Characteristics of Patients With Myelofibrosis Taking Ruxolitinib for 3 or More Years

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Abstract

CONTEXT: Ruxolitinib (RUX) was the first JAK1/2 inhibitor approved for patients with advanced phase of myelofibrosis (MF) with median therapy duration of about 3 years.

OBJECTIVE: We aimed to characterize clinical features of patients treated with RUX for ≥3 years.

PATIENTS and DESIGN: Retrospective review of medical records of 131 patients presented to our institution between January 2000 and July 2020 who received RUX for ≥3 years.

MAIN OUTCOMES: Major clinical features were reported by descriptive statistics. OS was analyzed using Kaplan-Meier model. Cox proportional hazard model (univariate, multivariate) was used for factors associated with OS.

RESULTS: Median age of patients was 67 years (range, 31-84), 56% were males. Less than 20% of patients had hemoglobin < 10 g/dL or platelets < 150 x 109/L, 30% had leukocytosis > 25 x 109/L. Only 8% of patients had ≥3% circulating blasts. JAK2 mutation was presented in 78% of patients. Among 62 patients with ≥ 28 gene next generation sequencing; 19, 24 and 19 patients had none, 1 and ≥2 additional mutations, respectively.

RUX as frontline therapy was given to 84% of patients. Median duration of RUX therapy was 76 months (95% CI, 56-88). At the time of last follow-up, 35% of patients continued on RUX. The most common disease-related reasons for discontinuation was MF progression (62%) and blastic phase (8%).

Median OS since therapy was 90 months (95% CI, 76-104) with 40% of patients being alive at 10 years.

Patients ≥ 65 years had median OS of 76 months (95% CI, 67-85). Patients with high risk DIPSS had median OS of 72 months (95% CI, 55-89).

The only factor retaining significance for OS on multivariate analysis was age > 65 years (HR 2.7, 95% CI 1.50-4.14, p < 0.001).

CONCLUSIONS: Forty percent of patients who remained on RUX for ≥3 years were alive at 10 years since their therapy initiation. Age remains the major predictive factor of survival on long RUX therapy.

Objective & Methods

To characterize clinical features of patients treated with RUX for ≥3 years.

Retrospective chart review of 131 patients who received RUX for at least 3 years and presented to us 01/2000-07/2020.

Major clinical features were reported by descriptive statistics.

OS was analyzed using Kaplan-Meier model from the time of RUX initiation.

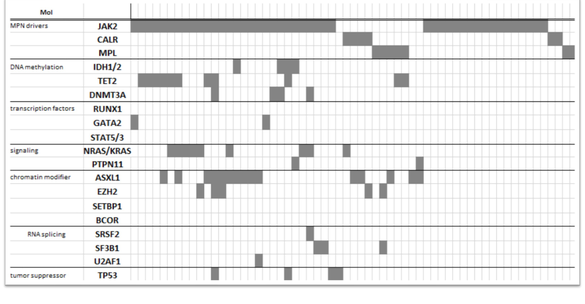
Cox proportional hazard model was used for factors associated with OS. Univariate analysis included all available clinical characteristics / disease features. Subsequently, variables with p < 0.05 were assessed in multivariate analysis.

Results

- 84% patients received RUX as frontline therapy
- Median time to RUX = 4 months (range, 0.1-123)
- Starting dose of RUX was ≥ 15 mg BID in 110 (84%), 10 mg BID in 17 (13%) and 5 mg BID in 4 (3%) patients
- Median duration of RUX Rx = 76 months (95% CI, 56-88)
- Table 1. summarized clinical features at RUX start

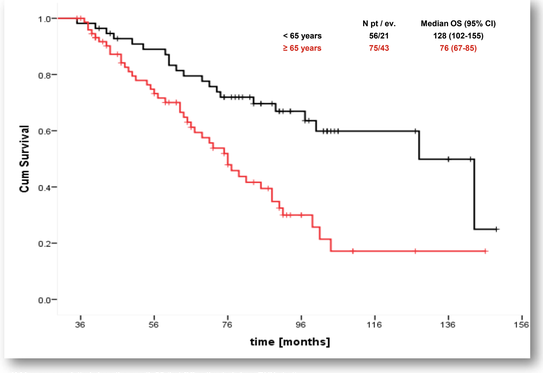
TABLE 1. N 131	Median (range), N (%)
Median Age	67 years (31-84)
Males	56%
White blood cells > 25 x 10⁹/L	38 (29)
Hemoglobin < 10 g/dL	24 (18)
Platelets < 150 x 10⁹/L	21 (16)
Neutrophils %	77 (30-98)
Monocytes %	3 (0.1-19)
Peripheral blasts ≥1% / ≥3%	58 (44) / 11 (8)
JAK2 / MPL / CALR	102 (78), 7 (5), 10 (8)
HMR, N 62 tested	22 (35)
Additional 0/1/2+ mol mutations	19 (15) / 24 (18) / 19 (15)
DIPSS intermediate 2 and high	88 (67)

- Mol Profile in 62 patients with NGS Sequencing (≥ 28 genes)

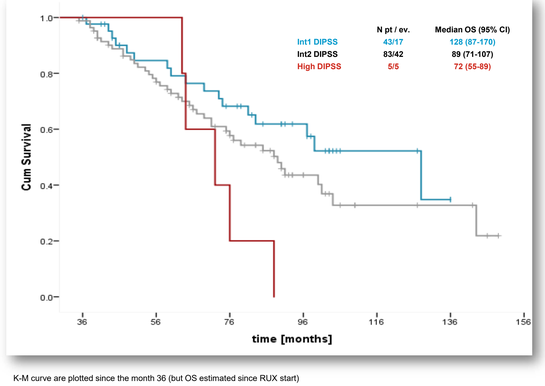


Results – cont.

- Median OS since therapy was 90 months (95% CI, 76-104)
- Estimated survival at 10 years since RUX start was 40%
- OS [since RUX] in MF subtypes are shown in Figures 1&2.



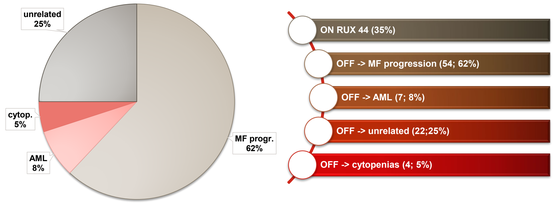
K-M curve are plotted since the month 36 (but OS estimated since RUX start)



K-M curve are plotted since the month 36 (but OS estimated since RUX start)

Results – cont.

- Discontinuation reasons and rates



- Significant factors ~ with OS: univariate & multivariate analysis

Univariate analysis for OS	HR (95% CI, p-value)
age > 65 years	2.56, 1.49-4.35, < 0.001
neutrophils %	0.97, 0.95-0.99, 0.006
blasts %	1.213, 1.035-1.421, 0.017
performance status <2	0.228, 0.069-0.752, 0.015

Multivariate analysis for OS	HR (95% CI, p-value)
age > 65 years	2.7, 1.50-4.14, < 0.001
neutrophils %	0.66, 0.29- 0.86, 0.012

Only statistically significant factors are shown

Conclusions

Patients taking RUX for ≥3 years have less cytopenias at the start of therapy. 30% had adverse molecular mutation.

Estimated survival at 10 since therapy initiation was 40%.

MF progression represents the leading cause of ultimate RUX discontinuation.

Age remains the major predictive factor of survival.

Contact

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