Ho-166-labeled microspheres (QuiremSpheres) in comparison to Y-90-SIR-Spheres

Secondary Outcome

- Prediction of therapeutically accumulation pattern (QuiremSpheres or SIR-Spheres) by accumulation pattern from pre-therapeutic evaluation (e.g. by Tc-99m-MAA)
- Dose response relationship
- Quality-of-Life
- Estimation of dysfunctional liver volume after RE by contrast media enhanced MRI
- Use of MRI (T2*) for dosimetry in Ho-166 labeled microspheres (QuiremSpheres)

Countries of recruitment

- DE **Germany**

Locations of Recruitment

- University Medical Center **Universitätsklinikum Magdeburg A.ö.R., Magdeburg**

Recruitment

- Planned/Actual: **Actual**
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Planned/Actual: **Actual**

(Anticipated or Actual) Date of First Enrollment: **2018/06/20**

- Target Sample Size: **100**
- Monocenter/Multicenter trial: **Monocenter trial**
- National/International: **National**

Inclusion Criteria

- Gender: **Both, male and female**
- Minimum Age: **18 Years**
- Maximum Age: **90 Years**

Additional Inclusion Criteria

- Patients with histopathological and cytological validated non-resectable and/or non-ablative intrahepatic mCRC od Mamma-CA with a liver-only or liver-predominant intra-hepatic spread after exhausted treatment compliant with standards,
- ECOG performance status of 0 - 1,
- Estimated life expectancy of at least 3 months without any active intervention/treatment,
- Patients have to be eligible for both treatment options (arm A: SIR-Spheres or arm B: QuiremSpheres) according to the clinical assessment of the treating observer/physician (considering labor-chemical evaluation, results from Tc-99m-MAA evaluation plus further results from clinically available imaging e.g. whole-body F-18-FDG PET/CT)

Exclusion criteria

- Liver-lung-shunt > 20 % or lung exposure >= 25 Gy from application of the radioembolisate,
- Preceding external radio therapy of the liver,
- Presence of a clinically liver insufficiency,
- Anormal vessel anatomy from pre-therapeutic angiogram, with possibility of a significant back flow of hepatic arterial blood into stomach, pancreas or bowel (extra-hepatic-abdominal accumulation from Tc-99m-MAA liver perfusion scintigraphy) which was unremedied by a re-evaluation (Dudeck et al 2012 CVIR),
- Treatment with Capecitabin during the last two months before therapy or a planned treatment with Capecitabin early after therapy with QuiremSpheres® or SIR-Spheres®,
- Conventional chemotherapy within the last two weeks. (CTx associated hepatotoxicity has to be decreased to < CTCAE grad 2),
- Kidney insufficiency restricting contrast-media enhanced imaging (e.g. angiography),
- Existence of a contraindication for contrast-media enhanced MRI (e.g. incompatible cardiac pacemaker, limiting kidney insufficiency),
- Intra-hepatic lesion immeasurable by RECIST criteria,
- Non-liver predominant tumor disease,

- Suspicion of untreated metastasis/metastases of the CNS from clinically or imaging examinations,
- Pregnancy or nursing,
- Within 28 days before randomization participation in an active part of another clinical study, potentially affecting any endpoint of the current study,
- Verification of a persisting active infection, affecting execution of treatment or outcome.

Addresses

■ **Primary Sponsor**

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Universitätsklinikum Magdeburg

Collaborator, Other Address

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Sources of Monetary or Material Support

- **Institutional budget, no external funding (budget of sponsor/PI)**

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Status

- Recruitment Status: **Recruiting ongoing**
- Study Closing (LPLV): **[---]***

Trial Publications, Results and other documents

- Approval of ethics comm. (mandatory for transfer to Studybox) **Votum der Ethikkomission**
- trial protocol (mandatory for transfer to Studybox) **Ethikantrag / Protocoll**

** This entry means the parameter is not applicable or has not been set.*
**** This entry means that data is not displayed due to insufficient data privacy clearing.*