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RUXOLITINIB IN MYELOFIBROSIS

A MULTICENTRE EXPERIENCE IN ENGLAND, NORTHERN IRELAND AND WALES

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BACKGROUND

Ruxolitinib (RUX), an oral Janus Kinase (JAK)1/2 inhibitor was approved in Europe in 2012 for disease-related splenomegaly & constitutional symptoms in adults with:

- **Primary Myelofibrosis (PMF)** or
- **Post-Polycythaemia Vera (PPV-MF)** or
- **Post-Essential Thrombocythaemia (PET-MF)**

In 2016, RUX was commissioned by the NHS in England and Northern Ireland (NI) for patients with Intermediate-2 (INT-2) or High-risk MF, following the results of the COMFORT trails.[1,2]

AIMS

Assess the safety and efficacy of RUX in a real-world cohort of MF patients treated in England, NI and Wales, and compare clinical outcomes for lower-risk (Low/INT-1 risk) vs higher-risk (INT-2/High-risk) patients.

METHODS

Multicentre retrospective analysis of JAK inhibitor-naïve adults with PMF or post-MPN MF treated with RUX at 13 centres in England, Wales and NI from Jan 2011–Dec 2019. Clinical data obtained from electronic medical records. Survival analysis using the Kaplan-Meier method and standard log-rank test.

DEMOGRAPHICS

188 MF patients received RUX at **13** centres in England, Northern Ireland, and Wales from Jan 2011–Dec 2019

178 patients were eligible for further analysis
10 patients were excluded (8 had insufficient data, 2 received an alternative JAKi).

Median age	**69** years (29–91)
Gender	**55**% male
Rux first-line	**36**%

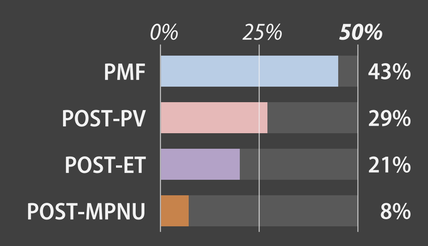
ACCESS TO RUX

Cancer Drugs Fund	**62**% (111/178)
NHS	**29**% (52/178)
Clinical trial	**8**% (15/178)

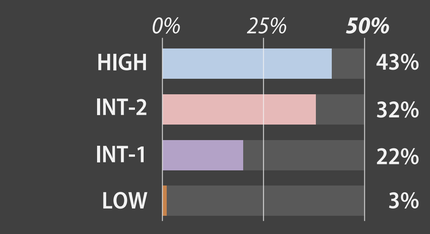
DRIVER MUTATIONS

JAK2+	**63**% (113/178)
CALR+	**4**% (8/178)
MPL +	**2**% (3/178)
None	**10**% (7/178)
Unknown	**21**% (37/178)

MF SUBTYPES



IPSS GROUP



RESULTS

MEDIAN OS, WHOLE COHORT FROM START OF RUX (N=178)

Whole Cohort	**3.5** years
Median follow-up	**3.5** years

MEDIAN OS, BY IPSS GROUP FROM START OF RUX (N=178)

LOW	not reached
INT-1	not reached
INT-2	**8.1** years
HIGH	**1.7** years

MEDIAN OS, SINCE MF DIAGNOSIS FROM DATE OF MF DIAGNOSIS (N=139)

Whole Cohort	**6.5** years
Low	not reached
INT-1	**12.3** y (4–NR)
INT-2	**10.0** y (4–14)
High	**3.8** y (3–6)
Hazard Ratio	**2.3** (2–3), p=0.000

3-YEAR OS, WHOLE COHORT FROM START OF RUX (N=178)

3y OS	**53**% (45–61)

3-YEAR OS, BY IPSS GROUP FROM START OF RUX (N=178)

Low	**100**%
INT-1	**76**%
INT-2	**57**%
High	**32**%
Hazard Ratio	**2.4** (2–3), p<0.0005

MEDIAN DURATION ON RUX

2.7 years (range 0 – 9)

