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634.MYELOPROLIFERATIVE SYNDROMES: CLINICAL AND EPIDEMIOLOGICAL

A Real World, Single-Centre Study of Young Adult Patients with Philadelphia Negative Myeloproliferative Neoplasms

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Classical 'Philadelphia negative' myeloproliferative neoplasms (MPNs) are clonal haematopoietic disorders and include essential thrombocythaemia (ET), polycythaemia vera (PV) and myelofibrosis (MF). MPNs have a heterogenous phenotype with an inherent risk of thromboembolic and haemorrhagic complications, and risk of blastic transformation. MPNs are commonly diagnosed in the 6 th decade or later, although up to 20% of patients are diagnosed < 40 years. Current risk stratification and treatment guidance, however, is frequently extrapolated from older cohorts.

Here, we present a comprehensive retrospective analysis of 107 MPN adolescent and young adult (AYA) patients diagnosed <40 years, representing 19.6% of the total outpatient MPN cohort at University College London Hospital. Median follow up was 78 months (range (r), 1 - 507). Table 1 displays clinicopathological details of the entire cohort. Median age at diagnosis was 32 years (r,13-40). There was a female preponderance (66%); 57.9% of patients were Caucasian. Most patients had a diagnosis of ET (57.9%), with 24.3% PV and 9.3% MF, respectively. The most common driver mutation was *JAK2* V617F, observed in 60.7%, followed by *CALR* (15.9%) and *MPL* (1.9%); 17% of patients were classified as triple negative (TN). Where data was available (n=27), median variant allelic frequency (VAF) for *JAK2* V617F was 19.7% (r, 4-75%) and for *CALR* 43% (r, 5.7 - 53). 9/107 (8.4%) of patients had additional pathogenic gene abnormalities, most commonly variants of NRAS (22.2%), TET2 (22.2%) and ASXL1 (22.2%).

We observed a high thrombosis rate of 19.6% (21/107); the majority had a diagnosis of ET (61.9%).. In 80% of such cases, this was the heralding event leading to the MPN diagnosis. Venous thrombosis was more frequent than arterial thrombosis (68% vs 33%). In particular, there was a disproportionate number of venous thromboses at unusual sites including cerebral venous sinus and splanchnic venous thromboses, representing 40% and 33% of total events, respectively. Only 3 (2.8%) patients were found to have a co-existent thrombophilia. Younger age at diagnosis appeared to associate with a higher rate of thrombosis (60% in patients aged <20, 18.2% in patients aged 20-30, and 17.2% in patients aged 31-40). Thrombotic events were most common in those with a *JAK2*V617 mutation (23.4%), followed by those who were TN (20.0%). Only 5.9% of *CALR* mutated cases had a thrombotic event. In terms of cardiovascular risk factors, 13.0% (14/107) and 6.5% (7/107) of patients had diagnoses of hypertension and type 2 diabetes, respectively.

Haemorrhagic events were reported in 8.4% (9/107) of patients; 3.7% (4/107) had grade 3 or 4 bleeding complications, requiring transfusion and/or surgical intervention. All who experienced haemorrhagic events were on treatment with an anti-platelet or anti-coagulant agent. 4.7% (5/107) were diagnosed with acquired von Willebrand's disease, of whom one experienced a grade 3 haemorrhagic event. No patients transformed during follow up. 33 patients reported pregnancies, with 7/33 (21%) reporting antenatal or perinatal medical complications.

Over 50% (55/107) of patients were commenced on cytoreduction. Most common agents employed were pegylated interferon (45.5%; 25/55) and hydroxycarbamide (43.6%%; 24/55). No patients required combination therapy. 92/107 (86%) patients were treated with an antiplatelet agent and 9/107 (8.4%) were on anti-coagulant treatment with the majority (88.8%) receiving warfarin rather than a DOAC.

AYA MPN patients have unique characteristics and heterogeneous clinico-biological features differentiating them from older MPN cohorts. Our data highlights a female preponderance, higher incidence of venous thrombosis (particularly atypical sites), and lower incidence of arterial thrombosis. Whilst traditionally younger patients are considered to have 'low risk' disease, this real-world study highlights a significant thrombosis rate of ~ 20% which may have associated morbidity considering the rela-

tively longer duration of the disease course and need for cytoreductive therapy. Specific AYA MPN directed risk stratification and therapeutic algorithms are required to inform holistic and age-appropriate patient management.

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	Total Cohort (n=107)	Age At Diagnosis		
		<20 (n=5)	20-30 (n=44)	31-40 (n=58)
Median Age at Diagnosis	32 (13-40)	15 (13-18)	26 (21-30)	35 (31-40)
Female	66	3	26	37
Male	41	2	18	21
ET	68	4	27	37
PV	26	0	12	14
MF	10	1	3	6
MPN-U	3	0	2	1
***JAK2* V617F**	65	0	24	38
CALR	17	3	9	8
MPL	2	0	1	1
***JAK2* exon 12**	3	0	1	2
***JAK2* exon 13**	1	0	1	0
Triple Negative	20	2	9	9

Table 1: Patient demographics, diagnosis and mutational status.

ET= essential thrombocythaemia, PV=polycythaemia vera, MF=myelofibrosis, MPN-U = myeloproliferative neoplasm unclassified

Figure 1