PHAZAR Basic Results Summary

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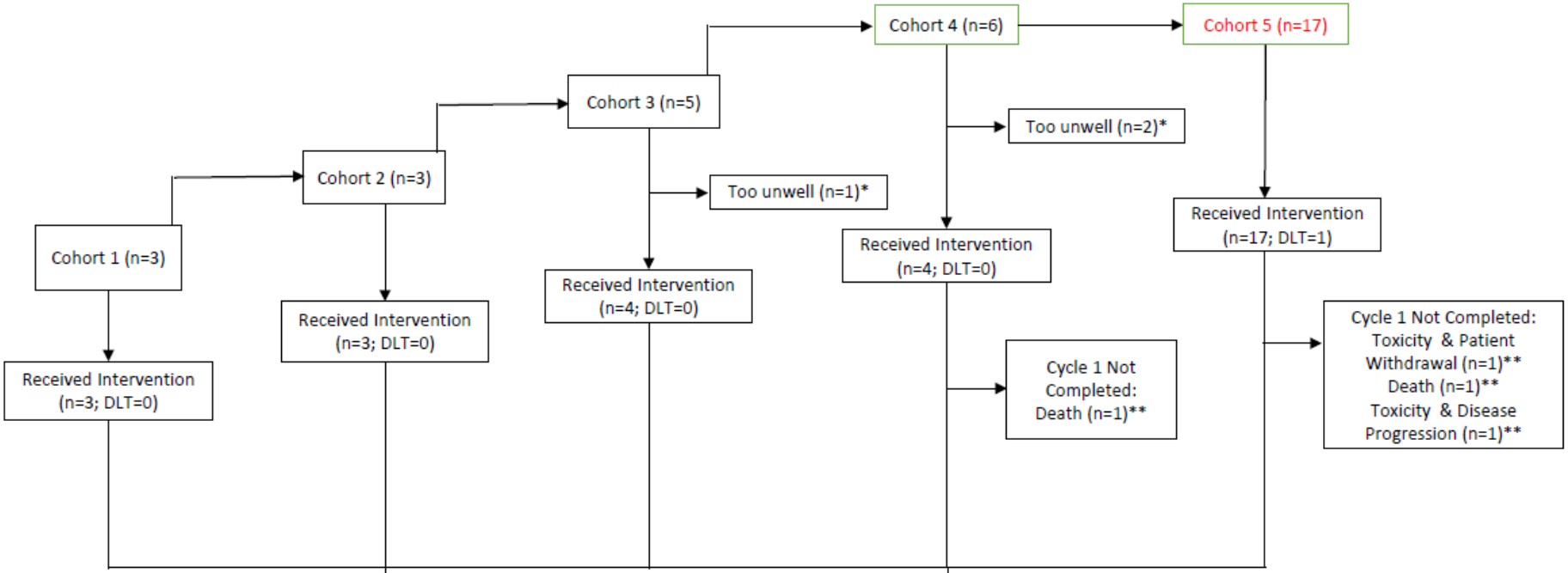
Interventional Component – Participant Flow



Modified Intention to Treat	n
Cohort 1	3
Cohort 2	3
Cohort 3	4
Cohort 4	4
Cohort 5	17
Excluded (*)	

Primary Outcome Evaluable	n
Cohort 1	3
Cohort 2	3
Cohort 3	4
Cohort 4	3
Cohort 5	14
Excluded (* & **)	

Interventional Component – Baseline Characteristics

	Dose 0: 10mg (3)	Dose 1: 15mg (3)	Dose 2: 20mg (5)	Dose 3: 25mg (23)	Overall (34)
Age (years)					
N	3	3	5	23	34
Mean (sd)	67.7 (9.1)	71.7 (3.2)	70.8 (4.1)	72.1 (6.9)	71.5 (6.4)
Median	64.0	73.0	69.0	72.0	72.0
Range	61.0, 78.0	68.0, 74.0	68.0, 78.0	55.0, 85.0	55.0, 85.0
Sex (N (%))					
Female	1 (33.3)	2 (66.7)	3 (60.0)	8 (34.8)	14 (41.2)
Male	2 (66.7)	1 (33.3)	2 (40.0)	15 (65.2)	20 (58.8)
Total	3 (100.0)	3 (100.0)	5 (100.0)	23 (100.0)	34 (100.0)
Disease Type (N (%))					
MPN-AP	2 (66.7)	2 (66.7)	2 (40.0)	13 (56.5)	19 (55.9)
MPN-BP	1 (33.3)	1 (33.3)	3 (60.0)	10 (43.5)	15 (44.1)
Total	3 (100.0)	3 (100.0)	5 (100.0)	23 (100.0)	34 (100.0)
Time from Diagnosis† (days)					
N	3	3	4	23	33
Mean (sd)	225.3 (89.1)	37.7 (52.3)	90.5 (94.4)	25.5 (19.0)	52.7 (72.6)
Median	230.0	10.0	78.5	24.0	26.0
Range	134.0, 312.0	5.0, 98.0	3.0, 202.0	2.0, 73.0	2.0, 312.0
Prior Polycythaemia Vera (N (%))					
No	2 (66.7)	3 (100.0)	3 (60.0)	12 (52.2)	20 (58.8)
Yes	1 (33.3)	0 (0.0)	2 (40.0)	8 (34.8)	11 (32.4)
Not Known	0 (0.0)	0 (0.0)	0 (0.0)	3 (13.0)	3 (8.8)
Total	3 (100.0)	3 (100.0)	5 (100.0)	23 (100.0)	34 (100.0)
Prior Essential Thrombocythaemia (N (%))					
No	2 (66.7)	1 (33.3)	2 (40.0)	11 (47.8)	16 (47.1)
Yes	1 (33.3)	2 (66.7)	3 (60.0)	10 (43.5)	16 (47.1)
Not Known	0 (0.0)	0 (0.0)	0 (0.0)	2 (8.7)	2 (5.9)
Total	3 (100.0)	3 (100.0)	5 (100.0)	23 (100.0)	34 (100.0)
Prior Myelofibrosis (N (%))					
No	0 (0.0)	0 (0.0)	2 (40.0)	11 (47.8)	13 (38.2)
Yes	3 (100.0)	3 (100.0)	3 (60.0)	12 (52.2)	21 (61.8)
Total	3 (100.0)	3 (100.0)	5 (100.0)	23 (100.0)	34 (100.0)

