1. ABSTRACT

- **Title**

Use of Bone Marrow Biopsies in Patients With Chronic Immune Thrombocytopenia: Predictors for, and Prognosis After – a Nordic Population-based Cohort Study and a Nested Case Control Study

[redacted], Department of Clinical Epidemiology, Aarhus University Hospital, Aarhus, Denmark; 29 May 2020

- **Keywords**

Bone marrow biopsy, cITP, hematological malignancy, chronic immune thrombocytopenia, observational study

- **Rationale and Background**

Primary immune thrombocytopenia (ITP) is a diagnosis of exclusion, with no diagnostic tests available to confirm the ITP diagnosis, but secondary causes of thrombocytopenia must be excluded before diagnosis of primary ITP can be made. The American Society of Hematology (ASH) has recommended since 2011 (per ITP guidelines) against a bone marrow examination as part of the diagnostic work-up, irrespective of age, in patients presenting with typical ITP. Therefore, ITP patients who undergo a bone marrow biopsy (BMB) probably represent a selected group of patients with less typical disease and a higher chance of having secondary thrombocytopenia.

- **Research Question and Objectives**

Primary objectives of this study are to:

- estimate prevalence of previous BMB at date of chronic ITP (cITP) diagnosis
- estimate the incidence of BMB among patients with cITP
- identify characteristics associated with an increased risk of having a BMB among patients with cITP, and to
- assess whether having a BMB is associated with a higher risk of death, hematological cancer, hospitalized bleeding events, or thrombotic events

- **Study Design**

A population-based cohort study and a nested case control study.

Case control design is used to identify predictors of BMB after cITP diagnosis and involves comparison of cITP patients who underwent a BMB after cITP diagnosis (cases) with a group consisting of cITP patients without a BMB at the index date (date of BMB of matched cases) matched (1:1) by country and year of cITP diagnosis (controls).

Cohort analysis of incident cITP patients to date of death, hematological cancer, hospitalized bleeding event, and thrombotic event (with BMB as a time varying exposure).

- **Setting**

This study was conducted in Denmark, Norway, and Sweden, using data previously collected in National Health Registry Systems (NHRSs) and medical records as part of patients' routine medical care.

- **Subjects and Study Size, Including Dropouts**

All adults (≥18 years) with two or more ITP diagnoses registered at least 6 months apart from 1 January 1996 to 31 December 2017.

A total of 4471 adult cITP patients were included in study.

- **Variables and Data Sources**

Administrative medical care data collected from respective National Health Registry Systems (NHRSs) and medical records of Denmark, Norway and Sweden.

- **Results**

Of the 4471 adult cITP patients included in study, 1683 (37.6%) had a BMB before date of cITP diagnosis while the cumulative incidence of bone marrow biopsies was 3.1% at 1 year and 7.5% at 5 year after cITP diagnosis date.

Predictors for having a BMB after cITP diagnosis included increasing age, male sex, platelet count < 50 x 10^9/L (measured within 90 days of cITP diagnosis), splenectomy, and number of different cITP treatments.

Patients who underwent BMB after cITP diagnosis had higher complications rates such as thrombotic events (1-year adjusted hazard ratio [HR] 1.53 [95% confidence interval [CI], 0.92-2.54]), hospitalized bleeding episodes (1-year adjusted HR 1.72 [95% CI, 1.15-2.58]) and all-cause mortality (1-year adjusted HR 1.97 [95% CI, 1.44-2.68]).

The 1-year rate of hematological cancer per 1000 person years was 266.88 (95% CI, 158.17-421.78) among cITP patients who had a BMB compared with 7.09 (95% CI, 4.78-10.12) in cITP patients who did not, 1-year adjusted HR was 35.26 (95% CI 17.67-70.34).

- **Discussion**

Patients who undergo a BMB after cITP diagnosis represent a highly selected group with more severe disease and increased rates of complications as well as hematological malignancies.

- **Marketing Authorization Holder(s)**

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