ELSEVIER

Blood 142 (2023) 3397–3399

The 65th ASH Annual Meeting Abstracts

# POSTER ABSTRACTS

## 654.MGUS, AMYLOIDOSIS AND OTHER NON-MYELOMA PLASMA CELL DYSCRASIAS: CLINICAL AND EPIDEMIOLOGICAL

### Risk Factors of Smoldering Multiple Myeloma: Results from the Screened Istopmm Study

*Sigrun Thorsteinsdottir, MDPhD*[1,2], *Ingigerdur Sverrisdottir, MD*[1,3], *Sæmundur Rögnvaldsson, MD PhD*[4,1], *Sara Ekberg, PhD*[5], *Malin Hultcrantz, MDPhD*[6], *Brynjar Vidarsson, MD*[4], *Pall T. Onundarson, MD*[4], *Bjarni Agnarsson, MD*[1,4], *Margret Sigurdardottir, MD*[4], *Ingunn Thorsteinsdottir, MDPhD*[4], *Isleifur Olafsson, MDPhD*[4], *Asdis Rosa Thordardottir*[1], *Jon Thorir Oskarsson, MSc*[7], *Gudrun Asta Sigurdardottir*[1], *Elias Eythorsson, MDPhD*[1,4], *Asbjorn Jonsson, MD*[8], *Gauti Gislason, MSc*[1], *Andri Olafsson*[1], *Jon Kristinn Sigurdsson*[1], *Thorir Einarsson Long, MDPhD*[9,10], *Brian GM Durie, MD*[11], *Stephen J. Harding, PhD*[12], *Ola Landgren, MD*[13], *Thorvardur Jon Love, MD PhD*[1,4], *Sigurdur Y. Kristinsson, MDPhD*[1,4]

[1] Faculty of Medicine, University of Iceland, Reykjavik, Iceland
[2] Department of Hematology, Rigshospitalet, København, Denmark
[3] Dept. of Haematology and Coagulation, Sahlgrenska University Hospital, Gothenburg, Sweden
[4] Landspitali, The National University Hospital of Iceland, Reykjavik, Iceland
[5] Red Door Analytics AB, Stockholm, Sweden
[6] Myeloma Service, Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, NY
[7] Faculty of Medicine, University of Iceland, Reykjavik, Iceland
[8] Akureyri Hospital, Akureyri, Iceland
[9] Faculty of Medicine, University of Iceland, Reykjavik, Iceland
[10] Skåne University Hospital, Lund, Sweden
[11] Samuel Oschin Comprehensive Cancer Institute, Cedars-Sinai Outpatient Cancer Center, Los Angeles, CA
[12] The Binding Site Inc., Birmingham, United Kingdom
[13] Sylvester Comprehensive Cancer Center, Myeloma Division, University of Miami, Miami, FL

**Introduction**

Smoldering multiple myeloma (SMM) is an asymptomatic precursor condition to multiple myeloma (MM) that carries a higher risk of progression to MM than monoclonal gammopathy of undetermined significance (MGUS). This study aimed to identify potential risk factors of SMM by analyzing the association of baseline characteristics, body mass index, smoking, alcohol consumption, prior diagnoses of autoimmune diseases and prior chronic infections and SMM in the screened Iceland Screens, Treats, or Prevents Multiple Myeloma (iStopMM) study cohort.

**Methods**

The iStopMM study is a screening study for MM precursors where 75,422 individuals over 40 years old in Iceland were screened with serum protein electrophoresis (SPEP) and free light chain (FLC) analysis. Those with a positive screening result were randomized to one of the three study arms, with clinical evaluation at the study center, including bone marrow sampling, performed in two of them. MGUS was defined by the presence of a serum M-protein concentration less than 30 g/L and less than 10% clonal plasma cells in the bone marrow, and SMM was defined as 10-60% bone marrow plasma cells and/or M-protein concentration over 30 g/L, both in the absence of MM defining events. IgM MGUS was excluded in this analysis. Height and weight were measured at the first visit to the study center, alcohol and smoking habits were evaluated with questionnaires. Information on previous diagnoses (ICD codes) was obtained from central health registries with almost 100% completeness. Logistic regression models were used to calculate odds ratio (OR) with 95% confidence interval (CI) to compare risk factors in SMM vs. MGUS and SMM vs. controls. All analyses were adjusted for age and sex.

**Results**

At the first study center evaluation, 210 individuals were diagnosed with SMM and 1,456 with MGUS. Data from 70,627 controls with negative SPEP and normal FLC analysis were included. Individuals with SMM were older and more frequently male than controls, however there was no statistically significant difference between the sex and age distribution of individuals with SMM and MGUS (Figure). Immunoparesis (OR 3.98; 95% CI: 2.74-5.76), abnormal FLC ratio (OR 3.61; 95% CI: 2.59-5.02), IgA isotype (OR 2.64; 95% CI: 1.83-3.83) and increasing M-protein levels (OR per g/L 1.33; 95% CI: 1.27-1.39) were all associated

with increased odds of SMM compared to MGUS. BMI measured at the first study visit was not significantly different between individuals with MGUS and SMM (overweight vs. normal weight OR 1.08; 95% CI: 0.74-1.56). Neither current or previous smoking nor alcohol consumption more than once per week (vs. less) was associated with increased risk of SMM compared to MGUS (OR 0.88; 95% CI: 0.60-1.31, and OR 0.97; 95% CI: 0.62-1.53, respectively) or controls (OR 0.92; 95% CI: 0.64-1.33, and OR 0.85; 95% CI: 0.57-1.27, respectively). Prior diagnosis of autoimmune disease was not associated with SMM as compared to MGUS (OR 1.19; 95% CI: 0.81-1.74) or controls (OR 1.21; 95% CI: 0.85-1.73). A previous diagnosis of a chronic infection was not statistically significantly associated with increased risk of being diagnosed with SMM as compared to MGUS (OR 1.53; 95% CI: 1.00-2.34) but an association was seen when compared to controls (OR 1.54; 95% CI: 1.05-2.28). In individuals with SMM, the most common chronic infections were varicella zoster virus and herpes simplex virus, no diagnoses of hepatitis virus or chronic bacterial infections were observed.

