Results from Phase 1/2 Clinical Trial of Tagraxofusp (SL-401) in Patients with Intermediate, or High Risk, Relapsed/Refractory Myelofibrosis

Naveen Pemmaraju[1], Vikas Gupta[2], Haris Ali[3], Abdulraheem Yacoub[4], Eunice Wang[5], Sangmin Lee[6], Gary Schiller[7], Megan Sardone[8], Halyna Wysowskyj[8], Janice Chen[8], Chris Brooks[8], Enrique Poradosu[8], Peter McDonald[8], Nicole Rupprecht[8], Animesh Pardanani[9], Ayalew Tefferi[9], Moshe Talpaz[10], Minakshi Taparia[11], Srdan Verstovsek[1], Joseph Khoury[1], Mrinal M. Patnaik[9]

[1]The University of Texas MD Anderson Cancer Center, Houston, [2]Princess Margaret Cancer Centre, Toronto, Canada, [3]City of Hope, Duarte, [4]Kansas University Cancer Center, Westwood, [5]Roswell Park Cancer Institute, Buffalo, [6]Weill Cornell Medical Center, New York, [7]Ronald Reagan UCLA Medical Center, Los Angeles, [8]Stemline Therapeutics, New York, [9]Mayo Clinic, Rochester, [10]University of Michigan Health System, Ann Arbor, [11]University of Alberta Hospital, Edmonton

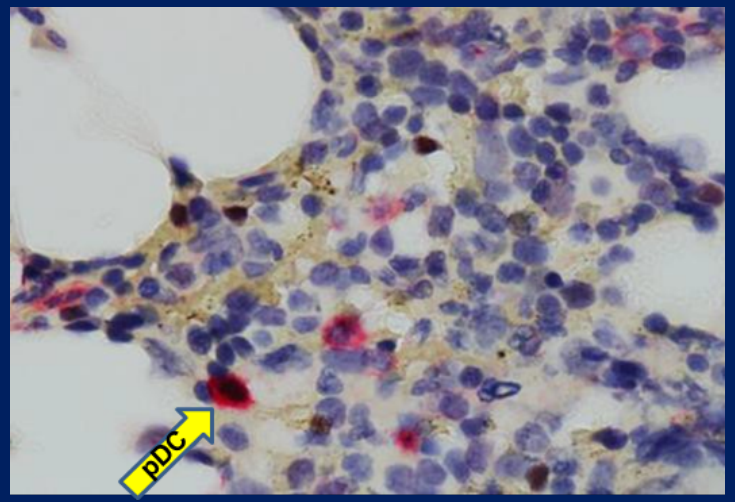
Tagraxofusp in MF: Background Myelofibrosis

- Survival in patients with relapsed/refractory (R/R) myelofibrosis (MF) is generally poor, with a median survival ~14 months
- Prognosis for patients with thrombocytopenia at baseline or during JAK1/2 therapy is worse
- Monocytosis is an independent predictor for inferior survival in primary MF
- Currently no approved therapies for patients with MF who have failed or are intolerant to the JAK 1/2 inhibitors (ruxolitinib, fedratinib)

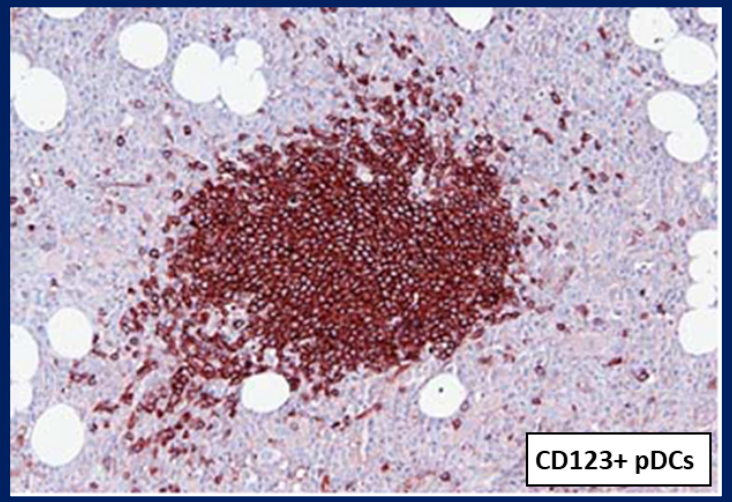
Newberry et al *Blood.* 2017 Aug 31;130(9):1125-1131
Kuykendall AT et al *Ann Hematol* 2018 Mar; 97(3):435-441
Tefferi A, et al. *Br J Haematol.* 2018;183(5):835-838.