† calculated as number of days from reported disease diagnosis to study entry date

Interventional Component – Outcome Measures

Primary outcome measure	
To determine the MTD of ruxolitinib in combination with 5-azacitidine; Timepoint(s): Within 1 cycle of treatment	25mg twice daily

Secondary outcome measures

1. **Best response following 3 cycles of treatment**
   Assessment will be made according to the following criteria: Proposed criteria for response assessment in patients treated in clinical trials for MPNs in blast phase (MPN-BP): Formal recommendations from the post-MPN acute myeloid leukaemia consortium (for patients with >20% blasts at baseline) OR International Working Group (IWG) response criteria in myelodysplasia (for patients with <20% blasts at baseline)

	Dose 0: 10mg (3)	Dose 1: 15mg (3)	Dose 2: 20mg (4)	Dose 3: 25mg (21)	Overall (31)
Response at Cycle 3					
CR	0 (0.0)	1 (33.3)	0 (0.0)	0 (0.0)	1 (3.2)
MCR	0 (0.0)	0 (0.0)	0 (0.0)	2 (9.5)	2 (6.5)
PR	0 (0.0)	0 (0.0)	0 (0.0)	2 (9.5)	2 (6.5)
ALR-P	0 (0.0)	1 (33.3)	0 (0.0)	2 (9.5)	3 (9.7)
SD	1 (33.3)	0 (0.0)	2 (50.0)	6 (28.6)	9 (29.0)
DP	1 (33.3)	0 (0.0)	1 (25.0)	1 (4.8)	3 (9.7)
NE	0 (0.0)	0 (0.0)	1 (25.0)	1 (4.8)	2 (6.5)
Not Outcome Evaluable	1 (33.3)	1 (33.3)	0 (0.0)	7 (33.3)	9 (29.0)
Total	3 (100.0)	3 (100.0)	4 (100.0)	21 (100.0)	31 (100.0)

CR – Complete Response, PR – Partial Response, MCR – Molecular Complete Response, CCR – Complete Cytogenetic Response, ALR-C – Acute leukaemia response-complete, ALR-P - Acute leukaemia response-partial, SD – Stable Disease, DP – Disease Progression, NE – Not Evaluable following assessment, Not Outcome Evaluable – no disease assessment performed.

Best response (criteria as above) following 6 cycles of treatment

	Dose 0: 10mg (3)	Dose 1: 15mg (3)	Dose 2: 20mg (4)	Dose 3: 25mg (21)	Overall (31)
Response at Cycle 6					
MCR	0 (0.0)	0 (0.0)	0 (0.0)	4 (19.0)	4 (12.9)
ALR-P	0 (0.0)	0 (0.0)	1 (25.0)	0 (0.0)	1 (3.2)
SD	0 (0.0)	1 (33.3)	0 (0.0)	4 (19.0)	5 (16.1)
DP	1 (33.3)	0 (0.0)	1 (25.0)	0 (0.0)	2 (6.5)
NE	0 (0.0)	0 (0.0)	1 (25.0)	1 (4.8)	2 (6.5)
Not Outcome Evaluable	2 (66.7)	2 (66.7)	1 (25.0)	12 (57.1)	17 (54.8)
Total	3 (100.0)	3 (100.0)	4 (100.0)	21 (100.0)	31 (100.0)

2. Change in the proportion of patients who require transfusion of red cells or platelets

Achievement of transfusion independence at the end of cycle 3 compared to baseline.

