A randomized, double-blind study of zinpentraxin alfa in patients with myelofibrosis who were previously treated with or ineligible for ruxolitinib: stage 2 of a phase II trial

Authors

Srdan Verstovsek,[1°] Moshe Talpaz,[2] Martha Wadleigh,[3] Alessandro Isidori,[4] Peter te Boekhorst,[5] Michael R. Savona,[6] Prithviraj Bose,[1] Olga Pozdnyakova,[7] Ruben Mesa,[8°] Tarec C. El-Galaly,[9°] Jennifer O'Sullivan,[10] Katia Gamel,[9] Brian Higgins,[11] Sudhakar Katakam,[9] Boyan Todorov,[9] Kerstin Trunzer[9] and Claire N. Harrison[10]

[1]The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [2]Michigan Medicine - The University of Michigan, Ann Arbor, MI, USA; [3]Dana-Farber Cancer Institute, Boston, MA, USA; [4]Hematology and Stem Cell Transplant Center, AORMN Hospital, Pesaro, Italy; [5]Erasmus Medical Center, Rotterdam, the Netherlands; [6]Vanderbilt-Ingram Cancer Center, Vanderbilt University School of Medicine, Nashville, TN, USA; [7]Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA; [8]Mays Cancer Center at UT Health San Antonio MD Anderson, San Antonio, TX, USA; [9]F. Hoffmann-La Roche, Ltd., Basel, Switzerland; [10]Guy's & St Thomas' NHS Foundation Trust, London, UK and [11]Genentech Inc, South San Francisco, CA, USA

°Current address of SV: Kartos Therapeutics, Redwood City, CA, USA °Current address of RM: Wake Forest Baptist Comprehensive Cancer Center, Winston-Salem, NC, USA

°Current address of TCE-G: Department of Hematology, Aalborg University Hospital, Aalborg, Denmark

Correspondence:
C.N. HARRISON - claire.harrison@gstt.nhs.uk

https://doi.org/10.3324/haematol.2023.284410

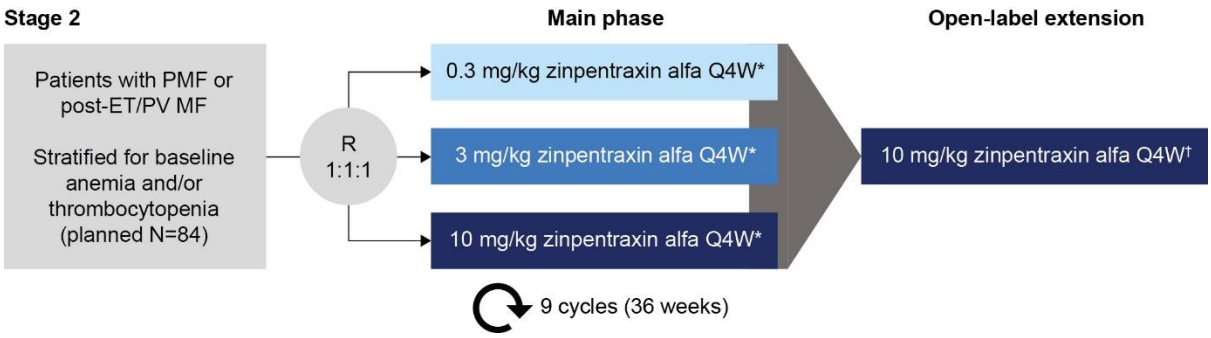
SUPPLEMENTARY MATERIAL

for

A randomized, double-blind study of zinpentraxin alfa in patients with myelofibrosis who were previously treated with or ineligible for ruxolitinib: Stage 2 of a Phase II trial

Srdan Verstovsek, Moshe Talpaz, Martha Wadleigh, Alessandro Isidori, Peter te Boekhorst, Michael R Savona, Prithviraj Bose, Olga Pozdnyakova, Ruben Mesa, Tarec C El-Galaly, Jen O'Sullivan, Katia Gamel, Brian Higgins, Sudhakar Katakam, Boyan Todorov, Kerstin Trunzer, Claire N Harrison

Supplementary Figure S1. Stage 2 study design.