Tagraxofusp in MF: Rationale for CD123-Directed Therapy

CD123 expression in MF



CD123 (red) and TCF4 (brown) staining in MF bone marrow



CD123^{+} staining in MF bone marrow

Thrombocytopenia in MF

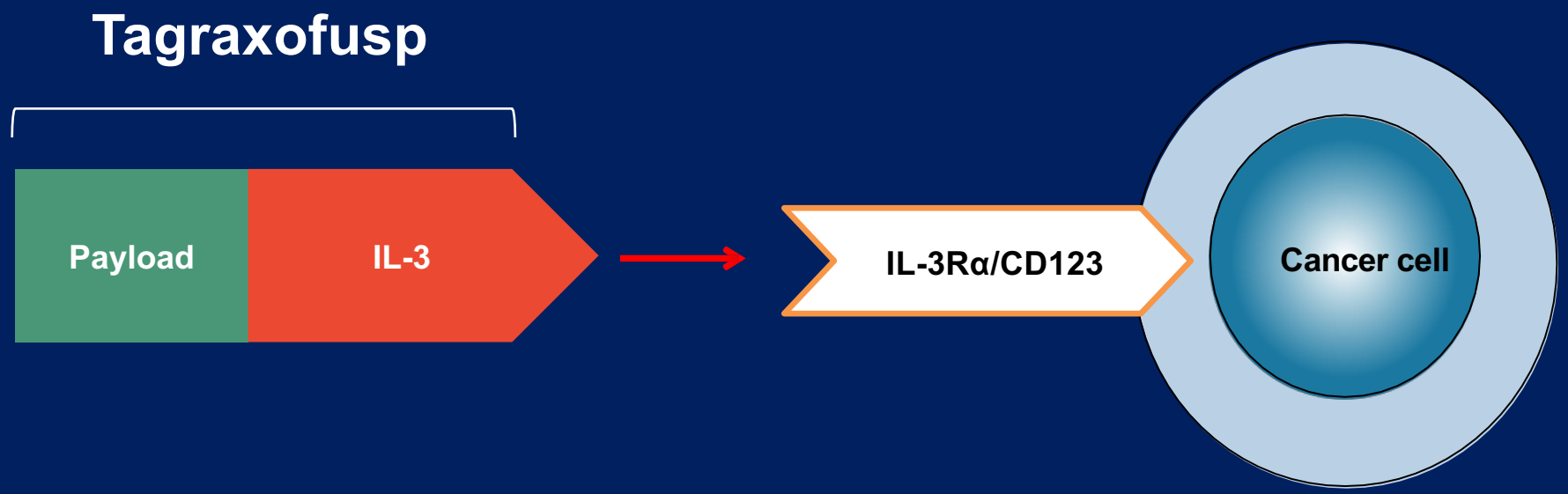
- Patients with thrombocytopenia may require dose interruptions, and/or dose reductions with standard therapies
- Aside from cycle 1, prolonged thrombocytopenia not observed with tagraxofusp

CMML-like features in MF

- Monocytosis (>1x10^{9}/L monocytes) associated with accelerated disease phase and poor prognosis
- Independent predictor of inferior survival in MF
- Monocytes and CD123+ pDCs share common progenitor

Facchetti et al. *Mod Pathol*. 2016 Feb;29(2):98-11
Solary et al. *Leukemia*. 2019 Oct;33(10):2466-2480

Tagraxofusp in MF: Novel CD123 Targeted Therapy



- Novel CD123-targeted therapy
- FDA-approved for the treatment of adult and pediatric patients, ages ≥ 2 with Blastic Plasmacytoid Dendritic Cell Neoplasm (BPDCN)
- CD123 is expressed on multiple myeloid and other malignancies including BPDCN, CMML, MF, AML, and others

Pemmaraju et al. *N Engl J Med*; 2019; 380(17):1628-1637

Tagraxofusp in MF: Study Design & Eligibility Criteria (n=29)

Stage 1 – Lead in (Complete)

Single-arm, n=4

- MPN: CMML, MF, SM, and PED
- Tagraxofusp: 7, 9, or 12 µg/kg via IV infusion, days 1-3 of a 21-day cycle (C1-4); 28-day cycle (C5-7); and 42-day cycle thereafter
- Key objectives: Determine optimal dose and regimen for Stage 2

