PLEASE NOTE: *This trial has been registered retrospectively.*

Trial Description

Title

Dose-escalating study to determine the maximum tolerated dose (MTD) of the mistletoe extract WEME 200 mg for intravesical instillation in patients with completely resected (R0) superficial bladder carcinoma (pTa low grade [multilocular or recurrence], pT1 low grade)

Trial Acronym

Mistletoe extract WEME 200 mg study

URL of the trial

[---]*

Brief Summary in Lay Language

The goal of the study is to determine the optimum intravesical (that means directly applied into the bladder) dosing of mistletoe extract. Another goal is to determine the maximum tolerated dose. In addition the influence of mistletoe extract on the tumour recurrence will be assessed.

Brief Summary in Scientific Language

To determine the maximum tolerated dose (MTD) of a mistletoe-extract (oak) manufactured by WELEDA (WEME 200 mg) in intravesical instillation in patients after transurethral R0-resection (TUR) of a histologically confirmed, superficial bladder carcinoma (pTa G2, pT1 G1-2), based on the incidence of dose-limiting toxicities (DLTs), to describe optimal dose ranges for putative phase II/III trials.

Organizational Data

- DRKS-ID: **DRKS00002070**
- Date of Registration in DRKS: **2012/12/12**
- Date of Registration in Partner Registry or other Primary Registry: **[---]***
- Investigator Sponsored/Initiated Trial (IST/IIT): **yes**
- Ethics Approval/Approval of the Ethics Committee: **Approved**
- (leading) Ethics Committee Nr.: **156/08 , Ethik-Kommission der Albert-Ludwigs-Universität Freiburg**

Secondary IDs

- EudraCT-No.
  (for studies acc. to Drug Law): **2008-000782-35**
- BfArM-No.: **4034263**

Health condition or Problem studied

- ICD10: **C67 - Malignant neoplasm of bladder**

Interventions/Observational Groups

- Arm 1: **DG-C: 1.0 ml WEME ad 50 ml NaCl 0.9% intravesical**
- Arm 2: **DG-D: 2.0 ml WEME ad 50 ml NaCl 0.9% intravesical**
- Arm 3: **DG-E: 3.0 ml WEME ad 50 ml NaCl 0.9% intravesical**
- Arm 4: **DG-F: 4.0 ml WEME ad 50 ml NaCl 0.9% intravesical**
- Arm 5: **DG-G: 5.0 ml WEME ad 50 ml NaCl 0.9% intravesical**
- Arm 6: **DG-H: 6.0 ml WEME ad 50 ml NaCl 0.9% intravesical**
- Arm 7: **DG-B: 0.5 ml WEME ad 50 ml NaCl 0.9% intravesical**
- Arm 8: **DG-A: 0.25 ml WEME ad 50 ml NaCl 0.9% intravesical**

Characteristics

- Study Type: **Interventional**
- Study Type Non-Interventional: **[---]***
- Allocation: **Other**
- Blinding: **[---]***
- Who is blinded: **[---]***
- Control: **Other**
- Purpose: **Treatment**
- Assignment: **Other**
- Phase: **I-II**
- Off-label use (Zulassungsüberschreitende Anwendung eines Arzneimittels): **Yes**

Primary Outcome

To determine the maximum tolerated dose (MTD) of a mistletoe-extract (oak) manufactured by WELEDA (WEME 200 mg) in intravesical instillation in the aforementioned patient population, based on the incidence of dose-limiting toxicities (DLTs), to describe optimal dose ranges for putative phase II/III trials.

Secondary Outcome

1. To investigate safety and tolerability of different dosages of intravesically applied mistletoe extract (WEME 200 mg).
2. To acquire first data about the clinical effects of intravesical instillation of WEME 200 mg in superficial bladder carcinoma.
a) To describe tumour recurrence rate 3, 6, 9 and 12 months after start of therapy.
b) To examine the binding of mistletoe-lectins to tumour tissue (ex vivo in vitro).

