I-ITP

Short title: Changes in immune profiles and platelet function after start TPO-RA in ITP

Principal investigator: R.E.G. Schutgens

Sponsor: UMC Utrecht

EudraCT nr. (if applicable): NA

Patient population:

Required no. of patients (if applicable): 20 with complete follow-up

Type of study: multicenter, prospective observational cohort study

Study objectives:

Primary objectives: To evaluate a possible change in immunologic profile and platelet function before start and during treatment with eltrombopag

Secondary objectives: To evaluate if there is a difference in platelet function or immunologic profile at baseline between responding and non-responding patients

Subject eligibility criteria:

Inclusion criteria:

- Age 16 years and older
- Previously confirmed diagnosis of primary ITP with current platelet counts of $<100x10^9/L$
- Will start treatment with eltrombopag
- Willing and be able to understand the study information and sign the informed consent form.

Exclusion criteria:

- Documented history of persisting severe anemia (defined as hemoglobin <6.0 mmol/L for men and women)
- Treatment with rituximab in the past 9 months
- Treatment with any immune modulating drug other than corticosteroids in the past 3 months

Status:
Inclusions ongoing

Participating sites:
UMC Utrecht
Diakonessenhuis Utrecht
St. Antonius ziekenhuis Utrecht
Meander Medisch Centrum

Contact for more information:
Uitvoerend onderzoeker:
Drs. W.E.M. van Dijk, arts-onderzoeker
Van Creveldkliniek UMC Utrecht
E-mail: w.e.m.vandijk-16@umcutrecht.nl, tel: 088-7567846

Hoofdonderzoeker UMC Utrecht:
dr. R.E.G. Schutgens, internist-hematoloog
Van Creveldkliniek UMC Utrecht
Tel: 088-7558450

Summary (optional):
Rationale: It has been suggested that prolonged use of TPO-receptor agonists (TPO-RA) can result in immune tolerance induction in patients with ITP. However, little is known about the effect of this kind of immune modulation on B- and T-cell profiles in ITP. Furthermore, the use of TPO-RA is associated with an increased rate of thromboembolic events, suggesting the possibility that TPO-RA alters the platelet function. The aim of this study is to test our hypothesis that TPO-RA increases platelet activity and alters immune profiles in ITP.

Objective: To evaluate possible changes in immune profiles and platelet function after start of eltrombopag, a TPO-RA.

Our secondary objective is to evaluate if there is a difference in platelet function or immunologic profile between responding and non-responding patients.

Study design: non-interventional, non-randomized, non-blinded, observational trial design.

Study population: We will analyse a cohort of adult patients with ITP who will start treatment with eltrombopag, as prescribed by their treating physician.

Study procedures: Five times an extra bloodsample (five tubes) withdrawal: before start of eltrombopag, at 2-3 weeks, and 3, 6 and 12 months after start of a TPO-RA. Patients might be asked to come to the UMC Utrecht for the withdrawal, depending on the laboratory facilities in their own treatment center. The withdrawal is usually done during a routine venipuncture as part of standard

of care; only before start of TPO-RA might an extra venipuncture be necessary due to the (semi)acute indication to start with eltrombopag.

For the Biobank, one extra tube per withdrawal and any remaining materials after analyses will be stored for additional testing in the future. **Main study parameters/endpoints:**

Primary endpoints: monitor B and T cell profiles and changes in platelet function and reactivity in adult patients with ITP who are treated with eltrombopag.

Nature and extent of the burden and risks associated with participation, benefit and group relatedness:

At least four out of five times, the blood sample will be taken during a scheduled venipuncture, as part of standard of care. Because only a small volume will be withdrawn, the risk is considered negligible. Possibly, one extra venipuncture is necessary. Venipunctures are carried out very often in ITP patients and the associated risk is considered low. Possible risks of the venipuncture are formation of a small, local hematoma and pain/discomfort.

If patients are asked to come the UMC Utrecht for the venipuncture, travel expenses and parking costs will be compensated. The blood results that are relevant for the patient's treatment will be sent to the patient's physician, so the study withdrawals will still be combined with the standard of care venipuncture, as mentioned above.