Stage 2 – Ongoing

Single-arm, n=25

- MPN: CMML or MF without evidence of transformation
- Tagraxofusp: 12 µg/kg via IV infusion, days 1-3 of a 21-day cycle (C1-4); 28-day cycle (C5-7); and 42-day cycle thereafter
- Key objectives: Further define safety and efficacy

Select Inclusion Criteria

- Patient population
  - Stage 1 - High-risk MPN-associated MF, CMML, SM, and PED
  - Stage 2 - CMML or MF without evidence of transformation
- Age ≥18; ECOG PS 0-2
- Adequate baseline organ function, including: LVEF ≥ LLN, creatinine ≤1.5 mg/dL, albumin ≥3.2 g/dL, bilirubin ≤1.5 mg/dL, AST/ALT ≤2.5 times ULN, creatine phosphokinase ≤2.5 times ULN, ANC ≥0.5 × 10^9/L

MF Response Criteria

- Revised International Working Group-Myeloproliferative Neoplasms Research and Treatment (IWG-MRT) and European LeukemiaNet (ELN) Response Criteria (Tefferi 2013; Barbui 2018)
- Efficacy: First assessment performed at the end of cycle 4

Tefferi A., et al. *Am J Hematol* 2013A; 88:142-150.
Barbui T, et al. *Leukemia.* 2018;32(5):1057-1069.

Tagraxofusp in MF: Study Demographics (n=29)

Age, years	
Median [range]	69 [54-87]
Gender [n, (%)]	
Female	15 (52)
ECOG	
Median [range]	1 [0-2]
Median Blast Count, %	
Median [range]	3 [0-16]
Baseline sites of disease [n, (%)]	
Spleen	23 (79)
Liver	5 (17)
Baseline Labs	**Median [range]**
Platelets (10^9/L)	59 [13-579]
50-100, [n, (%)]	8 (28)
≤50, [n, (%)]	11 (38)
Hemoglobin (g/dL)	8.6 [6-15.2]
WBC (K/uL)	14.6 [1.4-86.9]

Prior systemic therapy for MF [n, (%)]	
JAK 1/2 inhibitor (JAKi)	20 (77%)
Stem cell transplant (SCT)	2 (8%)
Hypomethylating agent (HMA)	2 (8%)
Median # of prior tx [range]	2 [0-4]
Myelofibrosis type	
Primary	19 (66)
Post-Polycythemia Vera	7 (24)
Post-Essential Thrombocythemia	3 (10)
DIPSS-plus score	
High	9 (31)
Intermediate-2	17 (59)
Intermediate-1	2 (7)

Cytogenetics (n=9)	
20q-	3
-7/7q-	3
-5/5q-	2
12p-	2
13q-	1
i(17q)	1
Molecular mutations (n=28)	
JAK2	19
CALR	3
MPL	1
ASXL1	5
U2AF1	4

Tagraxofusp in MF: Safety Analysis

MF (all doses): Stages 1 and 2 (n=29)

Most Common (≥10%) Treatment-Related Adverse Events (TRAEs)

