Mapping of Treatment Patterns and Transfusion Status in Danish and Swedish Myelofibrosis (MF) Patients

Observed differences in MF treatment patterns and healthcare resource utilisation between Denmark and Sweden likely reflect a lack of alignment in clinical practice during the study period, particularly in the management of MF patients with anaemia

Digital poster

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Erik Ahlstrand[1], Christen Lykkegaard Andersen[2], Anna Ravn Landtblom[3], Katja Nolvi[4], Mathias Lilja[5], Morten Johnsen[6], Lone Sander Dalsgaard[7], Ami Albihn[8]

[1]Örebro University Hospital, Örebro, Sweden; [2]Rigshospitalet, Copenhagen, Denmark; [3]Karolinska University Hospital, Stockholm, Sweden; [4]Quantify Research, Helsinki, Finland; [5]Quantify Research, Stockholm, Sweden; [6]Quantify Research, Copenhagen, Denmark; [7]GSK, Copenhagen, Denmark; [8]GSK, Stockholm, Sweden

Background

- Myelofibrosis (MF) is a rare myeloproliferative neoplasm, currently incurable in most patients[1]
- Janus kinase (JAK) inhibitors are becoming standard therapies for MF; however, the existing JAK inhibitors ruxolitinib and fedratinib may induce or aggravate anaemia[2,3]
- Consensus is lacking on how to manage treatment-related anaemia in the Nordic countries[4,5]

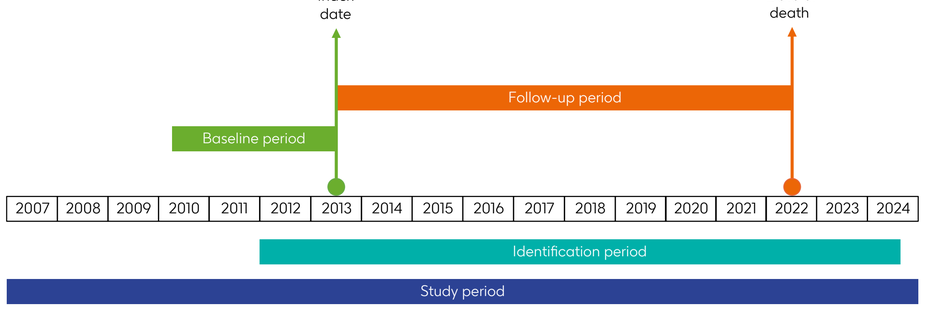
Aim

We collected real-world data on patients with MF in Denmark and Sweden with the aim to assess treatment patterns, associated outcomes and healthcare resource utilisation/costs related to anaemia and transfusion status

Methods

- This observational retrospective cohort study is based on quality registry data (2007–2024)*. Patients were identified using the International Classification of Diseases (ICD)/ICD-10 codes for MF in the Danish Cancer Registry (1 January 2012–31 December 2022) and the Swedish National Quality Registry for Myeloproliferative Neoplasms (MPN; 1 January 2012 –31 August 2024)
- The index dates were set as the date of MF diagnosis in each country at any time during 2012–2024. A 5-year baseline period was applied to collect clinical characteristic information prior to diagnosis, after which the patients were followed-up from 2012 onwards until death, emigration or last available data (**Figure 1**)
- Patients with an MF diagnosis in the study period were eligible for inclusion
- Exclusion criteria were:
  - Presence of other cancers at baseline
  - A post-index diagnosis of polycythaemia vera or essential thrombocythemia
  - Not being a national citizen at index
- Records of interventions and medication use were retrieved from hospital/prescription registries, and mortality data from causes of death registries
- At baseline, patients were categorised as non-anaemic (haemoglobin: ≥12 g/dL), or anaemic with mild (10–<12 g/dL), moderate (8–<10 g/dL) or severe anaemia (<8 g/dL)
- During follow-up, haemoglobin was one of three parameters used to define patient transfusion status as either transfusion-independent, -requiring or -dependent (**Supplementary Figure 1**)

Figure 1: **Study schema; *the study period spanned from 1 January 2007 until 31 August 2024 (Denmark), and until 31 December 2024 (Sweden)**



The index date and the date of death shown in the figure are illustrative of one fictional patient.