	Dose 0: 10mg (3)	Dose 1: 15mg (3)	Dose 2: 20mg (4)	Dose 3: 25mg (21)	Overall (31)
Change (N (%))					
Maintained	0 (0.0)	1 (33.3)	0 (0.0)	3 (14.3)	4 (12.9)
Achieved	0 (0.0)	0 (0.0)	0 (0.0)	1 (4.8)	1 (3.2)
Failed to maintain	0 (0.0)	0 (0.0)	1 (25.0)	6 (28.6)	7 (22.6)
Failed to achieve	1 (33.3)	1 (33.3)	2 (50.0)	5 (23.8)	9 (29.0)
Insufficient treatment	2 (66.7)	1 (33.3)	1 (25.0)	6 (28.6)	10 (32.3)
Total	3 (100.0)	3 (100.0)	4 (100.0)	21 (100.0)	31 (100.0)
Dependence Type (N (%))					
RBC Dependent	0 (0.0)	1 (100.0)	3 (100.0)	7 (63.6)	11 (68.8)
Platelet Dependent	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
RBC & Platelet Dependent	1 (100.0)	0 (0.0)	0 (0.0)	4 (36.4)	5 (31.2)
Total	1 (100.0)	1 (100.0)	3 (100.0)	11 (100.0)	16 (100.0)

Achievement of transfusion independence at the end of cycle 6 compared to cycle 3.

	Dose 0: 10mg (3)	Dose 1: 15mg (3)	Dose 2: 20mg (4)	Dose 3: 25mg (21)	Overall (31)
Change (N (%))					
Maintained	0 (0.0)	0 (0.0)	0 (0.0)	1 (4.8)	1 (3.2)
Achieved	0 (0.0)	0 (0.0)	0 (0.0)	4 (19.0)	4 (12.9)
Failed to maintain	0 (0.0)	0 (0.0)	0 (0.0)	2 (9.5)	2 (6.5)
Failed to achieve	0 (0.0)	0 (0.0)	2 (50.0)	2 (9.5)	4 (12.9)
Insufficient treatment	3 (100.0)	3 (100.0)	2 (50.0)	12 (57.1)	20 (64.5)
Total	3 (100.0)	3 (100.0)	4 (100.0)	21 (100.0)	31 (100.0)
Dependence Type (N (%))					
RBC Dependent	0 (.)	0 (.)	1 (50.0)	1 (25.0)	2 (33.3)
Platelet Dependent	0 (.)	0 (.)	0 (0.0)	1 (25.0)	1 (16.7)
RBC & Platelet Dependent	0 (.)	0 (.)	1 (50.0)	2 (50.0)	3 (50.0)
Total	0 (.)	0 (.)	2 (100.0)	4 (100.0)	6 (100.0)

3. Change in palpable splenomegaly

Percentage change in spleen size at cycles 3 and 6 compared to baseline reported by patient.

Allocated Dose	Time Point	Size of Spleen (cm)	Percentage Change (%)
10mg	Baseline	25	0.00
	Cycle 3	22	-12.00
20mg	Baseline	14	0.00
	Cycle 3	13	-7.14
	Cycle 6	8	-42.86
25mg	Baseline	21	0.00
	Cycle 3	13	-38.10
25mg	Baseline	17	0.00
	Cycle 3	7	-58.82
	Cycle 6	8	-52.94

Overall mean and median percentage change in spleen size at the start of each cycle compared to baseline.

	Cycle 1	Cycle 2	Cycle 3	Cycle 4	Cycle 5	Cycle 6
Allocated Dose: 10mg						
Percentage Change						
N	3	2	1	1	0	0
Mean (sd)	-41.7 (17.5)	-45.0 (24.0)	-12.0 (.)	-28.0 (.)	()	()
Median	-32.0	-45.0	-12.0	-28.0		
IQR	-61.9, -31.2	-61.9, -28.0	-12.0, -12.0	-28.0, -28.0	,	,
Allocated Dose: 15mg						
Percentage Change						
N	0	1	0	0	0	0
Mean (sd)	()	-50.0 (.)	()	()	()	()
Median		-50.0				
IQR	,	-50.0, -50.0	,	,	,	,
Allocated Dose: 20mg						
Percentage Change						
N	2	1	1	1	1	1
Mean (sd)	-18.5 (6.0)	7.1 (.)	-7.1 (.)	7.1 (.)	0.0 (.)	-42.9 (.)
Median	-18.5	7.1	-7.1	7.1	0.0	-42.9
IQR	-22.7, -14.3	7.1, 7.1	-7.1, -7.1	7.1, 7.1	0.0, 0.0	-42.9, -42.9
Allocated Dose: 25mg						
Percentage Change						
N	4	3	2	3	0	1
Mean (sd)	-32.1 (28.7)	-57.0 (34.4)	-48.5 (14.7)	-53.3 (21.5)	()	-52.9 (.)
Median	-38.1	-47.1	-48.5	-64.7		-52.9
IQR	-53.2, -11.0	-95.2, -28.6	-58.8, -38.1	-66.7, -28.6	,	-52.9, -52.9

For 10 patients it was reported that their spleen was not palpable at baseline or at any subsequent assessments, as such these patients have no available spleen sizes reported and are not included in the table above. A further 10 patients were not included in the percentage change analysis due to only baseline spleen size being reported (5), patients spleen size at baseline was either not known or not performed (2) and spleen was not palpable at baseline (but was later during the trial) (3).