**Conclusion**

In this large population-based screening study we did not find an association of smoking, alcohol consumption, BMI, or a prior diagnosis of autoimmune disease and SMM compared to MGUS. We found an association between a previous diagnosis of a chronic infection and SMM which could be explained by reverse causality, i.e., that SMM leads to immune impairment which increases the risk of viral infections. We found no significant age or sex difference between individuals with MGUS and SMM, but results from blood tests, including immunoparesis, abnormal FLC ratio, IgA-isotype, and higher levels of M-protein were all associated with SMM compared to MGUS. Our results indicate that neither lifestyle factors nor chronic inflammatory conditions increase the risk of SMM, and that the differences between individuals with MGUS and SMM can be detected in blood assessments associated with the plasma cell clone, but not in demographic or behavior related factors.

**Disclosures Hultcrantz:** *Amgen, Daiichi Sankyo, GlaxoSmithKline:* Research Funding; *Curio Science LLC, Intellisphere, Bristol Myer Squibb, GlaxoSmithKline:* Honoraria. **Harding:** *Bindingsite ltd.:* Current Employment, Membership on an entity's Board of Directors or advisory committees. **Landgren:** *Merck:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Other: Membership on independent data monitoring committees; *Amgen:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Other: Membership on independent data monitoring committees; *Takeda:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Other: Membership on independent data monitoring committees; *Janssen:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Other: Membership on independent data monitoring committees; *Celgene:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Other: Membership on independent data monitoring committees; *Adaptive:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Other: Membership on independent data monitoring committees; *Theradex:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Other: Membership on independent data monitoring committees. **Kristinsson:** *Celgene:* Research Funding; *Amgen:* Research Funding.

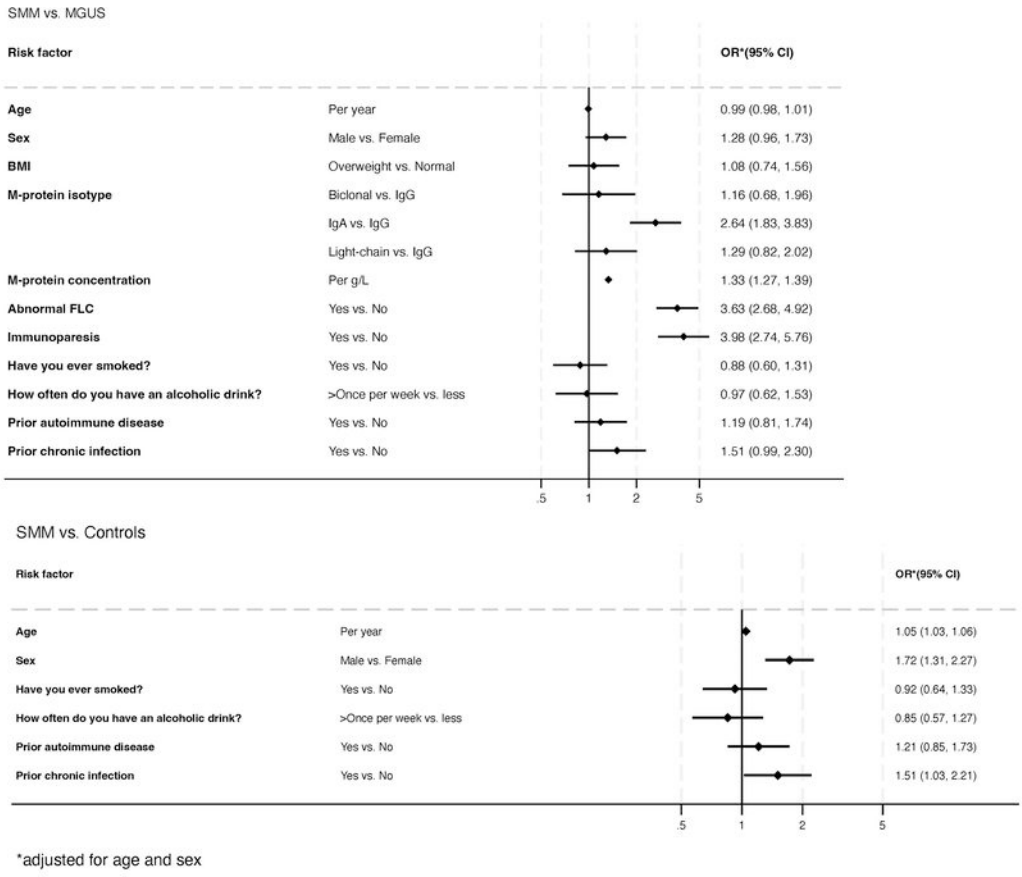


**Figure**: Forest plots showing odds ratios with 95% confidence intervals for the association of baseline characteristics, body mass index, smoking, alcohol consumption, prior diagnoses of autoimmune diseases and chronic infections, and smoldering multiple myeloma compared to monoclonal gammopathy of undetermined significance and controls

**Figure 1**

https://doi.org/10.1182/blood-2023-188469