2 SYNOPSIS

Name of Company: Roche Pharma AG	Individual Study Table Referring to Part ..... .of the Dossier Volume: Page:	(For National Authority Use Only)
Name of Finished Product: CellCept®		
Name of Active Ingredient: Mycophenolate mofetil (MMF)		

Study title:
Prospective study of whether patients receiving less than the recommended dose of EC-MPS due to gastrointestinal problems can be switched to a dose of MMF higher than the equimolar dose

Co-ordinating Investigator:
[redacted]

Centres:
The study was carried out in 6 hospitals in Germany.

Publication (reference):
None

Study period:	**Clinical development phase:**
Planned: 15 months **Actual:** 5 months (March 2007 – August 2007)	**IV**

Objective:
The primary objective of this study was to demonstrate that at least 30% of patients can be switched from EC-MPS to a dose of MMF higher than the equivalent dose without a deterioration in quality of life.
A further objective was to compare predose MPA, MPAG and AcMPAG concentrations before and after the change in treatment, as well as the safety and efficacy of the change and the dose increase.

Design:
This clinical trial was planned as a single-arm, prospective, open, multi-centre study.

Number of patients (planned and analysed):
Planned sample size: 100 patients
Actual sample size: 3 treated patients, 1 of whom dropped out of the study
ITT analysis: not applicable
PP analysis: not applicable

Diagnosis and main inclusion criteria:
Adult renal transplanted patients fulfilling the following criteria
- Age ≥ 18
- Patients receiving less than the recommended EC-MPS dose of 1,440 mg/day due to GI problems
- At least 6 months' treatment with EC-MPS
- Stable EC-MPS dose in the previous 2 months
- First or second transplant
- Written informed consent

Study medication, dose and administration, batch no.:
Mycophenolate mofetil hard capsules, 250 mg, batch no. [redacted], and mycophenolate mofetil tablets, 500 mg, batch no. [redacted], both taken orally, preferably with a meal.
The planned daily dose was 500–1,750 mg at visit 1 and 750–2,000 mg from visit 2, divided into 3 doses according to the treatment regimen.

Treatment duration:
Patients were switched from EC-MPS to the equimolar dose of MMF at the baseline visit. From visit 2, the daily dose of MMF was increased by 250 mg and divided into 3 daily doses. The planned total study duration for each patient was therefore 3 months.

Study medication, dose and administration, batch no.:
Not applicable

Planned evaluation criteria:

Efficacy:
- Proportion of patients who tolerated the dose increase without deterioration in quality of life
- MMF dose at visit 3
- Findings of differential diagnostic investigations in the case of gastrointestinal symptoms

Tolerability/safety:
- Adverse events,
- Acute rejection reactions,
- Laboratory parameters (change from baseline),
- Predose MPA, MPAG, AcMPAG concentration in all patients and in those patients who did not tolerate the dose increase

Statistics:
Confirmatory analysis of the primary endpoint was to be undertaken. Descriptive evaluation of the remaining parameters was planned specifying frequencies, means, medians, value ranges and confidence intervals.

Summary:
Efficacy findings:
Due to the small number of cases (only 3 patients treated), no efficacy analysis was performed.

Of the 3 treated patients, 1 patient tolerated the increase in the daily dose of MMF of 250 mg, 1 patient dropped out of the study after 32 days of treatment due to gastrointestinal problems following a dose increase not in line with the protocol, and the remaining patient was treated until the end of the study as planned following a dose reduction.

Safety findings:
No rejection reactions or clinically relevant changes in laboratory values were observed in any of the patients.

The range of adverse events that occurred is in accord with the information in the SPC for MMF. No serious adverse events were reported during the course of the study. One patient dropped out of the study because of adverse gastrointestinal effects following a dose increase from 500 to 1,000 mg which was not in line with the protocol. There were no changes in vital signs.

Conclusion:
The small number of patients does not allow any meaningful conclusions in relation to efficacy. The study was terminated early for administrative reasons, because of too low an inclusion rate. Neither the adverse events that occurred during the course of the study nor the analysis of laboratory parameters and vital signs give rise to safety concerns.

Date of final report: 31 March 2008