4. Change in palpable hepatomegaly

Percentage change in liver size at cycles 3 and 6 compared to baseline reported by patient

Allocated Dose	Time Point	Size of Liver (cm)	Percentage Change (%)
25mg	Baseline	1	0.00
	Cycle 3	1	0.00

Due to only one patient having available live size at baseline and a subsequent timepoint, the mean and median have not been presented.

For 20 patients it was reported that their liver was not palpable at baseline or at any subsequent assessments, as such these patients have no available liver sizes reported and are not included in the table above. A further 9 patients were not included in this analysis due to only baseline liver size being reported (4) and liver not palpable at baseline (but was later during the trial) (5).

5. Duration of Complete Response (CR) or Partial Response (PR)

Table of Duration of Response, presented for all patients and split by dose allocation.

Dose Allocation	Median DoR (months)
All Patients	7.2 (95%CI; 2.8, .)
Dose 1: 15mg	3.0 (95%CI; 3.0, NR)
Dose 2: 20mg	NR (95%CI; ., NR)
Dose 3: 25mg	9.5 (95%CI; 2.8, NR)

6. **12 months Progression-free survival (PFS)**

Table of Progression Free Survival outcomes, presented for MPN-AP patients and split by dose allocation

Dose Allocation	Median PFS (months)	Event Free at 12 Months	12 Month PFS Rate
All Patients	8.2 (95%CI; 2.9, 49.7)	5	42% (95%CI; 18, 65)
Dose 0: 10mg	2.5 (95%CI; 2.5, NR)	0	.% (95%CI; ., .)
Dose 1: 15mg	1.5 (95%CI; 1.5, NR)	1	50% (95%CI; 0, 91)
Dose 2: 20mg	2.3 (95%CI; 2.3, NR)	0	.% (95%CI; ., .)
Dose 3: 25mg	49.7 (95%CI; 3.9, NR)	4	56% (95%CI; 21, 81)

7. 12 months Leukaemia-free survival (LFS)

Table of Leukaemia Free Survival outcomes, presented for MPN-BP patients and split by dose allocation

Dose Allocation	Median LFS (months)	Event Free at 12 Months	12 Month LFS Rate
All Patients	7.3 (95%CI; 1.3, .)	2	26% (95%CI; 6, 51)
Dose 0: 10mg	NR (95%CI; ., NR)	1	100% (95%CI; ., .)
Dose 1: 15mg	NR (95%CI; ., NR)	0	.% (95%CI; ., .)
Dose 2: 20mg	7.3 (95%CI; 7.3, NR)	0	.% (95%CI; ., .)
Dose 3: 25mg	5.7 (95%CI; 0.3, 7.5)	1	13% (95%CI; 1, 44)

8. 12 months Overall survival (OS)

Table of Overall Survival outcomes, presented for all patients and split by dose allocation

Dose Allocation	Median OS (months)	Alive at 12 Months	12 Month OS Rate
All Patients	9.3 (95%CI; 5.7, 26.3)	9	42% (95%CI; 23, 59)
Dose 0: 10mg	NR (95%CI; 2.5, NR)	2	67% (95%CI; 5, 95)
Dose 1: 15mg	10.2 (95%CI; 1.5, NR)	1	33% (95%CI; 1, 77)
Dose 2: 20mg	7.3 (95%CI; 3.6, NR)	1	50% (95%CI; 6, 84)
Dose 3: 25mg	8.2 (95%CI; 5.1, NR)	5	37% (95%CI; 15, 59)

Here alive indicates patients that were known to be alive at 12 months, i.e. those with no death forms and those not censored pre 12 months

9. Duration of treatment

Duration of trial treatment, in months, reported for all patients in the modified Intention to Treat population and split by dose level

Allocated Dose	N	Mean (SD)	Median (Range)
All Patients	31	8.1 (11.7)	3.7 (2.1, 6.1)
10mg	3	2.5 (1.5)	2.1 (1.2, 4.1)
15mg	3	2.6 (1.3)	3.3 (1.1, 3.4)
20mg	4	5.0 (1.8)	5.8 (4.0, 6.0)
25mg	21	10.2 (13.7)	3.8 (2.1, 9.3)

10. Clinical improvement in haemoglobin level

Mean change in haemoglobin counts, alongside the range for each dose group as well as all patients with counts available at cycle 3 or 6.

Allocated Dose	Cycle 3 N	Cycle 3 Mean(sd)	Cycle 3 Range	Cycle 6 N	Cycle 6 Mean(sd)	Cycle 6 Range
10mg	2	2.0 (14)	-8, 12	1	18.0 (.)	18, 18
15mg	2	8.5 (30)	-13, 30	1	-2.0 (.)	-2, -2
20mg	3	-8.7 (14)	-19, 7	3	7.3 (17)	-9, 25
25mg	15	-5.2 (16)	-40, 20	9	-3.1 (11)	-22, 11
All Patients	22	-3.8 (16)	-40, 30	14	0.7 (13)	-22, 25

11. Clinical improvement in platelet count

Mean change in platelet counts, alongside the range for each dose group as well as all patients with counts available at cycle 3 or 6.

