Long-term follow-up on the outcome of patients with Essential Thrombocythemia

ET-2014-01

OBSERVATIONAL RETROSPECTIVE AND PROSPECTIVE MULTICENTER NATIONAL STUDY

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RATIONALE OF THE STUDY

The most frequently observed genetic mutation in essential thrombocythemia (ET) is the Janus-associated kinase (JAK)2 V617F mutation, present in about 50% of cases. In around 5% of patients, also mutations in the TPO receptor (MPL) gene have been found. Very recently, also mutations in the gene of CAL-reticuline (CALR) have been identified in approximately 70% of patients without the JAK2 V617F mutation. In view of the high incidence of CALR mutations in ET, the analysis of CALR has entered the routine diagnostic work-up of ET, together with the routine analysis of mutations in JAK2 and MPL genes. Despite the recent biological and therapeutic acquisitions, the clinical and laboratory characteristics of the disease remain to be clarified.

Objectives

Primary endpoint:

- To determine the impact of the clinical and laboratory characteristics on the outcome of patients with ET, in terms of long-term survival.

Secondary endpoints:

- To assess the incidence of thrombotic events, bleeding.
- To assess the incidence of second malignancies and acute leukemias.
- Evaluate the toxicity and the effects of conventional therapies.

Study Design

This is an observational study with a retrospective phase and with a prospective phase, involving patients with ET diagnosed according to the WHO 2008 criteria. ET patients diagnosed since 1980 will be enrolled. In each patient the following parameters will be considered: age, medical history, characteristics of onset of ET, histological, cytogenetic and molecular data at diagnosis or during follow-up, medical treatments performed, type of response to therapy, complications of such therapies and overall outcome.

The enrollment period is estimated at 60 months (June 2014 - June 2019). Observation time will be of 15 years.
Inclusion criteria

- Age of patients ≥ 18 years
- Patients with essential thrombocythemia diagnosed according to the PVSG 1997 or the WHO 2008 criteria
- Informed Consent signed, when applicable.

Exclusion Criteria

- None.

Follow-up visit:

For the prospective follow-up visits, the patients involved in the study will follow the normal process of care, in terms of frequency and examination procedures.

Collection and management of data and statistical analysis

The data will be collected in accordance with the guidelines for the collection of clinical data in the trials (Guidelines of July 2008). The parameters that will be collected are the following: demographics and disease onset, biochemical, haematological, molecular and cytogenetic data, previous treatments, type of treatments, response to therapy, disease characteristics, adverse events with grade and correlation with therapy, use of growth factors, erythropoietin and transfusions, date of last follow-up and disease status, possible date and cause of death. All parameters collected in the CRF will be documented in the medical record of the origin of the patients. All data will be collected by the principal investigator or by someone authorized by him, and with his review and approval, in accordance with ICH guidelines (November 2005). The demographic characteristics of the patients are reported as descriptive statistics: the quantitative parameters are expressed as mean ± standard deviation, the quality parameters are expressed as absolute and relative frequencies. The survival curves will be estimated according to the method of Kaplan-Meier. The analysis will be carried out with the program Stata 11 (StataCorp LP, TX) and statistical significance (p) will be set at ≤ 0.05.
The data will be collected anonymously giving each patient selected only a serial number. The Promoter of the study and the experimental station are the owners of the processing of personal data. The controller is the principal investigator of the center. The data that emerged from the analysis will be processed with statistical methods to extract information that are the purpose of the research. The study manager and his staff will have access to the information and will be bound by a duty of confidentiality and processing of data in accordance with current standards. The staff of the monitoring and verification, the Ethics Committee and the regulatory authorities will have direct access to the medical records to verify the study procedures and/or data, to the extent provided by law. The data will be stored anonymously and identified by unique code number assigned to the patient and will be kept for the period allowed by law. The results of the study will provide the material for a scientific publication in which the data will be reported anonymously.

Management of the informed consent

For patients presently related to the hematologic center, the Investigator must obtain informed consent of a subject or his/her designee prior to any study related procedures as per GCPs as set forth in the CFR and ICH guidelines. Documentation that informed consent occurred prior to the subject’s entry into the study and the informed consent process should be recorded in the subject’s source documents. The original consent form signed and dated by the subject and by the person consenting on behalf of the subject prior to the subject’s entry into the study, must be maintained in the Investigator’s study files.

For deceased patients, given the general authorization for the management of personal data carried out for scientific research issued by the Guarantor on March 1st, 2012 (Official Gazette n. 72, March 26th, 2012), the management of personal data is considered authorized upon the approval of the study by the Ethics Committee.

For patients no longer related to the hematologic center, many ethical reasons support the decision not to contact the patients. Given the oncologic nature of the disease, it is considered unadvisable or not proper to contact the patient specifically to ask for the consent, as it may urge anxiety and concerns. Therefore, given the general authorization for the management of personal data carried out for scientific research issued by the Guarantor on March 1st, 2012 (Official Gazette n. 72, March 26th, 2012), the management of personal data is considered authorized upon the approval of the study by the Ethics Committee.