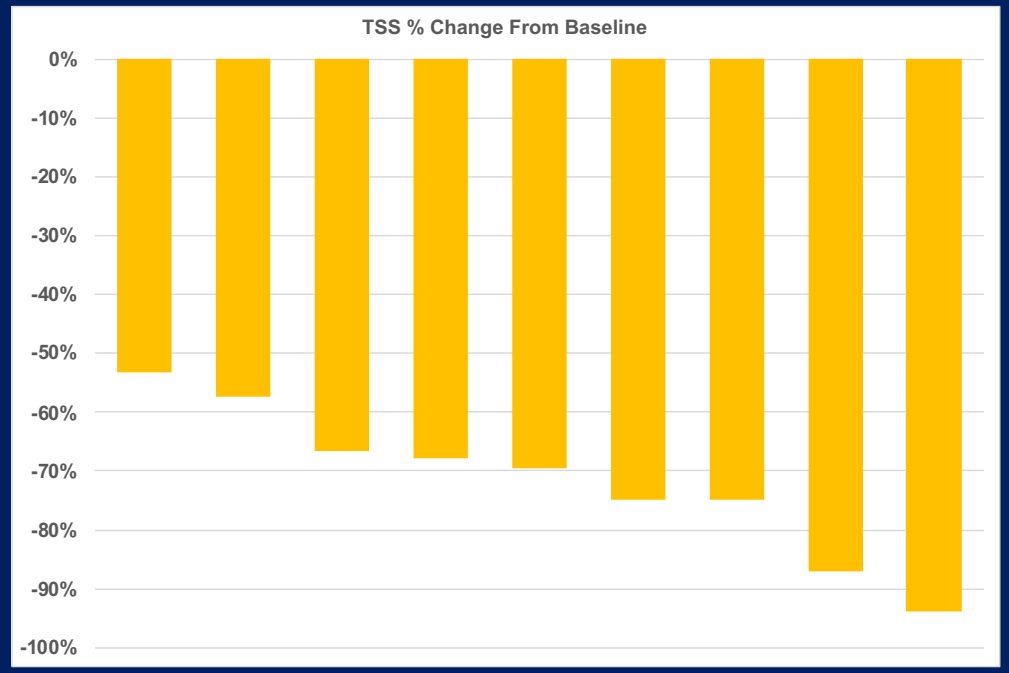
Adverse Event	All Grades, n (%)		TRAEs, n (%)			
	TRAEs	All AEs	G1 & 2	G3	G4	G5
Alanine aminotransferase increased	5 (17)	6 (21)	5 (17)	--	--	--
Headache	5 (17)	6 (21)	5 (17)	--	--	--
Hypoalbuminaemia	5 (17)	9 (31)	5 (17)	--	--	--
Anemia	4 (14)	9 (31)	0 (0)	4 (14)	--	--
Thrombocytopenia	4 (14)	7 (24)	2 (6)	1 (3)	1 (3)	--
Aspartate aminotransferase increased	3 (10)	3 (10)	3 (10)	--	--	--
Dizziness	3 (10)	7 (24)	3 (10)	--	--	--
Fatigue	3 (10)	8 (28)	2 (7)	1 (3)	--	--
Nausea	3 (10)	7 (24)	3 (10)	--	--	--

- There was one case of capillary leak syndrome, which was Grade 3

- Predictable and manageable safety profile
- No apparent cumulative AEs over multiple cycles
  - Thrombocytopenia was largely transient

Tagraxofusp in MF: Spleen Response & Improvement in TSS

Pt	Total Symptom Score (TSS)			Spleen Size at TSS Best Response		
	Baseline	Best ponse	Reduction	Baseline (cm)	Size	Reduction
1	81	26	68%	35	19	46%
2	47	20	57%	17	12	29%
3	36	11	69%	17	16	6%
4	23	3	87%	5	0	100%
5	32	2	94%	-	-	N/R
6	3	1	67%	19	10	47%
7	15	7	53%	-	-	N/R
8	8	2	75%	-	-	N/E
9	20	5	75%	3	0	100%



- 45% (9/20) of patients had symptom burden reduction, including 3 with symptom response per IWG-MRT 2013 MF response criteria
- Spleen responses correlate with TSS responses

Emanuel RM, et al. *J Clin Oncol*. 2012 Nov 20;30(33):4098-103

Tagraxofusp in MF: Spleen Size Reductions

Spleen Size Reductions	Patients with splenomegaly ≥5 cm BCM at baseline	Patients with Thrombocytopenia		Patients with Monocytosis
		Platelets $<100x10^9/L$	Platelets $<50x10^9/L$	Monocytes $\geq 1x10^9/L$
All spleen size reductions	53% (8/15)	64% (7/11)	60% (3/5)	100% (5/5)
>35% size reduction	20% (3/15)	18% (2/11)	20% (1/5)	40% (2/5)