Allocated Dose	Cycle 3 N	Cycle 3 Mean(sd)	Cycle 3 Range	Cycle 6 N	Cycle 6 Mean(sd)	Cycle 6 Range
10mg	2	-23.5 (25)	-41, -6	1	3.0 (.)	3, 3
15mg	2	73.5 (422)	-225, 372	1	-170.0 (.)	-170, -170
20mg	3	-188.0 (303)	-538, -9	3	-209.7 (361)	-626, 2
25mg	15	-58.1 (218)	-825, 96	9	-64.0 (374)	-887, 494
All Patients	22	-60.7 (231)	-825, 372	14	-98.0 (333)	-887, 494

12. Quality of Life

EORTC-QLQ-C30 (Cycles 1, 2, 4 and 6)

Patients were asked to provide the response that was most relevant to their health state in the week prior to completing the questionnaire. These responses were then coded as single digit numbers (1-4) indicating the severity level with higher numbers equating to worse functionality.
These single digit numbers were then be transformed to obtain a score in the range of 0-100. Here a high score is indicative of a higher response level. Following this a high score for a functional scale represents a high/healthy level of functionality, a high score for global health score/QoI represents a high quality of life however a high score for symptom scale and single items represents a low level of functionality. The transformations used were obtained from the EORTC QLQ-30 Scoring Manual.

Mean and median global health scores for patients within the interventional arm, split by dose allocation and time-point

Allocated Treatment	Timepoint	N	Mean(sd)	Median(IQR)	Range
10mg	Cycle 1 Day 1	3	38.89(12.73)	41.67(25.00, 50.00)	25.00, 50.00
	Cycle 2 Day 1	3	69.44(17.35)	75.00(50.00, 83.33)	50.00, 83.33
	Cycle 4 Day 1	1	58.33(.)	58.33(58.33, 58.33)	58.33, 58.33
15mg	Cycle 1 Day 1	3	44.44(41.94)	50.00(0.00, 83.33)	0.00, 83.33
	Cycle 2 Day 1	2	45.83(5.89)	45.83(41.67, 50.00)	41.67, 50.00
	Cycle 4 Day 1	2	33.33(0.00)	33.33(33.33, 33.33)	33.33, 33.33
	Cycle 6 Day 1	1	91.67(.)	91.67(91.67, 91.67)	91.67, 91.67
20mg	Cycle 1 Day 1	4	60.42(45.83)	70.83(25.00, 95.83)	0.00, 100.00
	Cycle 2 Day 1	4	56.25(42.70)	62.50(25.00, 87.50)	0.00, 100.00
	Cycle 4 Day 1	3	63.89(41.11)	83.33(16.67, 91.67)	16.67, 91.67
	Cycle 6 Day 1	3	47.22(31.55)	33.33(25.00, 83.33)	25.00, 83.33
25mg	Cycle 1 Day 1	21	48.41(31.14)	58.33(16.67, 75.00)	0.00, 91.67
	Cycle 2 Day 1	16	59.38(22.33)	66.67(45.83, 75.00)	16.67, 83.33
	Cycle 4 Day 1	11	62.88(19.14)	66.67(50.00, 75.00)	16.67, 83.33
	Cycle 6 Day 1	9	65.74(24.45)	75.00(66.67, 83.33)	16.67, 83.33

EQ-5D-5L (Cycles 1, 2, 4 and 6)

The EQ-5D-5L descriptive system spans five dimensions (mobility; self-care; usual-activities; pain or discomfort; and anxiety or depression). Each of these has five response levels contained within them (no problems; slight problems; moderate problems; severe problems; extreme problems). Patients are asked to indicate their health state on the day of questionnaire completion, these responses are then coded as single digit numbers (1-5) indicating the severity level selected with lower numbers equating to better functionality. The digits for each of the 5 dimensions can then be combined into a five digit code that describes the patients health state on the day of response.
These health states can then be transformed into an index state using country specific estimates, for this report the England specific estimation was used obtained from Devlin et al. (2018). Using this transformation the maximum index score (resulting from a health state of 11111, i.e no problems for all dimensions) is 1.00, whilst the minimum index score (resulting from a health score of 55555, i.e extreme problems for all dimensions) is -0.285. For this quality of life questionnaire, higher scores represent better functionality.