Results

- Baseline characteristics for eligible patients were split by country (**Table 1**): overall, 27% from Denmark and 22% of the patients with MF from Sweden had moderate to severe anaemia

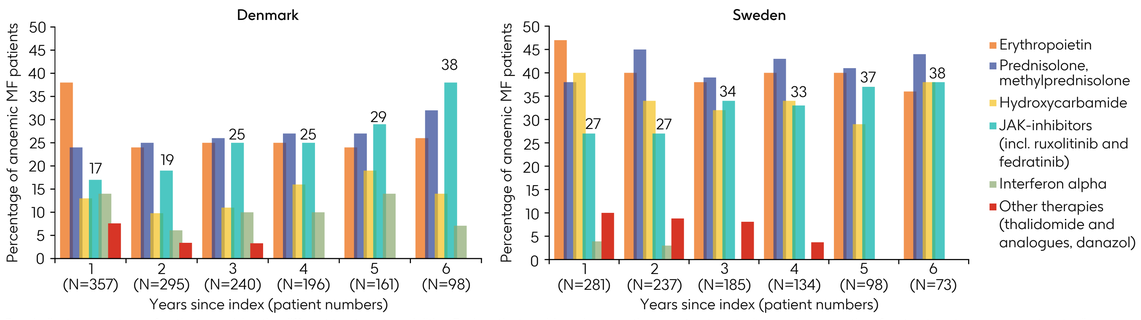
Table 1: **Overall, 794 patients from Denmark and 817 patients from Sweden were included**

	Denmark		Sweden	
	Actual	Missing, N (%)	Actual	Missing, N (%)
Demographics				
Number of patients, N	794		817	
Sex - Female, N (%)	334 (42)		353 (43)	
Age, median (IQR)	72 (15)		72 (16)	
Clinical characteristics				
Blood counts, median (IQR)				
Haemoglobin - g/dL	12.3‡ (3.2)	122 (15)	11.9 (3.3)	2 (0.2)
Platelets - 10^9/L	458.3‡ (492)	97 (12)	506.8‡ (529)	3 (0.4)
Leucocytes - 10^9/L	9.8 (8.1)	128 (16)	9.5 (7.4)	2 (0.2)
Blast cells - 10^9/L	0.3‡ (0.2)	505 (64)	0 (0.1)	195 (24)
Platelet subgroups, N (%)		97 (12)		3 (0.4)
Platelet count ≤50 x 10^9/L	26 (3.7)		22 (2.7)	
Platelet count ≤100 x 10^9/L	64 (9.2)		61 (7.5)	
Platelet count ≤200 x 10^9/L	150 (22)		158 (19)	
Anaemia status*†, N (%)		121 (15)		2 (0.2)
Non-anaemic	330 (49)		406 (50)	
Mild anaemia	164 (24)		236 (29)	
Moderate anaemia	141 (21)		143 (18)	
Severe anaemia	38 (5.6)		30 (3.7)	
Blood transfusions - yes†, N (%)	72 (9.1)	0 (0)	93 (11)	0 (0)
Whole blood	51 (6.4)		<5 (-)	
Platelets	9 (1.1)		<5 (-)	
RBC	19 (2.4)		91 (11)	
Sweden only				
Mutational status				65 (8.0)
JAK2 V617F			428 (52)	
JAK2 other			5 (0.6)	
MPL			40 (4.9)	
CALR			148 (18)	
No mutation			121 (15)	

*Haemoglobin levels; ≥12g/dL= non-anaemic; 10–<12g/dL= mild anaemia; 8–<10 g/dL or 1 blood transfusion = moderate anaemia; and <8g/dL or ≥2 blood transfusions = severe anaemia.
†Percentages shown are calculated from the MF patients where data were available.
‡Central value derived from a range around the median, based on data from ≥5 patient observations.
In Danish patients with no anaemia, mild anaemia or for whom haemoglobin data were missing at baseline, development of anaemia during the first year after diagnosis was assessed (**Supplementary Figure 2**)
CALR, calreticulin; IQR, inter-quartile range; MPL, myeloproliferative leukaemia virus oncogene; RBC, red blood cells.

