Supplementary material

Table S1. Patients' demographics and clinical characteristics at diagnosis of myelofibrosis

Variables	N. non missing	Values
Age, years, *mean (SD)*	1,010	63.7 (12.7)
Male sex, *n (%)*	1,010	605 (59.9)
Country, n (%)	1,010	
Italy		877 (86.8)
Spain		82 (8.1)
Sweden		51 (5.0)
Year of diagnosis, *n (%)*	1,010	
2001-2004		237 (23.5)
2005-2008		371 (36.7)
2009-2012		402 (39.8)
Type of MF, *n (%)*	1,010	
PMF		584 (57.8)
PET-MF		207 (20.5)
PPV-MF		219 (21.7)
IPSS score, *n (%)*	969	
Low		167 (17.2)
Intermediate-1		322 (33.2)
Intermediate-2		277 (28.6)
High		203 (20.9)
MYSEC-PM score (only for secondary MF), *n (%)*	346	
Low		131 (37.9)
Intermediate-1		155 (44.8)
Intermediate-2		51 (14.7)
High		9 (2.6)
Palpable spleen, *n (%)*	821	665 (81.0)
Spleen length ≥ 20cm (cm below costal margin), *n (%)*	623	33 (5.3)
Symptomatic disease at diagnosis, *n (%)*	922	451 (48.9)
Driver mutations, *n (%)*	1,010	
JAK2 V617F		541 (69.4)
MPL W515		37 (7.1)
CALR		81 (30.6)
Triple negative		26 (10.1)
Laboratory values, *n (%)*		
Presence of peripheral blood blasts, n (%)	928	231 (23.0)
Blood blasts, median (IQR) > 1%, n (%)	922	145 (15.7)
Hemoglobin, median (IQR) < 10 g/dl, n (%)	973	284 (29.2)
WBC count, median (IQR) > 25 x 10^9/L, n (%)	969	103 (10.6)
Platelets, median (IQR) < 100 x 10^9/L, n (%)	969	120 (12.4)
Support therapy, *n (%)*		

Splenic radiation	750	2 (0.3)
Corticosteroids	744	70 (9.4)
Immunomodulator (thalidomide)	730	10 (1.4)
ESA (Erythropoiesis Stimulating Agent)	734	28 (3.8)
Androgens	723	28 (3.9)
Other	953	77 (8.1)
Transfusion	649	71 (10.9)
Chelation therapy	36	2 (5.6)

Table S2. Characteristics of patients treated with Hydroxyurea and Ruxolitinib before and after Propensity Score (PS) matching

	BEFORE 1:1 PS-MATCHING			AFTER 1:1 PS-MATCHING		
	Hydroxyurea N=487	**Ruxolitinib N=108**	**P**	**Hydroxyurea N=50**	**Ruxolitinib N=50**	**P**
Age at first administration	67.0 (57.0-74.0)	64.5 (56.0-70.5)	0.022	63.0 (53.0-69.0)	62.5 (56.0-69.0)	0.96
Male gender	292 (60.0)	62 (57.4)	0.63	30 (60.0)	29 (58.0)	0.84
Type of MF						
PMF	273 (56.1)	61 (56.5)	0.96	21 (42.0)	27 (54.0)	0.46
PET-MF	91 (18.7)	21 (19.4)		10 (20.0)	7 (14.0)	
PPV-MF	123 (25.3)	26 (24.1)		19 (38.0)	16 (32.0)	
History of thrombosis						
None	346 (75.1)	75 (78.9)	0.77	35 (70.0)	36 (81.8)	0.38
Arterial	91 (19.7)	16 (16.8)		12 (24.0)	7 (15.9)	
Venous	21 (4.6)	4 (4.2)		3 (6.0)	1 (2.3)	
Cardiovascular risk factors**	181 (63.7)	67 (72.8)	0.11	22 (66.7)	29 (70.7)	0.71
DIPSS at first administration						
Low	64 (13.6)	12 (11.4)	0.36	3 (6.0)	6 (12.0)	0.40
Intermediate-1	188 (40.1)	48 (45.7)		19 (38.0)	20 (40.0)	
Intermediate-2	145 (30.9)	35 (33.3)		23 (46.0)	16 (32.0)	
High	72 (15.4)	10 (9.5)		5 (10.0)	8 (16.0)	
Year of diagnosis						
2001-2004	140 (28.7)	9 (8.3)	<0.001	5 (10.0)	3 (6.0)	0.83
2005-2008	190 (39.0)	32 (29.6)		18 (36.0)	19 (38.0)	
2009-2012	157 (32.2)	67 (62.0)		27 (54.0)	28 (56.0)	
Spleen palpable at first administration	368 (88.2)	93 (98.9)	0.002	50 (100.0)	49 (98.0)	0.31
Time from diagnosis to first administration	0.0 (0.0-1.2)	4.5 (2.2-6.7)	<0.001	3.2 (0.0-6.1)	2.5 (1.0-4.5)	0.71
Start within 2yrs from diagnosis	383 (78.6)	26 (24.1)	<0.001	22 (44.0)	24 (48.0)	0.69
Start over 2yrs after diagnosis	104 (21.4)	82 (75.9)		28 (56.0)	26 (52.0)	

**Chi-square test for categorical variables, Wilcoxon rank-sum test for continuous variables; **At least one among active smoking, hypertension, diabetes mellitus or hypercholesterolemia*