Allocated Treatment	Timepoint	N	Mean(sd)	Median(IQR)	Range
10mg	Cycle 1 Day 1	3	46.67(32.15)	60.00(10.00, 70.00)	10.00, 70.00
	Cycle 2 Day 1	3	68.33(17.56)	70.00(50.00, 85.00)	50.00, 85.00
	Cycle 4 Day 1	1	60.00(.)	60.00(60.00, 60.00)	60.00, 60.00
15mg	Cycle 1 Day 1	3	56.67(41.63)	70.00(10.00, 90.00)	10.00, 90.00
	Cycle 2 Day 1	2	42.50(31.82)	42.50(20.00, 65.00)	20.00, 65.00
	Cycle 4 Day 1	2	52.50(3.54)	52.50(50.00, 55.00)	50.00, 55.00
	Cycle 6 Day 1	0	.(.)	.(., .)	., .
20mg	Cycle 1 Day 1	4	67.50(37.97)	77.50(40.00, 95.00)	15.00, 100.00
	Cycle 2 Day 1	4	71.25(29.55)	80.00(50.00, 92.50)	30.00, 95.00
	Cycle 4 Day 1	2	57.50(38.89)	57.50(30.00, 85.00)	30.00, 85.00
	Cycle 6 Day 1	3	61.67(27.54)	75.00(30.00, 80.00)	30.00, 80.00
25mg	Cycle 1 Day 1	20	58.75(22.88)	60.00(42.50, 75.00)	10.00, 90.00
	Cycle 2 Day 1	16	65.31(17.93)	70.00(57.50, 80.00)	30.00, 85.00
	Cycle 4 Day 1	11	70.45(12.14)	75.00(65.00, 75.00)	50.00, 90.00
	Cycle 6 Day 1	9	74.44(17.76)	80.00(75.00, 85.00)	40.00, 90.00

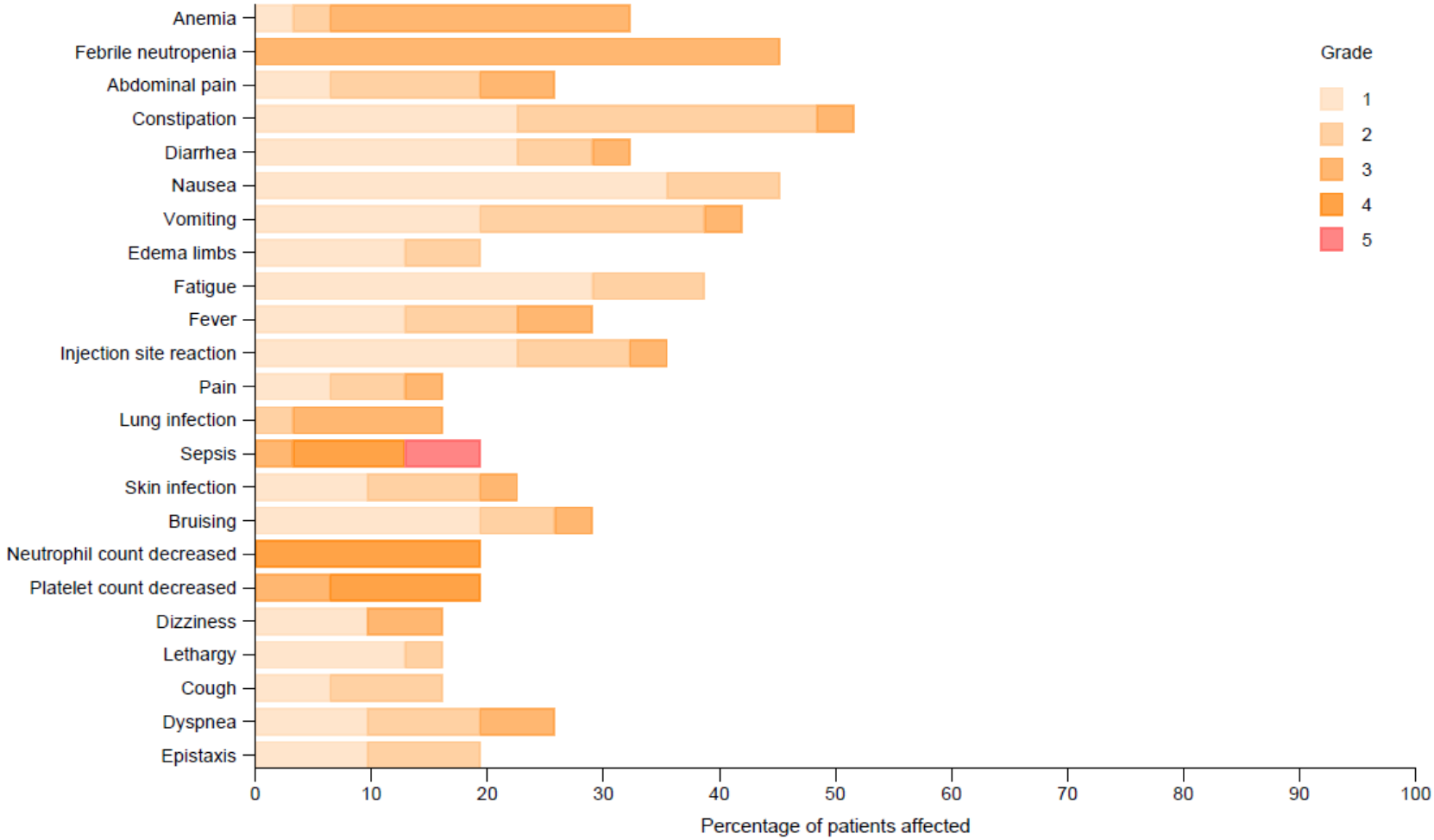
MPN SAF (Cycles 1, 2, 4 and 6)

The MPN-SAF is constructed of the 10 most clinically important items from the previously validated BFI and MPN-SAF surveys. This combination resulted in the inclusion 9 items from the MPN-SAF (early satiety; abdominal discomfort; inactivity; concentration problems; night sweats; itching; bone pain; fever and weight loss) and 1 from the BFI survey (fatigue). Each of these symptoms are measured on a scale ranging from 0 (Absent) to 10 (Worst Imaginable) and patients are asked to indicate how they had been affected by these symptoms in the week prior to questionnaire completion. Using this rating system, items can be classified into one of the following two categories: severe if symptoms were rated $\geq$7 or moderate if symptoms were rated $\geq$4 or $\leq$6. For patients who completed at least 6 of the items a total symptom score (TSS) could be calculated, this score was generated by taking the average of the answered items and multiplying this by 10 to achieve a possible range of 0-100.

