Trial Description

Title

OSAKA: A multicenter, four arm, randomized, open label clinical study investigating optimized dosing in a Prograf®/Advagraf®-based immunosuppressive regimen in kidney transplant subjects.
Short Title: OSAKA Study
(Optimizing ImmunoSuppression After Kidney Transplantation With Advagraf)
ISN: PMR-EC-1210Transplantation with ADVAGRAF)

Trial Acronym

[---]*

URL of the trial

[---]*

Brief Summary in Lay Language

Why is this study being conducted?
Different combinations of medications are known for preventing rejection of your new organ transplant. The well known immunosuppressive drug tacrolimus is authorised in two different dosage forms: Prograf®, which is taken twice a day, and a new formulation known as Advagraf®, which is taken just once a day. This study now shall be a study to investigate how well Advagraf® does work compared to Prograf® to prevent the rejection of your new kidney transplantat. In addition, you will take steroids, mycophenolat mofetil (MMF; Cellcept®) and probably basiliximab (Simulect®) during the study. In the past, this combination of immunosuppressive drugs (tacrolimus, MMF, Steroids, Basiliximab) has proven effective and safe in preventing rejection.

Brief Summary in Scientific Language

A multicenter, randomized, open, four armed, parallel group, comparative phase IIIb study. Subjects about to undergo kidney allograft transplantation will be randomized to one of the following Treatment Arms:
Arm 1:Prograf® (0.2mg/kg) + MMF + Corticosteroids (24 weeks)
Arm 2:Advagraf® (0.2mg/kg) + MMF + Corticosteroids (24 weeks)
Arm 3:Advagraf® (0.3mg/kg) + MMF + Corticosteroids (24 weeks)
Arm 4:Advagraf® (0.2mg/kg) + MMF + Basiliximab + Corticosteroids (Bolus)
- Randomization will include stratification according to age groups >= 18 to 59 years and >= 60 years will be performed.
- Study configuration is an open design.
- A Data Safety Monitoring Board (DSMB) will review the study at regular intervals during the course of the study.
- No interim analyses are planned.

Organizational Data

- DRKS-ID: **DRKS00000003**
- Date of Registration in DRKS: **2008/08/08**
- Date of Registration in Partner Registry or other Primary Registry: **2008/02/01**
- Investigator Sponsored/Initiated Trial (IST/IIT): **no**
- Ethics Approval/Approval of the Ethics Committee: **Approved**
- (leading) Ethics Committee Nr.: **034/08 , Ethik-Kommission der Albert-Ludwig-Universität Freiburg**

Secondary IDs

- EudraCT-Number: **2007-005376-13**
- Partner Registry-ID: **UKF001286 (Register Klinischer Studien des Universitätsklinikums Freiburg)**
- BfArM-No.: **4033897**
- Sponsor-ID: **ISN: PMR-EC-1210**

Health condition or Problem studied

- ICD10: **Z94.0 - Kidney transplant status**
- Free text: **Kidney transplant**

Interventions/Observational Groups

- Arm 1: **Prograf® (0.2mg/kg) + MMF + Corticosteroids (24 weeks)**
- Arm 2: **Advagraf® (0.2mg/kg) + MMF + Corticosteroids (24 weeks)**
- Arm 3: **Advagraf® (0.3mg/kg) + MMF + Corticosteroids (24 weeks)**
- Arm 4: **Advagraf® (0.2mg/kg) + MMF + Basiliximab + Corticosteroids (Bolus)**

Characteristics

- Study Type: **Interventional**
- Study Type Non-Interventional: **[---]***
- Allocation: **Randomized controlled trial**
- Blinding: **Open (masking not used)**
- Who is blinded: **[---]***
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Allocation: **Randomized controlled trial**

Blinding: **Open (masking not used)**

Who is blinded: **[---]***

Control: **Active control**

- Purpose: **Treatment**
- Assignment: **Parallel**
- Phase: **III**
- Off-label use (Zulassungsüberschreitende Anwendung eines Arzneimittels): **[---]***

Primary Outcome

The primary objective of this study is to compare the four therapy regimens with regard to efficacy failure rate. The secondary objective is to compare the efficacy and safety profiles of the four therapy regimens with each other. Efficacy failure rate will be assessed using a composite endpoint consisting of graft loss, biopsy confirmed acute rejection (BCAR) and graft dysfunction.