ESTIMATED DISCONTINUATION RATES

1-year	**32**%
3-year	**55**%
5-year	**64**%

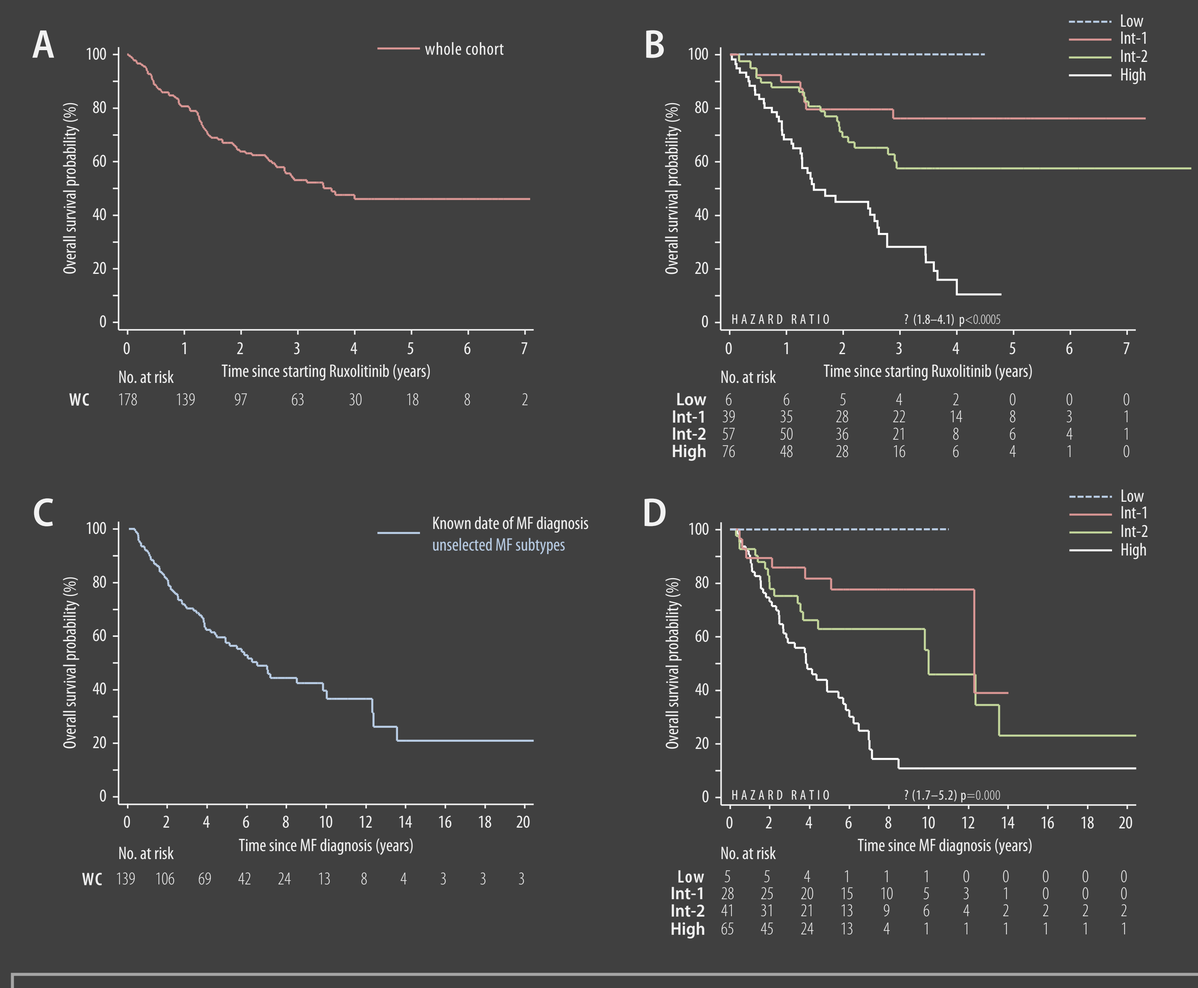


Figure 1. A. Kaplan-Meier (KM) curve of overall survival (OS) for whole cohort (WC) of myelofibrosis (MF) patients from the time of starting Ruxolitinib (RUX) (N=178). **B.** KM curve of OS for MF patients from the time of starting RUX, by IPSS group (N=178) **C.** KM curve of OS for whole cohort of MF patients from the time of MF diagnosis (N=139). **D.** KM curve of OS for MF patients from the time of MF diagnosis, by IPSS group (N=139).

CLINICAL RESPONSE

Weight and spleen response data currently only available for **57** and **101** patients, but is suggestive of a survival benefit associated with weight gain (p=0.0003).

Of the data collected to date:

Reduction in spleen size	**68**% (69/101)
Weight gain	**71**% (68/96)

ADVERSE EFFECTS (AE)

Thrombocytopaenia (Grade 3/4)	**25**%
Anaemia (Grade 3/4)	**38**%
Dose modification	**43**% (77/178)
Antimicrobial therapy	**36**% (62/178)

AT THE TIME OF ANALYSIS

Remain on RUX	**45**% (80/178)
Transformed to AML	**10**% (17/178)
Any-cause mortality	**47**% (83/178)

REASON FOR STOPPING RUX

Disease Progression	**30**% (29/98)
Death	**30**% (29/98)
Adverse Events	**22**% (22/98)
Allogeneic SCT	**9**% (9/98)
Patients Choice	**2**% (2/98)

DISCUSSION

Our whole cohort data support contemporary clinical trial results which show RUX to be well-tolerated and effective in improving disease-related splenomegaly and constitutional symptoms in unselected MF patients.

Haematological toxicity is common, but typically low grade and can be readily managed.

Rates of transformation to acute myeloid leukaemia were similar to published figures.

Uniform measures of response are limited within a retrospective study, but weight gain appears to be associated with improved clinical outcomes.

Longer follow-up is needed to assess the impact on survival and further studies into the use of ruxolitinib in lower-risk patients are required.

Further analysis is underway, including expansion of the dataset to other regions in the UK.

REFERENCES

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2. Harrison CN, Vannucchi AM, Kiladjian J-J, Al-Ali HK, Gisslinger H, Knoops L, et al. Long-term findings from COMFORT-II, a phase 3 study of ruxolitinib vs best available therapy for myelofibrosis. Leukemia. Nature Publishing Group; 2016;30(8):1701.

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