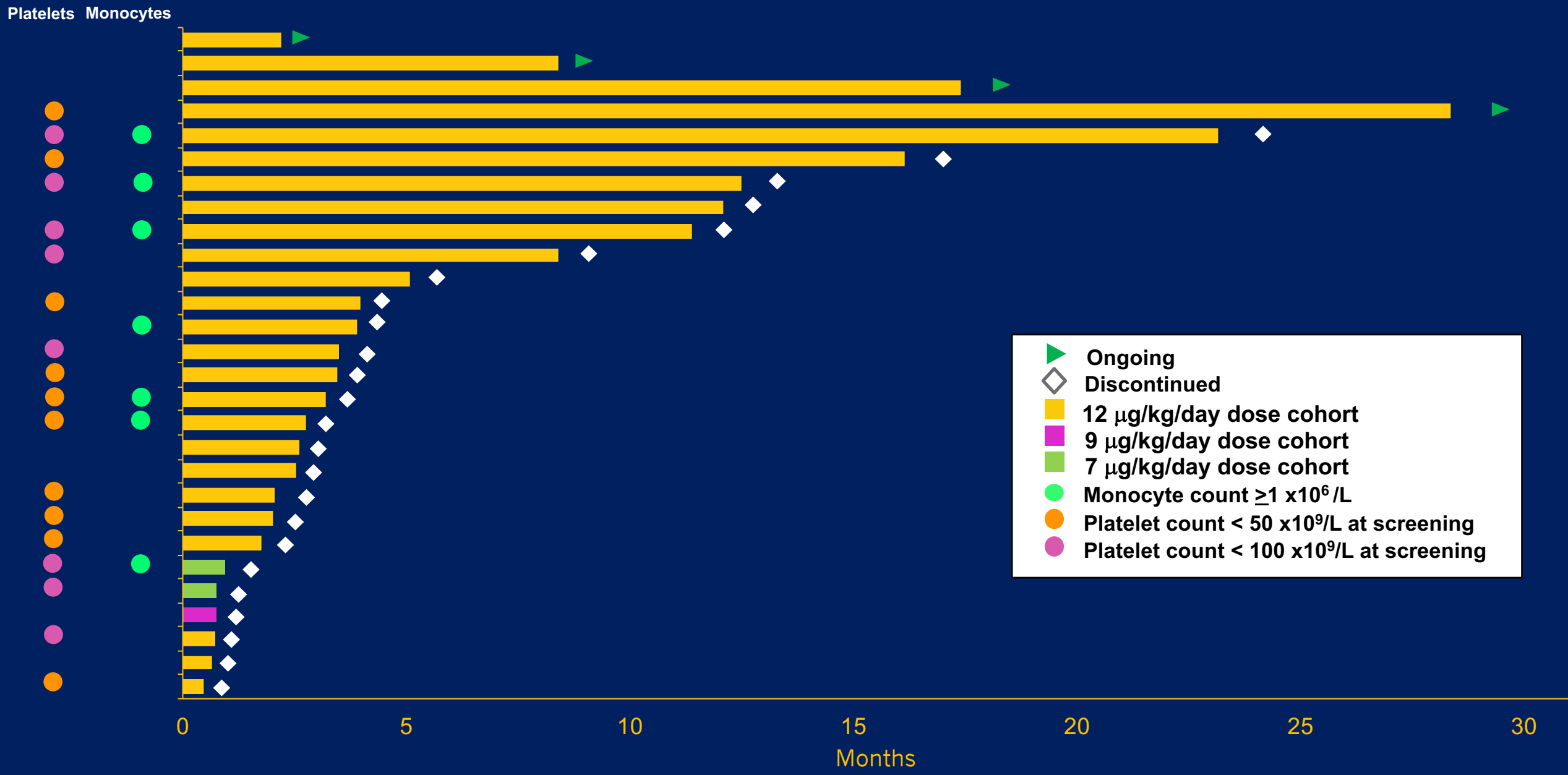
Tagraxofusp in MF: IWG 2013 Assessment & Patient Vignette

- 15 out of 28 patients were assessed as Stable Disease per IWG 2013
- 4 patients with Stable Disease also reported improvements in one or more the following response categories: clinical improvement, anemia, spleen, and/or symptom response per IWG

Patient vignette:

- 69 year-old woman; Baseline splenomegaly (5 cm BCM) and thrombocytopenia ($19x10^9/L$)
- Responses in four out of six subdomains; Currently on treatment (cycle 24, 28 months ongoing)
  - Anemia: Baseline Hb around 8-9 g/dl improved to 12 g/dl by cycle 16; currently stable
  - Spleen response: non-palpable after 1 cycle of tagraxofusp; Remains non-palpable
  - TSS: baseline score of 23, continued to improve over course of therapy, achieving a TSS best response of 3 at cycle 7