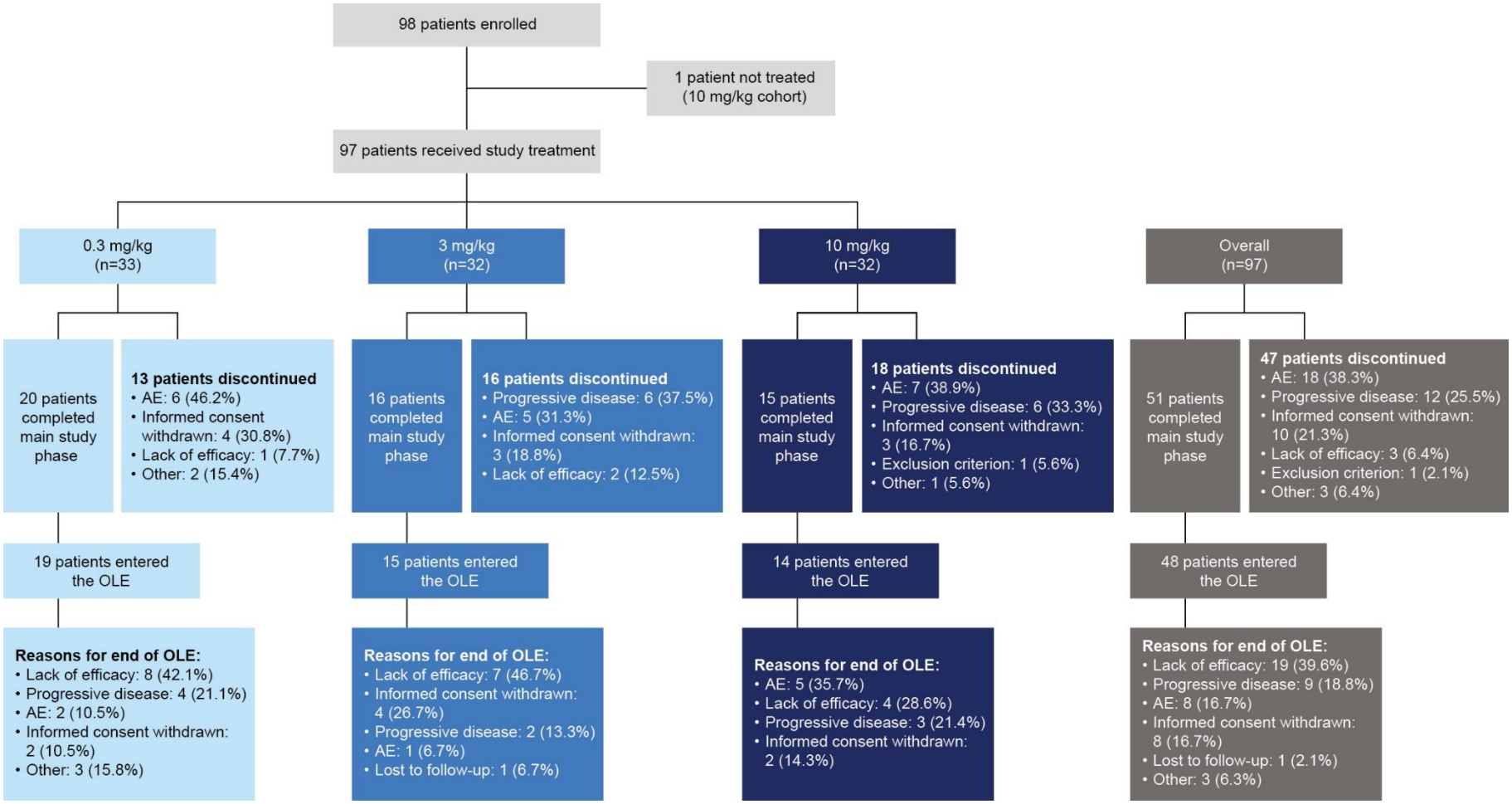
Stage 2 was a randomized, double-blind phase II study to determine the efficacy and safety of three different doses of zinpentraxin alfa in patients with PMF and post ET/PV MF who had discontinued or were not eligible for ruxolitinib treatment. Each patient participated in the main study phase for approximately 44 weeks, comprising a 4-week screening period, a treatment period of 9×4-week cycles, and an end of study visit 4 weeks after the end of the last cycle. After completion of 9 cycles, patients could continue with zinpentraxin alfa at 10 mg/kg in the OLE in the absence of disease progression or toxicity warranting discontinuation of therapy.

*Patients in the main phase of Stage 2 received additional loading doses of the assigned strength of zinpentraxin alfa at Days 3 and 5 during the first cycle.

†Patients in the OLE of Stage 2 received additional loading doses of 10 mg/kg zinpentraxin alfa at Days 3 and 5 of their first cycle after entering the OLE.

ET: essential thrombocythemia; MF: myelofibrosis; OLE: open-label extension; PMF: primary MF; PV: polycythemia vera; Q4W: every 4 weeks; R: randomized.

Supplementary Figure S2. Patient disposition.



AE: adverse event; OLE: open-label extension.

Supplementary Table S1. Key baseline demographics and disease characteristics in the all-treated population.