Secondary Outcome

Efficacy Variables:
- Renal function assessed by calculated GFR (Glomerular Filtration Rate) with MDRD formula at week 24 after transplantation
- Renal function assessed by calculated creatinine clearance with Cockcroft and Gault formula at week 24 after transplantation
- Acute rejection
*** Incidence of and time to first acute rejection**
*** Incidence of and time to first corticosteroid-resistant acute rejection**
*** Overall frequency of acute rejection episodes**
- Biopsy confirmed acute rejection
*** Incidence of and time to first biopsy confirmed acute rejection**
*** Incidence of and time to first biopsy confirmed corticosteroid-resistant acute rejection**
*** Overall frequency of biopsy confirmed acute rejection episodes**
*** Severity of biopsy confirmed acute rejections (Banff `97 criteria)**

Countries of recruitment

- DE **Germany**
- ES **Spain**
- IT **Italy**
- NL **Netherlands**

- AT **Austria**
- FR **France**

Locations of Recruitment

Recruitment

- Planned/Actual: **Actual**
- (Anticipated or Actual) Date of First Enrollment: **2008/06/02**
- Target Sample Size: **1200**
- Monocenter/Multicenter trial: **Multicenter trial**
- National/International: **International**

Inclusion Criteria

- Gender: **Both, male and female**
- Minimum Age: **18 Years**
- Maximum Age: **no maximum age**

Additional Inclusion Criteria

Subject is eligible for the study if all of the following apply:
1. Age >= 18 years.
2. End stage kidney disease and a suitable candidate for primary renal transplantation or
re-transplantation (unless the graft was lost from rejection within 12 month).
3. Receiving a kidney transplant from a cadaveric or living (non HLA identical) donor
with compatible ABO blood type.
4. Female subject of childbearing potential must have a negative serum pregnancy test at
enrollment and must agree to maintain effective birth control during the study.
5. Capable of understanding the purpose and risks of the study, fully informed and given
written informed consent (signed Informed Consent has been obtained).

Exclusion criteria

Subject will be excluded from participation if any of the following apply:
1. Receiving or having previously received an organ transplant other than a kidney.
2. Cold ischemia time of the donor kidney > 30 hours.
3. Receiving a graft from a non-heart-beating donor other than of Maastricht category 3

(withdrawn of support awaiting cardiac arrest).
4. Significant liver disease, defined as having continuously elevated SGPT/ALT and/or
SGOT/AST and/or total bilirubin levels >= 2 times the upper value of the normal range
of the investigational site or is receiving a graft from a hepatitis C or B positive donor.
5. Requiring initial sequential or parallel therapy with immunosuppressive antibody
preparation(s).
6. Requiring ongoing dosing with a systemic immunosuppressive drug prior to transplantation.
7. Significant, uncontrolled concomitant infections and/or severe diarrhea, vomiting,
active upper gastro-intestinal tract malabsorption or active peptic ulcer.
8. Pregnant woman or breast-feeding mother.
9. Subject or donor known to be HIV positive.
10. Known allergy or intolerance to tacrolimus, macrolide antibiotics, corticosteroids,
basiliximab or mycophenolate mofetil or any of the product excipients.
11. Diagnosis of new-onset malignancy prior to transplantation, with the exception of
basocellular or squamous cell carcinoma of the skin which had been treated successfully.
12. Currently participating in another clinical trial, and/or has taken an investigational drug
within 28 days prior to enrollment.
13. Any form of substance abuse, psychiatric disorder or condition which, in the opinion of
the investigator, may complicate communication with the investigator.
14. Unlikely to comply with the visits scheduled in the protocol.

Addresses

- **Primary Sponsor**

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Sources of Monetary or Material Support

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

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Germany

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Status

- Recruitment Status: **Recruiting complete, follow-up complete**
- Study Closing (LPLV): **2010/05/03**

Trial Publications, Results and other documents

** 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.*