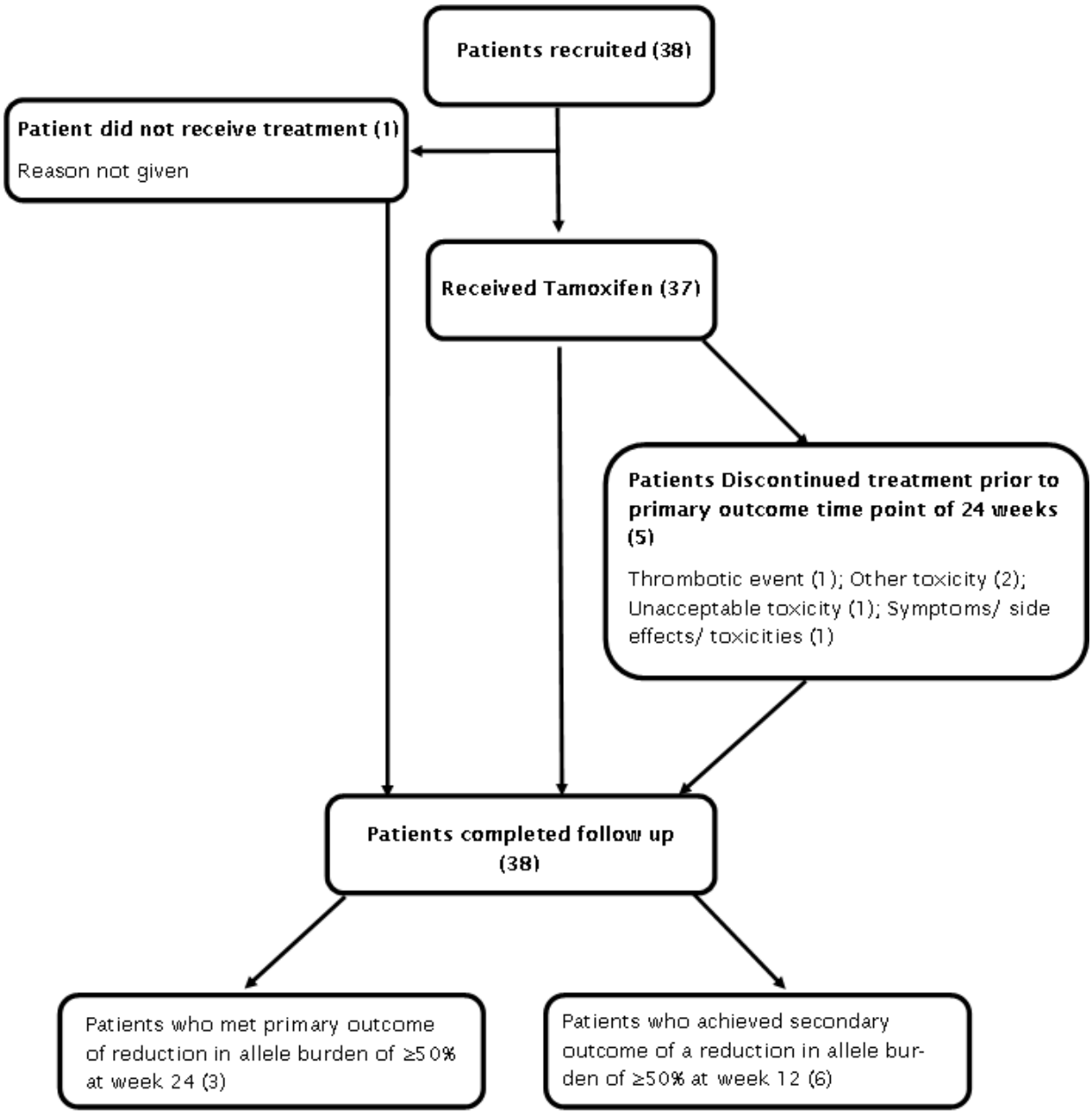
Participant Flow



Baseline Characteristics

Patient characteristics	
Age, years	
N	38
Median	65.5
IQR	62.0, 74.0
Range	50.0, 87.0
Sex	
Male	27 (71.1)
Female	11 (28.9)
Total	38 (100.0)
Height, m	
N	31
Median	1.8
IQR	1.7, 1.8
Range	1.1, 1.9
Weight, kg	
N	36
Median	83.0
IQR	74.5, 88.4
Range	53.7, 150.3
WHO Performance status	
0	27
1	5
Not applicable	1
Not known	3
Missing	1
Disease Type	
Essential Thrombocythaemia (ET)	14 (36.8)
Primary Myelobrosis (PMF)	6 (15.8)
Post-Essential Thrombocythaemia Myelofibrosis (PET-MF)	2 (5.3)
Polycythaemia Vera (PV)	11 (28.9)
Post-Polycythaemiai Vera Myelofibrosis (PPV-MF)	5 (13.2)
Total	38 (100.0)
Time since diagnosis, years	
N	38
Median	7.2
IQR	3.3, 10.2
Range	0.4, 22.1

Outcome Measures

Primary outcome measure

The primary outcome for the trial is the number of patients who experience a reduction of ≥50% in peripheral blood JAK2-V617F,CALR 5bp insertion (exon 9) or CALR 52bp deletion (exon 9) mutant allele burden at 24 weeks.