- Treatment of MF differed, including higher usage of interferon alpha and lower usage of hydroxycarbamide in Denmark than in Sweden
- There was a trend toward a higher usage of anaemia-related therapies in Sweden versus Denmark
- For both countries, the proportion of anaemic patients receiving JAK inhibitor treatment increased with time after index date (**Figure 2**)

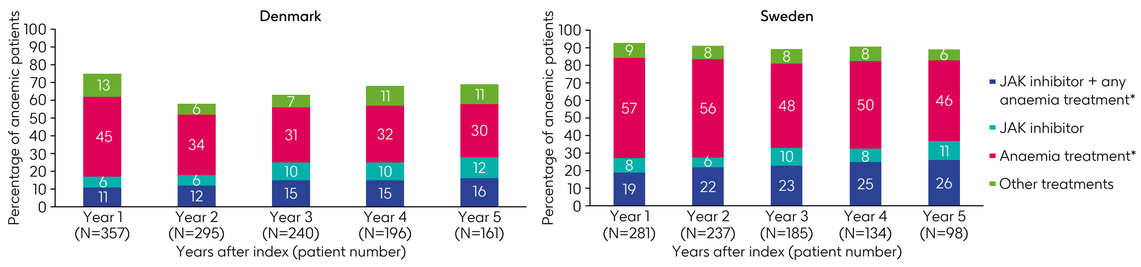
Figure 2: **Treatment patterns differed for patients with MF with anaemia in Denmark and Sweden**



Bars indicate percentage of patients receiving the different treatment modalities. Each patient could receive more than one treatment within a given year, therefore treatment groups are not mutually exclusive. Labels above light blue bars indicate percentage of patients receiving JAK inhibitors over the course of follow-up.

- Anaemia treatment alone decreased from Year 1 to Year 5, usage of JAK inhibitor + anaemia treatment increased and, in a few cases, patients received JAK inhibitor treatment alone (**Figure 3**)

Figure 3: **Most patients received anaemia treatment while some received JAK inhibitor therapy (with/without concomitant anaemia treatment)**



Including erythropoietin, corticosteroids (prednisolone, methylprednisolone), thalidomide and analogues, or danazol.

- In total, 228 Swedish patients with MF received ≥1 dispensation of ruxolitinib; one quarter of whom received 10mg BID as an initial dose, only 15% received the full starting dose at 20mg twice daily (BID), while 30% initiated their treatment on 15mg BID and 29% on 5mg BID (**Table 2**)

Table 2: **Patients received an initial dose of ruxolitinib followed by another at 3 months, which varied per individual**

	Patients with ≥1 ruxolitinib dispensation, N	Patients on 5mg BID, n (%)	Patients on 10mg BID, n (%)	Patients on 15mg BID, n (%)	Patients on 20mg BID, n (%)
Initial dose	228	66 (29)	58 (25)	69 (30)	35 (15)
Dose at 3 months	172	48 (28)	49 (29)	50 (29)	25 (15)

- Throughout the observation period, fewer patients with haemoglobin <10 g/dL received ruxolitinib 3 months after, than 3 months before anaemia related treatment or transfusion (=event, **Table 3**). This was less pronounced in all 191 MF patients with events, especially when assessing individual follow-up years (**Table 3** and not shown)

Table 3: **Over the whole observation period, 191 Swedish patients with MF received either anaemia related drug treatments or transfusions**

	Over whole treatment period		
	Number of patients, N	3 months prior to drug treatment or transfusion event	3 months after drug treatment or transfusion event
		Patients with ≥ 1 ruxolitinib dispensation, n	Patients with ≥ 1 ruxolitinib dispensation, n
Anaemia related treatment or transfusion	191	171	156
Haemoglobin <8 g/dL	11	9	*
Haemoglobin <10 g/dL	64	45	28

