SYNOPSIS ***ANNEX I***

Name of Sponsor/Company: Klinikum der Universität München Marchioninistr. 15 81377 München Sponsors Delegate Person: Prof. Dr. Martin Dreyling Medizinische Klinik III Tel.: 089 7095 2202 Fax: 089 7095 2201 Email: martin.dreyling@med.uni-muenchen.de	Individual Study Table Referring to Part of the Dossier not applicable	*(For National Authority Use only)*
Name of Finished Product: Revlimid	Volume: not applicable	
Name of Active Ingredient: Lenalidomid	Page: not applicable	

Title of Study:

Feasibility and efficacy of Lenalidomide maintenance after salvage immuno-chemotherapy induction in relapsed or refractory mantle cell lymphoma – a phase II study of the European MCL network
Short title: MCL2008-01
Version 3 vom 29.01.2010, EudraCT-Nr.: 2008-000678-19, Vorlagen-Nr.: 4035676

Investigators:
LKP: Prof. Dr. Martin Dreyling (contact data: see above)

Study centre(s):

not applicable

Publication (reference):

not applicable

Studied period (years): (date of first enrolment) (date of last completed) not applicable	Phase of development: II

Objectives:
Evaluation of efficacy and safety of lenalidomide maintenance in patients with relapsed or refractory MCL in remission after salvage immunochemotherapy

Methodology: Phase II study (see statistical methods)

Number of patients (planned and analysed):

Planned were approximately 60 patients, but no patient was included as the study was terminated early.

Diagnosis and main criteria for inclusion:

1. Histologically confirmed, refractory or relapsed mantle cell lymphoma according to the WHO classification
2. Histological material available for reference pathology

3. Relapse or progression following at least one adequate prior line of anti-neoplastic therapy
4. Complete or partial remission after salvage induction of 3-4 courses R-FC(M), R-B(M) or 4-6 cycles R-CHOP
5. Prior high-dose chemotherapy treatment with autologous stem cell transplantation (at least 6 months ago) or not eligible for a high dose approach
6. Age = > 18 years at the time of signing the informed consent
7. Written informed consent
8. ECOG performance status of < = 2 at study entry
9. Able to adhere to the study visit schedule and other protocol requirements
10. Laboratory test result within these ranges:
    - Absolute neutrophil count = > 1.5 x 10^9 / L
    - Platelet count = > 100 x 10^9 / L
    - Serum Creatinine < 2.0 mg/dL
    - Total serum bilirubin < = 2.0 mg/dL
    - AST (SGOT) and ALT (SGPT) < = 3 x ULN
11. special requirements for female patients of childbearing potential regarding contraception and pregnancy tests
12. special requirements for male patients regarding contraception and fathering a child
13. requirements for all patients regarding donating blood and handling study drug
14. Disease free of other malignancies for > = 3 years with exception of basal cell carcinoma of the skin, incidental histological finding of prostate cancer (TNM stage of T1a or T1b) or cervical cancer in situ
15. Able to take aspirin (100 mg) daily as prophylactic anticoagulation. Patients intolerant to ASA may use low molecular weight heparin or coumarin, respectively an equivalent vitamine K antagonist.
16. Negative serology for HIV, Hepatitis B and C at most 4 weeks before inclusion

Test product, dose and mode of administration, batch number:

Le4nalidomide 15 mg daily for up to 2 years
not applicable

Duration of treatment:

Up to 2 years (planned)

Reference therapy, dose and mode of administration, batch number:

not applicable

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Criteria for evaluation:

Efficacy:

Secondary endpoints are

- Response duration (RD): time from registration to progression of lymphoma or death from any cause. Response duration of patients alive without progression will be censored at the date of the latest tumor assessment.
- Overall survival (OS): time from registration to death from any cause. Overall survival of patients alive will be censored at the date of the latest follow-up.

Safety: The *primary* endpoint is the percentage of patients in which lenalidomide maintenance is not stopped prematurely. A premature stop of maintenance is any stop except due to lymphoma progression. In addition, a delay of maintenance due to ANC, platelets or toxicity lasting longer than 4 weeks is considered as premature stop of maintenance.

Secondary endpoints are Type, frequency and severity of adverse events determined by various biochemical parameters and clinical side effects according to the common toxicity criteria (CTC, Appendix IV).

Statistical methods:

The main question will be answered using a one-sided binomial test with null hypothesis
H0: FR $\leq$ 60%
and alternative hypothesis
H1: FR > 60%.
If the FR is only 60% or even lower, lenalidomide maintenance will not be considered further in this setting. Thus, a one-sided alternative hypothesis is sufficient to answer the main question.
With the significance level set to α = 0.05, the critical value for the number of patients without premature stop of maintenance is calculated using the binomial distribution with probability 60%. The null hypothesis will be rejected, if the number of patients without premature stop of patients exceeds the critical value.

The FR rate will be estimated with exact 95% confidence interval in the PP set. RD and OS will be estimated in the PP and ITT sets using the Kaplan-Meier method. One- and two-year survival probabilities will be calculated with 95% confidence intervals. For efficacy evaluation, RD and OS will be compared to the results from the preceding GLSG trial for patients with relapsed MCL (FCM-trial, Forstpointner 2004). Comparisons will be done using the log rank test and performing multiple Cox regression adjusting for important prognostic factors as potential confounders including the MIPI prognostic factors (Hoster et al., 2008), the number of previous therapies and the time between diagnosis and study registration.

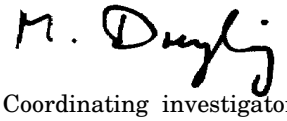
Frequency and severity of side effects will be analyzed by calculating absolute numbers and percentages

in the PP set. In addition, SUSAR's will be tabulated. The frequency of dose reductions or delays will be estimated also according to dose levels in the PP set. Time to first dose reduction and time to premature stop of maintenance will be evaluated using the Kaplan-Meier method. Patients with ongoing maintenance and patients with progression or death will be censored at the date of last contact.

The number of premature stops of maintenance will monitored continuously at the data center. If the number of patients with premature stop of patients reaches the number for which the null hypothesis cannot be rejected any more, recruitment will be stopped.
Data about recruitment, documentation, efficacy, and safety will be analyzed every 6 months according to recruitment by the sponsor. These data will also be reported to the study group members during regular meetings.
The final analysis will be performed, when all recruited patients are evaluable for the primary parameter..

SUMMARY - CONCLUSIONS

According to data of the European MCL network, a maintenance therapy with Rituximab represents the latest standard for treatment of mantle cell lymphoma. For this reason, the sponsor decided that this clinical trial involving a maintenance therapy with Lenalidomid, should not be conducted.
This decision was made after approval of the BfArM (competent authority) and of the Ethics Committee, but before activation of sites. For this reason, no patients were enclosed.
The termination of the study was on 03.02.2011, the notification to the BfArM was on 24.02.2011.



Coordinating investigator

Date of the report: 28.06.2012