# Abstract: P817

# Title: VALIDATION OF THE SECOND REVISED INTERNATIONAL STAGING SYSTEM (R2-ISS) IN A LARGE POPULATION-BASED, NATIONWIDE COHORT OF PATIENTS WITH NEWLY DIAGNOSED MULTIPLE MYELOMA

**Abstract Type: Poster Presentation**

**Session Title: Myeloma and other monoclonal gammopathies - Biology & Translational Research**

**Background:**

The revised international staging system (R-ISS) was recently updated as the second R-ISS (R2-ISS; D'Agostino et al., JCO, 2022) and refined the prognosis in patients with newly diagnosed multiple myeloma (NDMM).

**Aims:**

To validate the R2-ISS in a population-based nationwide cohort.

**Methods:**

We included all Danish patients registered with NDMM in the Danish Myeloma Database (2005 through 2019) via the Danish Lymphoid Cancer Research (DALY-CARE) database. We excluded patients without an indication for treatment (according to CRAB criteria) and patients who had not started anti-myeloma therapy within three months from diagnosis. To calculate R-ISS and R2-ISS, we retrieved information on international staging system (ISS; albumin and beta-2-microglobulin levels), lactate dehydrogenase (LDH) level, and adverse fluorescence in situ hybridization (FISH) cytogenetics; t(4;14), t(14;16), del(17p), and amp(1q). LDH levels above 205 U/L were considered elevated regardless of age and geographical region. FISH aberrations were dichotomized as either present or absent despite varying lower detection levels at different laboratories. In general, a cutoff of 10% was used for FISH analyses.

We calculated overall survival (OS) from time of diagnosis until death with censoring at end of follow-up. Patients were grouped according to R-ISS and R2-ISS to compare median OS and calculated Harrell's C-index to assess discrimination capabilities. The study was approved by the Danish National Ethics Committee (1804410) and Data Protection Agency (P-2020-561).

**Results:**

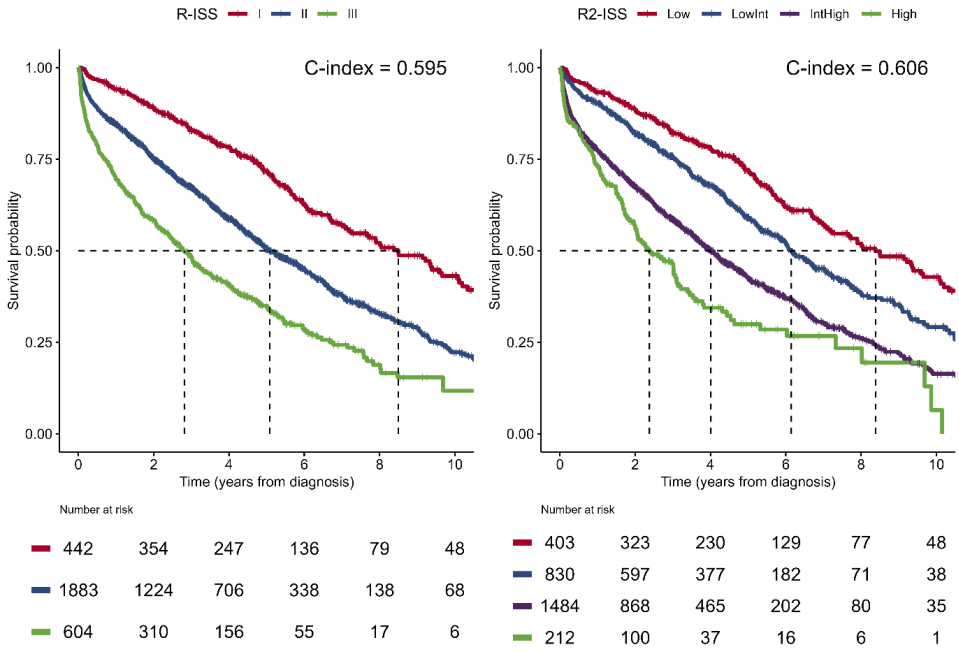
We identified 5492 patients with NDMM. FISH data were available in 2929 patients (53.3%): 188 patients had t(4;14), 77 had t(14;16), 238 had del(17p) and 546 had amp(1q). In total, adverse cytogenetics for R-ISS (del[17p], t[4;14], and t[14;16]) and R2-ISS (del[17p] and amp[1q]) were detected in 452 (15.4%) and 721 (24.6%) patients, respectively. Baseline characteristics for the 2929 patients with available FISH data demonstrated a median age of 70 years (IQR, 62-77), 56.5% were male (n = 1655) and the median LDH was 184 U/L (IQR, 151-226) with an elevated LDH in 35.1% of patients (n = 1027). The original ISS stage was I, II, and III in 693 (23.7%), 1091 (37.2%), and 1145 (39.1%) patients, respectively. Further, R-ISS was I, II and III in 442 (15.1%), 1883 (64.3) and 604 (20.6%) patients, respectively, while R2-ISS was low, low-intermediate, intermediate-high, and high-risk in 403 (13.8%), 830 (28.3%), 1484 (50.7%), and 212 (7.2%) patients, respectively.

The median follow-up was 5.2 years (IQR, 3.1-7.8) for the 2929 patients with available R-ISS and R2-ISS. The median OS for patients with R-ISS I, II, and III was 8.5, 5.1, and 2.8 years, respectively ($P<0.0001$; C-index 0.595), while the median OS for patients with R2-ISS low, low-intermediate, intermediate-high, and high-risk was 8.4, 6.1, 4.0, and 2.4 years, respectively ($P<0.0001$; C-index 0.606).

**Summary/Conclusion:**

This is, to our knowledge, the first validation of the R2-ISS in a population-based, nationwide cohort of patients

with multiple myeloma. We found that the R2-ISS demonstrated superior discriminatory capabilites when compared with R-ISS. R2-ISS primarily refined the prognosis for patients previously classified as R-ISS II (nearly two-thirds of patients), while the prognosis for patients with R-ISS I and III was similar to those with R2-ISS low and high risk, respectively.




**Keywords:** Multiple myeloma, Prognosis, FISH, Staging