Secondary disclosure

- Of 228 Swedish patients initiated on treatment with ruxolitinib; 50% of patients were estimated to remain alive and on ruxolitinib treatment for just over 1 year after initiation (**Figure 4**); this is a shorter median treatment persistence than the 2-3 years that has previously been reported[6,7]
- In Denmark, a high percentage of the transfusion-dependent patients with MF received concomitant anaemia-specific medical treatments, spanning from more than 50% to nearly 80% of all transfusion-dependent patients with MF from Years 1–6 after index (**Figure 5**). Numbers are similar in Sweden (not shown)

Figure 4: **Kaplan–Meier analysis of Swedish patients who initiated ruxolitinib**

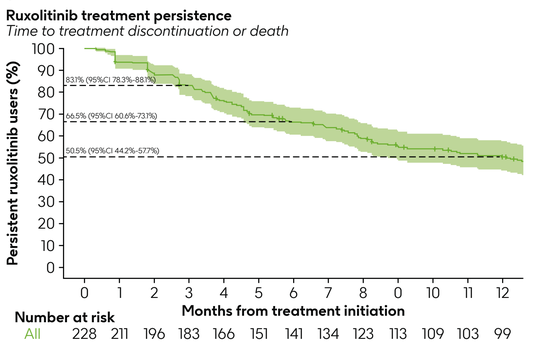
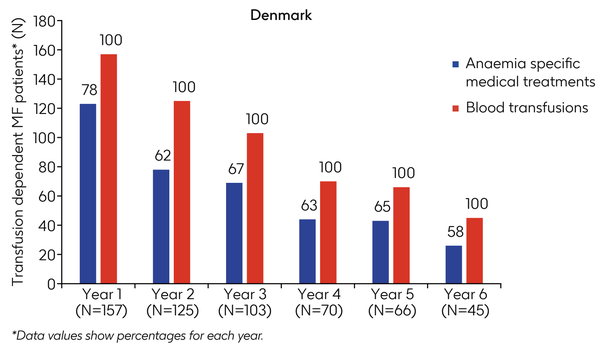


Figure 5: **Concomitant anaemia treatments remained high in Denmark from Years 1 to 6 after index**



Data values show percentages for each year.

- In Denmark, blood transfusion cost was €779,578 for 794 patients in Year 1 and €393,243 for 372 patients in Year 5. Patients received 1.8–2 average transfusions per year, with an average cost per patient of €981–1056. Transfusion-dependent patients received an average of 7.1-7.4 transfusions per year, corresponding to €3770–3946 per patient (**Supplementary Table 1**)
- In Sweden, blood transfusion cost was €316,610 for 817 patients in Year 1 and €133,234 for 327 patients in Year 5. The average number of transfusions per year was 0.5–0.6 per patient, resulting in an average cost of €375–409. In transfusion-dependent patients, the average number of transfusions increased from 3.6 to 5.3 over the 5-year period, giving an average cost per patient of €2602–3797 (**Supplementary Table 1**)
- The median survival for the studied MF patients was aligned with what has previously been reported for MF patients, 5.3 years in Denmark and 6.8 years in Sweden (**Supplementary Figure 3**). Acute myeloid leukaemia transformation is discussed in the supplementary material

Conclusions

- Danish and Swedish quality registries with high coverage, level of completeness and detail, and traceability allows analysis of MF treatment patterns, anaemia status, transfusion dependency and clinical and economic outcomes[8,9]
- The observed differences in MF treatment patterns and healthcare resource utilisation between Denmark and Sweden likely reflect a lack of alignment in clinical practice during the study period, particularly in the management of MF patients with anaemia
- Therapies that can improve transfusion independence rate and lower transfusion burden can lead to reductions in patient burden and healthcare utilisation costs in both countries.

Abbreviations

BID, twice daily; CALR, calreticulin; ICD, International Classification of Diseases; IQR, inter-quartile range; JAK, Janus kinase; MF, myelofibrosis; MPL, myeloproliferative leukaemia virus oncogene; MPN, myeloproliferative neoplasms; RBC, red blood cells.

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Presenter: Ami Albihn | ami.x.albihn@gsk.com