Tagraxofusp in MF: Treatment Duration

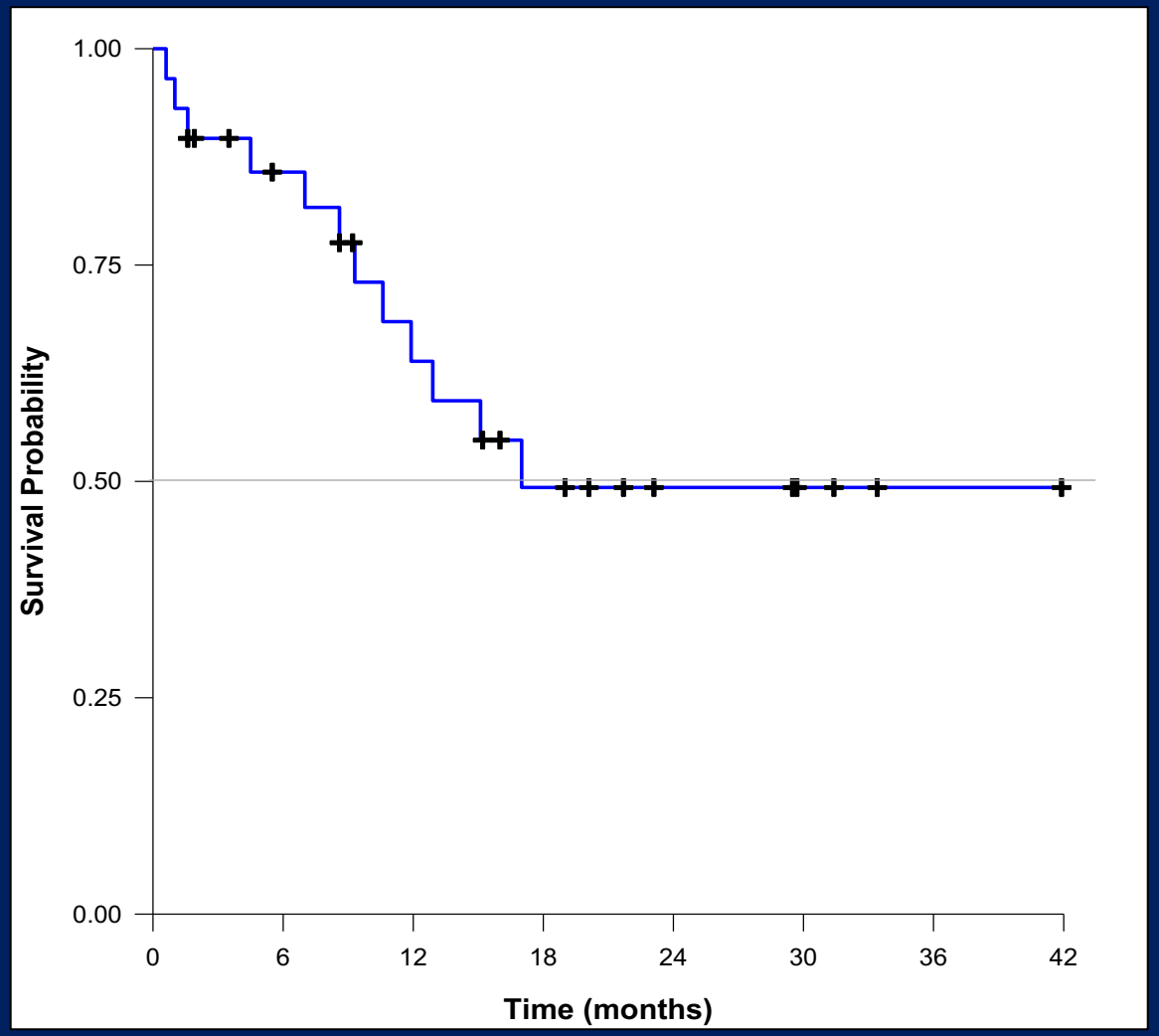


Tagraxofusp in MF: Patient Disposition

- 25/29 (86%) patients now off study

Reason	N
Progressive Disease	7
Physician Decision	5
AE	4
Withdrawal by Patient	4
Death	3
Other/concomitant medical conditions	1
Patient went onto allogenic transplant	1

Tagraxofusp in MF: Overall Survival (n=29)



- OS-18: 43% (9/21; 95% CI: 0.22, 0.66)
- OS-24: 29% (5/17; 95% CI: 0.10, 0.55)

Tagraxofusp in MF: Conclusions

- Tagraxofusp has demonstrated clinical efficacy with a predictable and manageable safety profile in this ongoing Phase I/II MF study cohort including patients with poor prognostic features, including thrombocytopenia, monocytosis and clonal evolution
- Current cohort is being expanded to continue to evaluate tagraxofusp in patients with relapsed/refractory MF
- Additional areas for further development include MF subsets with:
  - Thrombocytopenia
  - Monocytosis (CD123-overexpressed subsets)

Tagraxofusp in MF: Acknowledgements

We would like to thank our patients and their families, as well as:

- Investigators, co-investigators, Sponsor: Stemline and study teams