Characteristic	Group 1[a] (n=33)	Group 2[b] (n=32)	Group 3[c] (n=32)	Overall (N=97)
Median (range) age, years	70.0 (52-82)	71.0 (54-79)	69.0 (49-87)	70.0 (49-87)
Type of MF, n (%)				
Primary MF	20 (60.6)	20 (62.5)	26 (81.3)	66 (68.0)
Post-PV MF	8 (24.2)	6 (18.8)	2 (6.3)	16 (16.5)
Post-ET MF	5 (15.2)	6 (18.8)	4 (12.5)	15 (15.5)
Mean (SD) time since diagnosis, years	3.48 (5.90)	3.28 (2.49)	4.69 (5.06)	3.81 (4.72)
Risk group (IWG-MRT DIPSS), n (%)				
Low	0	0	0	0
Intermediate-1	5 (15.2)	6 (18.8)	3 (9.4)	14 (14.4)
Intermediate-2	24 (72.7)	22 (68.8)	20 (62.5)	66 (68.0)
High	4 (12.1)	4 (12.5)	9 (28.1)	17 (17.5)
Baseline central BM fibrosis grade,[d] n (%)				
MF – 0	0	1 (3.1)	0	1 (1.0)
MF – 1	2 (6.1)	2 (6.3)	1 (3.1)	5 (5.2)
MF – 2	12 (36.4)	6 (18.8)	10 (31.3)	28 (28.9)
MF – 3	19 (57.6)	21 (65.6)	21 (65.6)	61 (62.9)
Not evaluable	0	2 (6.3)	0	2 (2.1)
Previously treated with ruxolitinib, n (%)				
Yes	25 (75.8)	27 (84.4)	22 (68.8)	74 (76.3)
No	8 (24.2)	5 (15.6)	10 (31.3)	23 (23.7)
Intolerant to ruxolitinib, n (%)				
n	25	27	22	74
Yes	18 (72.0)	20 (74.1)	10 (45.5)	48 (64.9)
No	7 (28.0)	7 (25.9)	12 (54.5)	26 (35.1)
RBC transfusion dependency,[e] n (%)				
Dependent	14 (42.4)	11 (34.4)	13 (40.6)	38 (39.2)
Independent	19 (57.6)	21 (65.6)	19 (59.4)	59 (60.8)
Hemoglobin at baseline, n (%)				
<100 g/L	26 (78.8)	27 (84.4)	28 (87.5)	81 (83.5)
≥100 g/L	7 (21.2)	5 (15.6)	4 (12.5)	16 (16.5)

Platelet transfusion dependency,[f] n (%)				
Dependent	3 (9.1)	2 (6.3)	10 (31.3)	15 (15.5)
Independent	30 (90.9)	30 (93.8)	22 (68.8)	82 (84.5)
Platelet count at baseline, n (%)				
$\leq 25\times10^9$/L	10 (30.3)	10 (31.3)	10 (31.3)	30 (30.9)
$>25\times10^9$/L to $\leq 50\times10^9$/L	11 (33.3)	8 (25.0)	10 (31.3)	29 (29.9)
$>50\times10^9$/L to $\leq 100\times10^9$/L	5 (15.2)	4 (12.5)	4 (12.5)	13 (13.4)
$>100\times10^9$/L	7 (21.2)	10 (31.3)	8 (25.0)	25 (25.8)
Driver mutation,[g] n (%)				
n	26	25	28	79
Yes	24 (92.3)	22 (88.0)	25 (89.3)	71 (89.9)
No	2 (7.7)	3 (12.0)	3 (10.7)	8 (10.1)
HMR mutation status,[g,h] n (%)				
n	26	25	28	79
≥1 high-risk mutation	13 (50.0)	12 (48.0)	14 (50.0)	39 (49.4)
No high-risk mutation	13 (50.0)	13 (52.0)	14 (50.0)	40 (50.6)

[a]Group 1 was treated with zinpentraxin alfa 0.3 mg/kg Q4W.

[b]Group 2 was treated with zinpentraxin alfa 3 mg/kg Q4W.

[c]Group 3 was treated with zinpentraxin alfa 10 mg/kg Q4W.

[d]BM fibrosis grades according to World Health Organization criteria (as determined by central adjudication). Results were available for 95 patients. Local BM fibrosis grade was used to determine study eligibility.

[e]Baseline PRBC transfusion dependency was defined as ≥2 units PRBC every 4 weeks for 12 weeks prior to Cycle 1 Day 1, regardless of baseline hemoglobin level.

[f]Baseline platelet transfusion dependency was defined as ≥2 platelet transfusions in any 12 weeks prior to Cycle 1 Day 1, regardless of baseline platelet level.

[g]Results from at least one timepoint were available for 79 patients. Driver mutation status was derived irrespective of the timepoint the sample was taken.

[h]High-risk mutation was defined as having mutations in the following genes: *ASXL1*, *IDH1*, *IDH2*, *SRSF2*, *EZH2* or *U2AF1* Q157 mutation.

BM: bone marrow; HMR: high molecular risk; IWG-MRT DIPSS: International Working Group-Myeloproliferative Neoplasms Research and Treatment Dynamic International Prognostic Scoring System; MF: myelofibrosis; post-ET MF: post-essential thrombocythemia myelofibrosis; post-PV MF: post-polycythemia vera myelofibrosis; Q4W: every 4 weeks; RBC: red blood cell; SD: standard deviation.