Allocated Treatment	Timepoint	N	Mean(sd)	Median(IQR)	Range
10mg	Cycle 1 Day 1	3	38.85(9.92)	35.56(31.00, 50.00)	31.00, 50.00
	Cycle 2 Day 1	3	12.33(5.03)	13.00(7.00, 17.00)	7.00, 17.00
	Cycle 4 Day 1	1	23.00(.)	23.00(23.00, 23.00)	23.00, 23.00
15mg	Cycle 1 Day 1	3	20.33(6.51)	20.00(14.00, 27.00)	14.00, 27.00
	Cycle 2 Day 1	2	30.00(1.41)	30.00(29.00, 31.00)	29.00, 31.00
	Cycle 4 Day 1	2	32.50(12.02)	32.50(24.00, 41.00)	24.00, 41.00
20mg	Cycle 1 Day 1	4	25.25(23.20)	25.50(6.00, 44.50)	0.00, 50.00
	Cycle 2 Day 1	4	23.33(28.64)	15.67(1.67, 45.00)	0.00, 62.00
	Cycle 4 Day 1	2	30.00(35.36)	30.00(5.00, 55.00)	5.00, 55.00
	Cycle 6 Day 1	3	20.30(17.56)	18.00(4.00, 38.89)	4.00, 38.89
25mg	Cycle 1 Day 1	19	24.08(16.40)	25.00(11.00, 29.00)	0.00, 66.67
	Cycle 2 Day 1	14	23.92(17.86)	20.00(11.00, 36.00)	1.00, 58.89
	Cycle 4 Day 1	10	14.07(7.75)	13.00(9.00, 17.00)	2.00, 26.67
	Cycle 6 Day 1	9	14.89(9.24)	12.00(10.00, 19.00)	5.00, 35.00

Interventional Component – Adverse Events

Proportion of patients affected by adverse events experienced in at least 15% of patient recruited to the interventional arm. Coloured by maximum grade experienced.

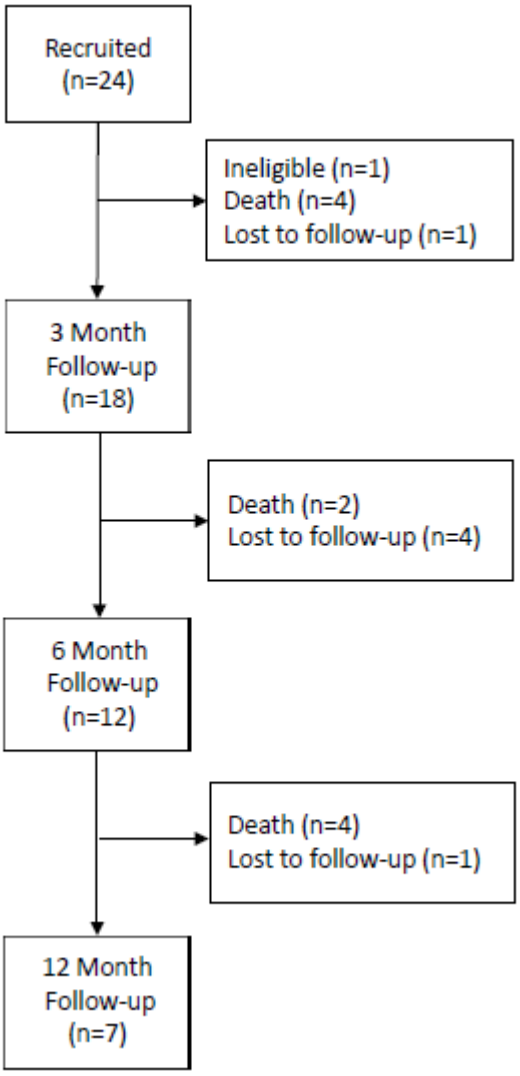


Serious Adverse Events

List of the 15 most common admitting events for SAEs reported for those in the interventional cohort of the trial

Category	Toxicity	Events(Affected)
Blood and lymphatic system disorders	Febrile neutropenia	17 (17)
Infections and infestations	Sepsis	7 (7)
General disorders and administration site conditions	Fever	6 (6)
Gastrointestinal disorders	Abdominal pain	3 (3)
Infections and infestations	Lung infection	3 (3)
Gastrointestinal disorders	Diarrhea	2 (2)
Respiratory, thoracic and mediastinal disorders	Dyspnea	2 (2)
Infections and infestations	Cellulitis	2 (2)
Blood and lymphatic system disorders	Anemia	2 (2)
Musculoskeletal and connective tissue disorders	Arthralgia	2 (2)
Gastrointestinal disorders	Lower gastrointestinal hemorrhage	2 (2)
Gastrointestinal disorders	Vomiting	2 (2)
Respiratory, thoracic and mediastinal disorders	Epistaxis	2 (2)
Infections and infestations	Skin infection	2 (2)
Eye disorders	Preseptal cellulitis	1 (1)

