Trial Description

Title

A Confirmatory, Prospective, Open-label, Single-arm, Reader-blinded Multi-centre Phase 3 Study to Assess the Diagnostic Accuracy of Ferumoxtran-10-enhanced Magnetic Resonance Imaging (MRI) and Unenhanced MRI in Reference to Histopathology in Newly-diagnosed Prostate Cancer (PCA) Patients, Scheduled for Radical Prostatectomy (RP) With Extended Pelvic Lymph Node Dissection (ePLND).

Trial Acronym

SPL-01-001

URL of the trial

https://ferrotran.com/

Brief Summary in Lay Language

The aim of this study is to assess if Ferumoxtran-10 is suitable contrast agent for magnetic resonance imaging (MRI) to identify small lymph nodes metastasis in the pelvic region. This study is conducted to evaluate the diagnostic accuracy and safety of Ferumoxtran-10. The study is intended for patients suffering from prostate cancer with an intermediate to high risk for metastasis and which are scheduled for a prostatcetomy with extended lymph node removal.
Ferumoxtran-10 consists of ultra small iron-particles and is sensitive and specific for the detection of lymph node metastases. A solution of Ferumoxtran-10 is administered via injection into the vein and will be taken up in healthy tissue but not in cancer tissue.
In the imaging process the Ferumoxtran-10 particles which are distributed to the whole body can be made visible. Healthy tissue appears darkened because the Ferumoxtran-10 was takes up whereas the cancer tissue stayes lighter.
This method allows the detection of very small lymph nodes (2 mm) in comparison to normally used scans which can identify metastases from a size of 7-8 mm.

Brief Summary in Scientific Language

This will be a confirmatory, prospective, open-label, single-arm, reader-blinded, multi-centre phase 3 study to assess the diagnostic accuracy and safety of Ferrotran®-enhanced MRI in comparison to unenhanced MRI in the detection of pelvic lymph node metastases in newly-diagnosed patients with prostate cancer and an intermediate to high risk for lymph node metastases, based on the D'Amico criteria.

Do you plan to share individual participant data with other researchers?

No

Description IPD sharing plan

[---]*

Organizational Data

- DRKS-ID: **DRKS00019106**
- Date of Registration in DRKS: **2020/02/26**
- Date of Registration in Partner Registry or other Primary Registry: **2020/02/10**
- Investigator Sponsored/Initiated Trial (IST/IIT): **no**
- Ethics Approval/Approval of the Ethics Committee: **Approved**
- (leading) Ethics Committee Nr.: **19/0223-EK 11 , Ethik-Kommission des Landes Berlin**

Secondary IDs

- EudraCT-No.
(for studies acc. to Drug Law): **2018-004310-18**
- Primary Registry-ID: **NCT04261777 (ClinicalTrials.gov)**
- Sponsor-ID: **SPL-01-001 (Saving Patients' Lives Medical B.V.)**

Health condition or Problem studied

- ICD10: **C61 - Malignant neoplasm of prostate**
- Free text: **metastasised lymph nodes in the pelvic region**
- Free text: **high risk prostate cancer**

Interventions/Observational Groups

- Arm 1: **After signing the consent form, inclusion and exclusion criteria are checked and screening examinations (e.g. blood pressure, pulse, 12-channel electrocardiogram (ECG) and normal MRI) are performed.**
On the day of treatment (day 0), a physical examination, vital signs an weight again assessed before administration of Ferumoxtran-10 (0.13 mL/kg). The contrast medium is administered via slow infusion over a period of 30 minutes. During this time and and for the following 30 min (60 minutes in total), the patient is closely monitored by the study staff to detect any possible allergic or infusion-related reactions. Another physical examination as well as vital signs and laboratory paramateres will be performed four hours after the end of the infusion.
The next day (day 1) the Ferumoxtran-10 enhanced MRI scan is performed.
Seven days after the Ferumoxtran-10 infusion, another physical examination and assessment of vital signs are performed as well as blood and urine samples are taken.
Days 7 to 42: During this period, the planned prostatectomy (removal of the prostate) with extended removal of the lymph nodes in the pelvic area is performed. Prior to this surgery (on the same day or one day before) the same examinations are performed as on day 7.

About 8 weeks after the surgery, blood and urine samples are assessed again and a normal MRT is also performed.

