PLEASE NOTE: *This study has been imported from ClinicalTrials.gov without additional data checks.*

Trial Description

Title

A Single Arm, Open-label Multicenter Phase II Trial of Everolimus in Patients With Relapsed/Refractory Germ Cell Cancer

Trial Acronym

RADIT

URL of the trial

[---]*

Brief Summary in Lay Language

The purpose of this study is to determine whether the drug everolimus is effective in the treatment of patients with relapsed cancer of the testis. This is a phase II study where all patients will receive the study drug (everolimus 10 mg daily). The primary endpoint of the study is the rate of patients that have no progressive disease after 12 weeks of treatment.

Twenty-five evaluable patients will be treated in this study.

Brief Summary in Scientific Language

Rationale

Patients with metastatic germ cell cancer and relapse after two or more courses of cisplatin-based chemotherapy or after high-dose chemotherapy have a poor prognosis and few treatment options. Everolimus is a derivative of rapamycin and acts as a signal transduction inhibitor. Its target is mTOR (mammalian target of rapamycin), a key protein kinase regulating cell growth, proliferation and survival. The mTOR pathway activity is modulated by the PI3K1AKT pathway and is known to be deregulated in numerous human cancers, including germ cell tumors. Everolimus is being investigated as an anticancer agent based on its potential to act:

- Directly on tumor cells by inhibiting tumor cell growth and proliferation

- Indirectly by inhibiting angiogenesis leading to reduced tumor vascularity

Study design

An open-label, single arm, non-randomized, single stage phase II study.
Screening phase:
Baseline evaluations will be performed within 2 weeks before the first dose of study drug.
Treatment phase: All patients will receive everolimus until disease progression (by RECIST
or tumor markers) or unacceptable toxicity or study discontinuation for other reasons. A
treatment cycle consists of 3 weeks. Dose reductions and dose interruptions (for up to 2
weeks) are allowed for intolerable toxicity. Follow-up phase: All patients will be followed
for survival.

Visit schedule

Tumor Response and progression will be assessed using the RECIST criteria and assessments
with tumor markers. Tumor measurements by a CT scan or MRI will be performed at screening
within 2 weeks prior to the first dose of study drug. During the study period, the CT
scan/MRI will be performed every 6 weeks (± one week), and at the time of discontinuation of
study drug (within 2 weeks). The same type of scan (CT or MRI) used at screening must be
used for all subsequent follow-up assessments. A partial or a complete response warrants a
confirmation no sooner than 4 weeks and no later than 6 weeks after its observation.

Tumor markers (AFP, HCG) will be assessed every 3 weeks. A tumor marker reduction > 90%
without an increase in tumor size is considered a partial response. A tumor marker increase
> 25% without an increase in tumor size is considered progressive disease when confirmed 3
weeks after its observation.

Translational research

The following retrospective pathological examinations of tumor samples will be performed in
those patients that gave additional informed consent:

- immunohistochemistry for the mismatch repair genes hMLH1, hMSH2, hMSH6, and PMS2, and
the cell signalling effectors pMAPK, pAKT, pS6K and PTEN.

- mutation analysis for PTEN, BRAF, p53, and examination of microsatellite instability
This information will be correlated with treatment response (CR, PR, SO or PD) at week
12 in an exploratory analysis.

Organizational Data

- DRKS-ID: **DRKS00004049**
- Date of Registration in DRKS: **2012/10/26**
- Date of Registration in Partner Registry or other Primary Registry: **2010/11/16**
- Investigator Sponsored/Initiated Trial (IST/IIT): **yes**
- Ethics Approval/Approval of the Ethics Committee: **[---]***
- (leading) Ethics Committee Nr.: **[---]***

Secondary IDs

- EudraCT-No.
(for studies acc. to Drug Law): **2009-014383-18**
- Primary Registry-ID: **NCT01242631 (ClinicalTrials.gov)**
- Sponsor-ID: **CRAD001CDE21T (Hannover Medical School)**
- Other Secondary-ID: **2009-014383-18**

Health condition or Problem studied

- Free text: **Testicular Cancer**
- Free text: **Germ Cell Cancer**
- ICD10: **C62 - Malignant neoplasm of testis**

Interventions/Observational Groups

- Arm 1: **Drug: Everolimus**

Characteristics

- Study Type: **Interventional**
- Study Type Non-Interventional: **[---]***
- Allocation: **Single arm study**
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Study Type: **Interventional**

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Blinding: **[---]***

- Who is blinded: **[---]***
- Control: **Uncontrolled/Single arm**
- Purpose: **Treatment**
- Assignment: **Single (group)**
- Phase: **II**
- Off-label use (Zulassungsüberschreitende Anwendung eines Arzneimittels): **[---]***

Primary Outcome

- Progression-free rate at 12 weeks; time frame: 12 weeks; Percentage of patients that have not progressed after 12 weeks of treatment.