Observational Component – Participant Flow



Observational Component – Baseline Characteristics

Age (years)	
N	24
Mean (sd)	66.0 (13.8)
Median	68.5
Range	29.0, 85.0
Sex (N (%))	
Female	8 (33.3)
Male	16 (66.7)
Total	24 (100.0)
Disease Type (N (%))	
MPN-AP	13 (54.2)
MPN-BP	11 (45.8)
Total	24 (100.0)
Time from Diagnosis† (days)	
N	24
Mean (sd)	407.4 (967.8)
Median	51.0
Range	4.0, 4666.0
Prior Polycythaemia Vera (N (%))	
No	13 (54.2)
Yes	10 (41.7)
Not Known	1 (4.2)
Total	24 (100.0)
Prior Essential Thrombocythaemia (N (%))	
No	14 (58.3)
Yes	7 (29.2)
Not Known	3 (12.5)
Total	24 (100.0)
Prior Myelofibrosis (N (%))	
No	11 (45.8)
Yes	12 (50.0)
Not Known	1 (4.2)
Total	24 (100.0)

† calculated as number of days from reported disease diagnosis to study entry date

Observational Component – Outcome Measures

1. To determine treatment and outcome of Accelerated Phase MPN (MPN-AP) and Blast Phase MPN (MPN-BP) patients

18/24 patients had available follow-up forms. Of these, 10 reported receiving treatment for their disease.

Treatment received by patients in the observational cohort.

ID	Follow-up Month	Treatment	Length of Treatment (days)	Response
42	3	Daunorubicin + Cytarabine DA 3+10	Ongoing (No end date reported)	Complete Response
42	6	Unrelated donor reduced intensity haematopoietic cell transplantation	0	Complete Response
140	3	Ruxolitinib	Ongoing (No end date reported)	Not Evaluated
486	3	CPX-351 (AML 19 Trial)	46	Progressive Disease
486	6	FLAG/IDA	5	Progressive Disease
1131	3	FLAG IDA	21	Not Evaluated
2490	3	Low dose Cytarabine	113	Progressive Disease
1280	3	DA Chemotherapy	9	Complete Response
1280	6	Flu/BU/ATG VUD	0	Progressive Disease
1280	12	Splenic Radiotherapy	20	Progressive Disease
1085	3	Daunorubicin and Ara-C Chemotherapy	9	Not Evaluated
1085	6	Allogenic Tranplant (VUD with busulfan, fludarabine and ATG conditioning)	365	Complete Response
129	3	Hydroxycarbomide	Ongoing (No end date reported)	Not Evaluated
129	3	Pegasys	Ongoing (No end date reported)	Not Evaluated
129	12	stem cell transplant	0	Not Evaluated
4606	3	Azacitidine	Ongoing (No end date reported)	Not Evaluated
3650	3	allograft	0	Not Evaluated

Proportion of observational patients reporting complete or partial response at any time

Disease Response (N (%))	
Responder	5 (20.8)
Non-responder	8 (33.3)
Not evaluated	5 (20.8)
Non outcome evaluable	6 (25.0)
Total	24 (100.0)

2. Quality of life

EORTC QLQ-C30 (at registration, 3 months and 6 months)
Mean and median global health scores for patients within the observational arm, split by timepoint

Timepoint	N	Mean(sd)	Median(IQR)	Range
Registration	18	47.69(29.68)	50.00(16.67, 83.33)	8.33, 91.67
Month 3	12	62.50(26.94)	70.83(45.83, 83.33)	0.00, 83.33
Month 6	9	57.41(23.36)	50.00(50.00, 75.00)	16.67, 83.33

EQ-5D-5L (at registration, 3 months and 6 months)
Mean and median health scores for patients within the observational arm, split by time-point

Timepoint	N	Mean(sd)	Median(IQR)	Range
Registration	17	54.71(23.98)	60.00(35.00, 75.00)	10.00, 98.00
Month 3	11	60.91(27.91)	65.00(50.00, 80.00)	0.00, 95.00
Month 6	9	62.78(20.17)	60.00(50.00, 75.00)	30.00, 90.00

MPN SAF (at registration, 3 months and 6 months)
Mean and median TSS for patients within the observational arm, split by time-point

Timepoint	N	Mean(sd)	Median(IQR)	Range
Registration	17	34.27(13.74)	34.00(24.00, 46.00)	8.89, 53.00
Month 3	12	26.77(19.79)	26.50(11.50, 34.50)	2.22, 77.00
Month 6	9	26.67(17.24)	31.00(11.00, 39.00)	2.00, 51.00

Observational Component – Adverse Events

There were no adverse events associated with the observational component.