Characteristics

- Study Type: **Interventional**
- Study Type Non-Interventional: **[---]***
- Allocation: **Single arm study**
- Blinding: **[---]***
- Who is blinded: **[---]***
- Control: **Uncontrolled/Single arm**
- Purpose: **Diagnostic**
- Assignment: **Single (group)**
- Phase: **III**
- Off-label use (Zulassungsüberschreitende Anwendung eines Arzneimittels): **No**

Primary Outcome

**Lymph node metastases will be detected by MRI scan (Ferumoxtran-10-enhanced and unenhanced).
True positive fraction and false positive fraction of identified tumour tissue in pelvic lymph nodes will be analysed by histopathology as established reference method. Based on these parameters the sensitivity and specificity will be evaluated.**

Secondary Outcome

**- Number and regions of lymph node metastases present in the follow-up MRI in comparison to pre-surgery MRI (unenhanced and Ferrotran®-enhanced)
- Frequency of occurrence and severity of abnormal findings in safety investigations (physical examination, vital signs, 12-lead ECG, clinical laboratory, concomitant medication, adverse events)
- Percentage of subjects for whom the patient management plan would be changed based on the Ferrotran®-enhanced MRI**

Countries of recruitment

- DE **Germany**
- CH **Switzerland**
- NL **Netherlands**
- BE **Belgium**

Locations of Recruitment

- University Medical Center **Charité Benjamin-Franklin, Berlin**
- University Medical Center **Universitätsklinikum Düsseldorf, Düsseldorf**
- University Medical Center **Universitätsspital, Bern**
- University Medical Center **Universitätsklinikum Carl Gustav Carus, Dresden**
- University Medical Center **Universitätsklinikum Bonn, Bonn**
- University Medical Center **Universitätsklinikum Köln, Köln**
- University Medical Center **Universitätsklinikum Schleswig-Holstein , Lübeck**
- University Medical Center **Nederlands Kanker Instituut Antoni van Leeuwenhoek, Amsterdam**
- Medical Center **Canisius-Wilhelmina Ziekenhuis Nijmegen, Nijmegen**
- University Medical Center **Radboud University Medical Center, Nijmegen**
- Medical Center **Vivantes Am Urban, Berlin**
- University Medical Center **Universitätsklinikum Essen , Essen**
- University Medical Center **Universitätsklinikum Leipzig, Leipzig**
- University Medical Center **Universitair Ziekenhuis , Ghent**
- University Medical Center **Universitätsmedizin Mannheim Medizinische Fakultät Mannheim der Universität Heidelberg, Mannheim**

Recruitment

- Planned/Actual: **Actual**
- (Anticipated or Actual) Date of First Enrollment: **2020/05/27**
- Target Sample Size: **200**
- Monocenter/Multicenter trial: **Multicenter trial**
- National/International: **International**

Inclusion Criteria

- Gender: **Male**
- Minimum Age: **18 Years**
- Maximum Age: **no maximum age**

Additional Inclusion Criteria

1. Voluntarily given and written informed consent.
2. Male ≥18 years of age.
3. Histologically newly-confirmed adenocarcinoma of the prostate.
4. Medium to high risk for lymph node metastasis, defined by either:
a. PSA ≥10 ng/mL or
b. Gleason-Score ≥7 or
c. Stage cT2b or cT2c or T3 or T4
5. Patients scheduled for radical prostatectomy (RP) with extended lymph node dissection (ePLND) between Day 7 and Day 42 after Ferrotran®-enhanced MRI.
6. Consent to practice contraception until end of study, including female partners of childbearing potential. Effective contraceptive measures include hormonal oral, injected or implanted female contraceptives, male condom, vaginal diaphragm, cervical cap, intrauterine device.