Percentage change in allele burden from baseline to 24 weeks	Responder	n (%)
Reduction of 50% or more	Major	3 (7.9)
Reduction of between 25% and 50%	Minor	5 (13.2)
Reduction of less than 25%	Non-responder	18 (47.4)
No change or percentage increase		6 (15.8)
Sample did not pass		2 (5.3)
No entry		4 (10.5)

Secondary outcome measures

1. Proportion of patients with a reduction in the peripheral blood JAK2-V617F, CALR 5bp insertion (exon 9), or CALR 52bp deletion (exon 9) mutant allele burden of ≥50% at 12 weeks

Change in allele burden (N (%))	
50+% decrease	1 (2.6)
25-50% decrease	5 (13.2)
0-25% decrease	15 (39.5)
0-25% increase	11 (28.9)
25-50% increase	2 (5.3)
50+% increase	1 (2.6)
No valid sample, on trt.	2 (5.3)
No valid sample, off trt.	1 (2.6)
Total	38 (100.0)
Responders (N (%))	
Primary (50%+)	1 (2.6)
Secondary (25-50%)	5 (13.2)
Non-responder	29 (76.3)
Non-responder (no valid sample, on trt.)	2 (5.3)
Non-responder (no valid sample, off trt.)	1 (2.6)
Total	38 (100.0)

2. Toxicity measured as the number of grade 3 and 4 adverse events reported.

TNO	Disease type	Category	Toxicity	Grade	Relatedness	Duration
[redacted]	ET	Skin and subcutaneous tissue disorders	Skin ulceration	3	Unrelated	Not known
[redacted]	PV	Infections and infestations	Urinary tract infection	3	Unrelated	6 days

3. The number of thrombotic events of any grade reported and validated.

TNO	Disease type	Event date	Treatment status at start of event	Weeks of treatment received	Event term	Grade	Duration
[redacted]	ET	21-Nov-17	Discontinued treatment	28	Superficial thrombophlebitis	2	24 hours or longer
[redacted]	ET	22-Apr-19	On treatment	20	Deep Vein Thrombosis	2	24 hours or longer

4. Haematological response, assessed at weeks 12 and 24, for patients who enter the study in response (CR or PR). Haematological response is defined according to 2009 ELN criteria for ET/PV patients and no evidence of disease progression for MF patients according to IWGMRT response criteria (for criteria see Appendices 5 & 6).

		Week (n, %)	
Disease Type	**Response category**	**12**	**24**
PV/ET (n = 25)	Complete response	6 (24.0)	4 (16.0)
	Partial response	14 (56.0)	15 (60.0)
	No response	3 (12.0)	2 (8.0)
	Missing	2 (8.0)	4 (16.0)
MF (n = 13)	No evidence of progression	13 (100.0)	11 (84.6)
	Evidence of progression	0 (0.0)	0 (0.0)
	Missing	0 (0.0)	2 (15.4)

5. Proportion of patients in each response category according to IWG-MRT response criteria for MF patients and 2013 ELN response criteria for ET/PV patients at 24 weeks of treatment.

PV/ET responses at Week 24 (N (%))	
Complete Response	2 (8.0)
Partial Response	14 (56.0)
No response	4 (16.0)
Missing	5 (20.0)
Total	25 (100.0)
MF responses at Week 24 (N (%))	
CR	1 (7.7)
PR	1 (7.7)
Stable disease	8 (61.5)
Missing	3 (23.1)
Total	13 (100.0)
MF response criteria selected at Week 24 (N (%))	
CR; Spleen response; Stable disease	1 (7.7)
Missing (no criteria selected)	3 (23.1)
PR; Stable disease	1 (7.7)
Stable disease	8 (61.5)
Total	13 (100.0)

6. Proportion of patients showing an improvement in response category at 24 weeks compared to baseline according to 2009 ELN criteria for ET/PV patients [1] and according to IWG-MRT response criteria [2] for MF patients. Patients who are in a higher category at week 24 compared to baseline will be classed a success. Patients who enter the trial in CR and who maintain a CR will also be classed as a success in this outcome.

