SYNOPSIS OF RESEARCH REPORT
PROTOCOL ML18690

COMPANY: Hoffmann-La Roche NAME OF FINISHED PRODUCT: CellCept Zenapax Rapamune NAME OF ACTIVE SUBSTANCES: mycophenolate mofetil daclizumab sirolimus	(FOR NATIONAL AUTHORITY USE ONLY)

TITLE OF THE STUDY / REPORT No. / DATE OF REPORT	Final Clinical Study Report – ML18690 - An Open-Label Study Comparing a Steroid Sparing Versus a Standard Steroid Regimen in Combination with CellCept, Zenapax and Sirolimus in the Prevention of Acute Renal Allograft Rejection – 21 September 2007. The Sponsor decided to terminate the study early after the decision of the [redacted] company to early discontinue treatment in other studies after observing a significantly higher number of acute rejections confirmed by biopsy and a higher number of deaths in the groups where the treatment design was IL2R Ab + Rapamune + mycophenolate mofetil + corticosteroids.
INVESTIGATORS / CENTERS AND COUNTRIES	Four centers in Spain
PUBLICATION (REFERENCE)	Not applicable
PERIOD OF TRIAL	The maximum follow-up time of the patients was 12 weeks versus the 56 planned in the study.
CLINICAL PHASE	IV
OBJECTIVES	The primary study objective was to compare the acute rejection rate confirmed by biopsy of a steroid-free regimen based on daclizumab, mycophenolate mofetil, and sirolimus versus the same at standard doses of steroids 24 hours after patient randomization that had been performed at 12 weeks post-transplant.
STUDY DESIGN	A multicenter, national, randomized, open-label, prospective clinical trial.
NUMBER OF SUBJECTS	It was planned to include approximately 144 patients in order to randomize at least 115 patients. At the time of study termination, a total of 17 patients were included, of which 3 patients had been randomized.

DIAGNOSIS AND MAIN CRITERIA FOR INCLUSION	Male and female patients >18 years of age, who were receiving their first renal allogenic transplant, were enrolled in the study.
TRIAL DRUG / STROKE (BATCH) No.	CellCept (mycophenolate mofetil) Zenapax (daclizumab) Rapamune (sirolimus)
DOSE / ROUTE / REGIMEN / DURATION	Treatment regimens were prescribed at a standard dosage regimen.
REFERENCE DRUG / STROKE (BATCH) No.	CellCept (mycophenolate mofetil) Zenapax (daclizumab) Rapamune (sirolimus) Steroids
DOSE / ROUTE / REGIMEN / DURATION	Treatment regimens were prescribed at a standard dosage regimen.
CRITERIA FOR EVALUATION	
EFFICACY:	The primary efficacy endpoint was the acute rejection rate confirmed by biopsy 24 weeks post-randomization of patients (i.e., Week 36 post-transplant [Visit 7]).
PHARMACODYNAMICS:	Not applicable
PHARMACOKINETICS:	Not applicable
SAFETY:	The safety profile of both treatment groups was measured from the adverse events (AEs), opportunistic infections, and development of neoplasms occurring in each group throughout the study.
STATISTICAL METHODS	A descriptive analysis of the variables was provided: centralization and dispersion measures for quantitative variables and absolute and relative frequencies for qualitative variables. No statistical tests were performed for the above referring to the sample size reached.

METHODOLOGY

This was a multicenter, national, randomized, double-blind, comparative study of a steroid-free regimen versus a standard steroid regimen in combination with daclizumab, mycophenolate mofetil, and sirolimus in patients > 18 years of age from both sexes and who were receiving their first renal allogenic transplant. It was planned to include approximately 144 patients in order to randomize at least 115 patients. This study was prematurely terminated and at the time of termination a total of 17 patients enrolled in the study, of which 3 patients had been randomized. None of the randomized patients completed the post-randomization period.

EFFICACY RESULTS

A total of 9 of 17 patients (52.9%) reported an acute rejection. However, in one case, rejection was not confirmed by biopsy, and, of the eight patients biopsied, rejection was not confirmed in one patient. Therefore the acute rejection rate confirmed by biopsy was 41% to Week 12.

With regard to the severity of confirmed acute rejections, 3 patients (42.9%) had a severity/seriousness of 2A.

PHARMACODYNAMIC RESULTS

Not applicable

PHARMACOKINETIC RESULTS

Not applicable

SAFETY RESULTS

All enrolled 17 patients had at least 1 AE during the study. A total of 81 AEs were reported during study. The most common AEs were edema (16.0%) followed by urinary infection (12.3%) and anemia (11.1%). No opportunistic infection was reported.

CONCLUSIONS

Due to the low number of patients recruited at the time of study termination, no conclusions regarding the efficacy and safety of the treatment regimens could be drawn.