Exclusion criteria

1. Any contraindication to MRI, as per standard criteria.
2. Any radiation therapyor systemic antiproliferative (chemo-, immuno, or hormonal) therapy for prostate cancer (Lupron, Taxotere, Casodex, Eulexin, Zoladex, etc.) prior to screening and until after post-surgery FUP MRI.
3. Known hypersensitivity to Ferrotran® or its components such as dextran.
4. Known hypersensitivity to other parenteral iron products.
5. Acute allergy, including drug allergies and allergic asthma.
6. Evidence of iron overload or disturbances in the utilisation of iron (e.g., haemochromatosis, haemosiderosis, chronic haemolytic anaemia with frequent blood transfusions).
7. Presence of liver dysfunction.
8. Any other investigational medicinal product within 30 days prior to receiving study medication until end of study visit.
9. Simultaneous participation in any other clinical trial.
10. Abnormal safety laboratory values at screening or baseline that are assessed by the principal investigator as clinically relevant.
11. Patients not able to declare meaningful informed consent on their own (e.g. with legal guardian for mental disorders), or other vulnerable patients (e.g. under arrest).

12. Patients with acute SARS-CoV-2 infection

Addresses

■ **Primary Sponsor**

Saving Patients' Lives Medical B.V. (SPL Medical)
Transistorweg 5
6534 AT Nijmegen
Netherlands

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■ **Contact for Scientific Queries**

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■ **Contact for Public Queries**

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SPL-01-001 Team
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- **Collaborator, Other Address**

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  Blasewitzer Str. 78-80
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  Germany

  Telephone: **0049 351 21 444 0**
  Fax: **[---]***
  E-mail: **info at abx-cro.com**
  URL: **[---]***

Sources of Monetary or Material Support

- **Commercial (pharmaceutical industry, medical engineering industry, etc.)**

  Saving Patients' Lives Medical B.V.(SPL Medical)
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  Fax: **[---]***
  E-mail: **info at splmed.com**
  URL: **[---]***

Status

- Recruitment Status: **Recruiting ongoing**
- Reason, if "Recruitment stopped after recruiting started" or "Recruiting withdrawn before recruting started": **[---]***
- Reason, if Reason for Recruiting Stop "Other": **[---]***
- Study Closing (LPLV): **[---]***
- Number of Participants in Germany after Recruiting complete: **[---]***
- Total Number of Participants (all Sites worldwide) after Recruiting complete: **[---]***

Trial Publications, Results and other documents

- Background literature **Harisinghani MG, Barentsz J, Hahn PF, Deserno WM, Tabatabaei S, van de Kaa CH, de la Rosette J, Weissleder R. Noninvasive detection of clinically occult lymph-node metastases in prostate cancer. N Engl J Med. 2003 Jun 19;348(25):2491-9. doi: 10.1056/NEJMoa022749. Erratum in: N Engl J Med. 2003 Sep 4;349(10):1010. PMID: 12815134.**
- Background literature **Heesakkers RA, Hövels AM, Jager GJ, van den Bosch HC, Witjes JA, Raat HP, Severens JL, Adang EM, van der Kaa CH, Fütterer JJ, Barentsz J. MRI with a lymph-node-specific contrast agent as an alternative to CT scan and**

lymph-node dissection in patients with prostate cancer: a prospective multicohort study. Lancet Oncol. 2008 Sep;9(9):850-6. doi: 10.1016/S1470-2045(08)70203-1. Epub 2008 Aug 15. PMID: 18708295.

- Background literature **Heesakkers RA, Jager GJ, Hövels AM, de Hoop B, van den Bosch HC, Raat F, Witjes JA, Mulders PF, van der Kaa CH, Barentsz JO. Prostate cancer: detection of lymph node metastases outside the routine surgical area with ferumoxtran-10-enhanced MR imaging. Radiology. 2009 May;251(2):408-14. doi: 10.1148/radiol.2512071018. PMID: 19401573.**
- Background literature **D'Amico et al, 1998; Biochemical Outcome After Radical Prostatectomy, External Beam Radiation Therapy, or Interstitial Radiation Therapy for Clinically Localized Prostate Cancer**

Additional Trial Attributes

- *Urological disease:* ***prostate cancer***
- *If other, please specify:* ***[---]****
- *Onset of therapy:* ***other***
- *If other, please specify:* ***[---]****
- *If other, please specify:* ***[---]****
- *Study recommendations:* ***trial sites in demand***
- *If other, please specify:* ***[---]****
- *German director of clinical investigation:*

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  Hindenburgdamm 30
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- *Further contact:*

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  Fax: **[---]***
  E-mail: **[---]***
  URL: **[---]***

- *Function of contact:* ***[---]****
- *Non-interventional study:* ***[---]****
- *Stage:* ***metastasized***

** 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.*