Countries of recruitment

- DE **Germany**

Locations of Recruitment

- Medical Center **Universitätsklinik Freiburg, Freiburg im Breisgau**
- Medical Center **Universitätsklinik Mannheim, Mannheim**

Recruitment

- Planned/Actual: **Actual**
- (Anticipated or Actual) Date of First Enrollment: **2009/11/19**
- Target Sample Size: **24**
- Monocenter/Multicenter trial: **Multicenter trial**
- National/International: **National**

Inclusion Criteria

- Gender: **Both, male and female**
- Minimum Age: **18 Years**
- Maximum Age: **80 Years**

Additional Inclusion Criteria

1. Age: 18 - 80 years.
2. Histologically confirmed superficial bladder carcinoma: pTa G2 or pT1 G1-2; re-resected tumours included.
3. No evidence of lymph node involvement and/or metastasis.
4. Transurethral R0-resection of the bladder tumour within 2 - 7 weeks before inclusion into the study; re-resection of the tumour included.
5. Patient information according to applicable national legislation and international guidelines
followed by signing and dating the informed consent form.
6. Female, pre-menopausal patients must provide negative pregnancy test within two weeks before

study entry and are willing to apply a highly effective birth-control method.

Exclusion criteria

**1. Bladder carcinomas with one or more of the following characteristics:
Carcinoma in situ (pTis),
pT2-4, N1-3, M1, G3-4; furthermore are excluded pTa-tumours with G1-grading.
2. Previous intravesical instillation therapy within the last 6 months.
3. Previous radiation therapy.
4. Bladder resection.
5. Contracted bladder with capacity < 100 ml.
6. Inadequately treated acute or chronic urinary tracts infections.
7. Secondary neoplasia.
8. Co-morbidity with one of the following: active tuberculosis, active thyroid hyperfunction, known
secondary cancer, HIV-infection/ AIDS, other severe systemic diseases as cardiac insufficiency,
parasitosis or Crohn's disease, acute inflammatory diseases with body temperature > 38 °C.
9. Other concomitant diseases likely to make participation of the patient difficult at the discretion of
the investigator.
10. Clinically relevant cardiac arrhythmias.
11. Severe allergic illness (including asthma); known hypersensitivity to mistletoe products.
12. Any other current or planned oncological therapy (surgery, radiotherapy, chemotherapy, other
mistletoe products including s.c. therapy with Iscador®).
13. Previous medical therapy that could interfere with the objectives of this study including mistletoe
therapy within the last month.
14. Concomitant treatment with other immunomodulatory medications.
15. Known abuse of medicaments, alcohol or illegal drugs.
16. Laboratory parameters outside the following limits:
Creatinine > 2x upper limit of normal
Bilirubine > 3x upper limit of normal
Transaminases > 3x upper limit of normal
17. Pregnancy or breast-feeding.
18. Pre-menopausal women not applying an effective birth control method.
19. Doubt concerning the compliance.
20. Previous participation in this clinical trial earlier in study course. Participation in any other clinical
trial currently or within the last month.
21. Subjects which are in a state of dependence in relation to the sponsor's or investigator's institutions
or which are their employees.**

Addresses

■ **Primary Sponsor**

WELEDA AG
Möhlerstr. 2-5
73525 Schwäbisch-Gmünd

Primary Sponsor

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■ **Contact for Scientific Queries**

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Sources of Monetary or Material Support

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

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  URL: **[---]***
- **Private sponsorship (foundations, study societies, etc.)**

  Verein für Krebsforschung
  Kirschweg 9
  4144 Arlesheim
  Switzerland

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

Status

- Recruitment Status: **Recruiting complete, follow-up complete**
- Study Closing (LPLV): **2011/09/30**

Trial Publications, Results and other documents

- Paper **Elsässer-Beile U, Leiber C, Wetterauer U, Bühler P, Wolf P, Lucht M, Mengs U. Anticancer Res. 2005 Nov-Dec;25(6C):4733-6.**

- Paper **Elsässer-Beile U, Leiber C, Wolf P, Lucht M, Mengs U, Wetterauer U. J Urol. 2005 Jul;174(1):76-9.**