Secondary Outcome

- Objective response rate; time frame: 6 months
- Overall survival; time frame: 12 months
- Safety profile; time frame: 6 months

Countries of recruitment

- DE **Germany**

Locations of Recruitment

- **Vivantes Klinikum am Urban, Berlin**
- **Universitatsklinikum Essen, Essen**
- **Universitatsklinikum Hamburg-Eppendorf, Hamburg**
- **Hannover Medical School, Hannover**
- **Universitatsklinikum Schieswig-Holstein - Campus Kiel, Kiel**
- **Universitatsklinikum Marburg, Marburg**
- **Klinikum Harlaching München, München**

- **Universitatsklinikum der Eberhard-Karls-Universitat Tübingen, Tübingen**

Recruitment

- Planned/Actual: **[---]***
- (Anticipated or Actual) Date of First Enrollment: **2010/11/30**
- Target Sample Size: **25**
- Monocenter/Multicenter trial: **Multicenter trial**
- National/International: **[---]***

Inclusion Criteria

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

Additional Inclusion Criteria

- Male patients >= 18 years old.

- Patients with histologically proven seminomatous or non-seminomatous germ cell cancer

- Disease progression during cisplatin-based chemotherapy or

- Disease progression or relapse after high-dose chemotherapy or

- Disease progression or relapse after at least 2 different cisplatin-based regimens and contraindications for high-dose chemotherapy.

- Patients must have received prior combination chemotherapy with gemcitabine, oxaliplatin and paclitaxel (GOP). Prior treatment with a combination of two of these drugs is allowed in case of contraindications for GOP.

- Disease progression at study entry: progressive disease according to RECIST criteria in baseline examinations or tumor marker increase > 25% within 4 weeks before study entry.

- ECOG performance status <= 2.

- Life expectancy >= 3 months.

- Adequate bone marrow function: absolute neutrophil count >= 1.5 x 109/1, platelets >= 75 x 109/1, hemoglobin >= 9 g/dl.

- Adequate liver function: serum bilirubin: <= 1.5x ULN, ALT and AST <= 2.5x ULN. For patients with known liver metastases: AST and ALT <= 5x ULN.

- Adequate renal function: serum creatinine <= 2.0x ULN.

- Patients must be surgically sterile or must agree to use effective contraception during study treatment.

- Signed written informed consent.

Exclusion criteria

- Systemic antitumor treatment within 21 days before study entry.

- Simultaneous radiotherapy of the only target lesion(s).

- Patients who have undergone major surgery within 4 weeks prior to starting study drug (e.g. intra-thoracic, intra-abdominal, or intra-pelvic) or significant traumatic injury, or who have not recovered from the side effects of any of the above

- Patients who have previously received mTOR inhibitors (sirolimus, temsirolimus, everolimus).

- Patients receiving chronic systemic treatment with corticosteroids (dose of >= 20 mg/day methylprednisone equivalent) or another immunosuppressive agent.

- Patients with unstable angina pectoris, myocardial infarction <= 6 months prior to first study treatment, congestive heart failure NYHA III-IV or serious uncontrolled cardiac arrhythmias.

- Patients with severely impaired lung function: spirometry or DLCO < 50% of the normal predicted value.

- Uncontrolled diabetes: fasting serum glucose > 2.0x ULN.

- Patients with an active or uncontrolled infection, incl. chronic Hepatitis B or C

- Patients who have a history of another primary malignancy and are off treatment for <= 3 years, with the exception of non-melanoma skin cancer.

- Patients who have participated in another clinical trial within 30 days before study

entry.

- Other serious medical conditions that could impair the ability of the patient to participate in the study.

- Patients unwilling or unable to comply with the protocol.

Addresses

■ **Primary Sponsor**

Hannover Medical School

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URL: **[---]***

Sources of Monetary or Material Support

■ **[---]***

Bitte wenden Sie sich an den Sponsor / Please refer to primary sponsor

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

Status

- Recruitment Status: **Recruiting complete, follow-up complete**
- Study Closing (LPLV): **2014/03/01**

Trial Publications, Results and other documents

The parameters in ClinicalTrials.gov and DRKS are not identical. Therefore the data import from ClinicalTrials.gov required adjustments. For full details please see the DRKS FAQs.
- Translation on version: 5
- Last processed date by ClinicalTrials.gov: 2016/01/14
Please note:
There are additional attributes available concerning this trial. To open an extended view please click here.