	Disease Type		
Change in response	**PV/ET (n = 25)**	**MF (n = 13)**	**Overall (n = 38)**
Improved	0 (0.0)	2 (15.4)	2 (5.3)
Maintained CR	2 (8.0)	0 (0.0)	2 (5.3)
Unchanged (less than CR)	9 (36.0)	6 (46.2)	15 (39.5)
Worsened	8 (32.0)	1 (7.7)	9 (23.7)
Not evaluable	6 (24.0)	4 (30.8)	10 (26.3)

Adverse Events

	No. of events (related)				
Toxicity	Grade1	Grade2	Grade3	Grade4	Any Grade
Mucosal infection	0 (0)	1 (1)	0 (0)	0 (0)	1 (1)
Alanine aminotransferase increased	0 (0)	1 (1)	0 (0)	0 (0)	1 (1)
Lymphedema	0 (0)	1 (1)	0 (0)	0 (0)	1 (1)
Superficial thrombophlebitis	0 (0)	1 (1)	0 (0)	0 (0)	1 (1)
Flashing lights	1 (1)	0 (0)	0 (0)	0 (0)	1 (1)
Eye disorders - Other	1 (1)	0 (0)	0 (0)	0 (0)	1 (1)
Oral pain	1 (1)	0 (0)	0 (0)	0 (0)	1 (1)
Skin infection	1 (1)	0 (0)	0 (0)	0 (0)	1 (1)
Cholesterol high	1 (1)	0 (0)	0 (0)	0 (0)	1 (1)
Generalized muscle weakness	1 (1)	0 (0)	0 (0)	0 (0)	1 (1)
Peripheral sensory neuropathy	1 (1)	0 (0)	0 (0)	0 (0)	1 (1)
Agitation	1 (1)	0 (0)	0 (0)	0 (0)	1 (1)
Urinary frequency	1 (1)	0 (0)	0 (0)	0 (0)	1 (1)
Urinary tract pain	1 (1)	0 (0)	0 (0)	0 (0)	1 (1)
Vaginal dryness	1 (1)	0 (0)	0 (0)	0 (0)	1 (1)
Rash acneiform	1 (1)	0 (0)	0 (0)	0 (0)	1 (1)
Flushing	1 (1)	0 (0)	0 (0)	0 (0)	1 (1)
Skin ulceration	0 (0)	0 (0)	1 (0)	0 (0)	1 (0)
Blood and lymphatic system disorders - Other	0 (0)	1 (0)	0 (0)	0 (0)	1 (0)
Palpitations	0 (0)	1 (0)	0 (0)	0 (0)	1 (0)
Retinal detachment	0 (0)	1 (0)	0 (0)	0 (0)	1 (0)
Eye infection	0 (0)	1 (0)	0 (0)	0 (0)	1 (0)
Memory impairment	0 (0)	1 (0)	0 (0)	0 (0)	1 (0)
Wheezing	0 (0)	1 (0)	0 (0)	0 (0)	1 (0)
Cardiac disorders - Other	1 (0)	0 (0)	0 (0)	0 (0)	1 (0)
Ear pain	1 (0)	0 (0)	0 (0)	0 (0)	1 (0)
Tinnitus	1 (0)	0 (0)	0 (0)	0 (0)	1 (0)
Ear and labyrinth disorders - Other	1 (0)	0 (0)	0 (0)	0 (0)	1 (0)
Blurred vision	1 (0)	0 (0)	0 (0)	0 (0)	1 (0)
Eye pain	1 (0)	0 (0)	0 (0)	0 (0)	1 (0)
Abdominal distension	1 (0)	0 (0)	0 (0)	0 (0)	1 (0)
Constipation	1 (0)	0 (0)	0 (0)	0 (0)	1 (0)
Diarrhea	1 (0)	0 (0)	0 (0)	0 (0)	1 (0)
Flatulence	1 (0)	0 (0)	0 (0)	0 (0)	1 (0)
Vomiting	1 (0)	0 (0)	0 (0)	0 (0)	1 (0)
Chills	1 (0)	0 (0)	0 (0)	0 (0)	1 (0)
Non-cardiac chest pain	1 (0)	0 (0)	0 (0)	0 (0)	1 (0)
Pain	1 (0)	0 (0)	0 (0)	0 (0)	1 (0)
Hepatic pain	1 (0)	0 (0)	0 (0)	0 (0)	1 (0)
Bruising	1 (0)	0 (0)	0 (0)	0 (0)	1 (0)
Weight loss	1 (0)	0 (0)	0 (0)	0 (0)	1 (0)
Hypertriglyceridemia	1 (0)	0 (0)	0 (0)	0 (0)	1 (0)
Myalgia	1 (0)	0 (0)	0 (0)	0 (0)	1 (0)
Neck pain	1 (0)	0 (0)	0 (0)	0 (0)	1 (0)
Lethargy	1 (0)	0 (0)	0 (0)	0 (0)	1 (0)
Paresthesia	1 (0)	0 (0)	0 (0)	0 (0)	1 (0)
Vaginal discharge	1 (0)	0 (0)	0 (0)	0 (0)	1 (0)
Reproductive system and breast disorders - Other	1 (0)	0 (0)	0 (0)	0 (0)	1 (0)
Nasal congestion	1 (0)	0 (0)	0 (0)	0 (0)	1 (0)
Pleuritic pain	1 (0)	0 (0)	0 (0)	0 (0)	1 (0)
Rash maculo-papular	1 (0)	0 (0)	0 (0)	0 (0)	1 (0)

NB. The brackets contain the number of potentially related AE's for that toxicity.