2. SYNOPSIS

Name of the sponsor: NV ROCHE SA	Individual Study table Referring to part of the dossier	*(For national Authority use only)*
Name of the finished product: NeoRecormon®	Volume	
Name of Active Ingredient(s): Epoetin Beta, Ro 205-3859	Page	
Title of Study An open label, single-arm, multicenter study to assess the safety and efficacy of once weekly administration of NEORECORMON® using the 30,000 IU pre-filled syringe in anaemic adult patients with solid tumors treated with non-platinum containing chemotherapy: "THE PANTHER TRIAL"		
Principal or Coordinating Investigator [redacted]		
Study Centers 14 centers in Belgium (+ 12 inactive centers; list in appendix 16.1.4)		
Publications None		
Study Period 24 January 2006 (First patient enrolled) 23 August 2006 (Last patient observation)		
Phase of Development Phase IV		
Methodology Open-label, single-arm, multicenter study, 12 weeks treatment, 4 weeks follow-up.		
Number of Patients (Planned and Analyzed) Planned: Minimum 50 Analyzed: 52		

Diagnosis and Main Criteria for Inclusion:

- Adult (≥ 18 years) patients with solid tumors treated with non-platinum containing chemotherapy, which is scheduled for at least 12 weeks
- Haemoglobin ≤11 g/dL at Visit 1
- WHO performance status grade 0-2
- Life expectancy > 6 months
- Written informed consent

Length of study
16 weeks (NeoRecormon® treatment for 12 weeks and 4 weeks of follow-up)

Test Product, Dose, Mode of Administration, and Batch No.
Test Product: NeoRecormon® (epoetin beta) 30,000 IU pre-filled syringe
Dose and mode of administration: subcutaneous injection of 30,000 IU NeoRecormon® administered once weekly.
If after 4 weeks treatment haemoglobin (Hb) had not increased by at least 1 g/dL versus Visit 1 or blood transfusion were necessary in the last week the dose was to be doubled, i.e. 60,000 IU per week.
If the Hb level exceeds 13 g/dL, the administration of the study drug was to be interrupted. The study drug could be re-administrated at 50% of the last dose when the Hb level was again below 13 g/dL
Batch No.: [redacted]

Comparator drug
None

Criteria for Evaluation

Primary variable
Incidence of Adverse Events during the treatment period.

Secondary safety variables

- Incidence of possibly treatment related Adverse Events during treatment period
- Change and abnormalities in laboratory safety parameters
- Vital signs

Primary efficacy variable
Increase in haemoglobin of at least 1 g/dL at Week 4.

Secondary efficacy variables

- % of patients with Hb increased ≥ 1 g/dL at Week 4
- % of response * at Week 12
- Time to response *
- Change in Hb between Visit 1 and subsequent visits
- Proportion of patients with Hb controlled within target range (12 g/dL ≤ Hb ≤ 13 g/dL at 12 weeks
- Need for transfusion
- Number of units transfused

* Response is defined as an increase in Hb concentration ≥ 12 g/dL without red blood cell transfusion within the previous 28 days.

Statistical Methods
Frequencies and exact 95 % confidence intervals were calculated for the number of patients reporting adverse events and possibly related adverse events, overall and by body system.
A descriptive analysis was performed for all efficacy and safety outcome measures.
Time to response was evaluated using Kaplan-Meier survival analysis.

SUMMARY – CONCLUSION

Safety Results

The mean treatment duration was 76 days, ranging from 28 to 91 days. Eight patients discontinued prematurely the study mainly because of AEs (5 patients). Forty-six patients experienced AEs mainly in gastrointestinal disorders, general disorders and administration site conditions, musculoskeletal and connective tissue disorders, vascular disorders, infections and infestations, respiratory, thoracic and mediastinal disorders System Organ Classes (each reported by > 15% of the patients). SAEs were reported for 14 patients and the outcome was death due to the progression of the pathology for 5 patients.
Only 2 of the reported AEs (musculoskeletal pain and swelling face) and none of the SAEs were considered related to NeoReormon®.
Laboratory values with a deviation code 4 were recorded for 4 patients in the following parameters: Leucocyte count (one patient), platelets (one patient) and potassium (2 patients).
No major changes were observed in vital signs and in the WHO performance status between the first and follow-up visits.

Efficacy Results

A total of 52 patients, 43 females and 9 males, with age ranging from 31 to 62 years, were enrolled in the study and received once weekly dose of NeoReormon®. Patients received at least 4 weeks of treatment and 48% of them received 12 weeks of treatment.

The average Hb concentration increases during the first 6 weeks before stabilizing (from 10.2 ± 0.8 g/dL on Day 1 to 11.0 ± 1.3 g/dL on Week 4 and to 11.7 ± 1.6 g/dL at Week 6).
The Hb concentration increased by at least 1 g/dL in 42% of the patients after 4 weeks of the treatment and in 77% of the patients (34/44) after 12 weeks of treatment.

CONCLUSIONS

The results presented in this report demonstrate that 30,000 UI NeoReormon® given subcutaneously once per week is well tolerated by the study population and enables an increase of Hb concentrations in a 6 weeks administration window.

Date of the report: 8 October 2008