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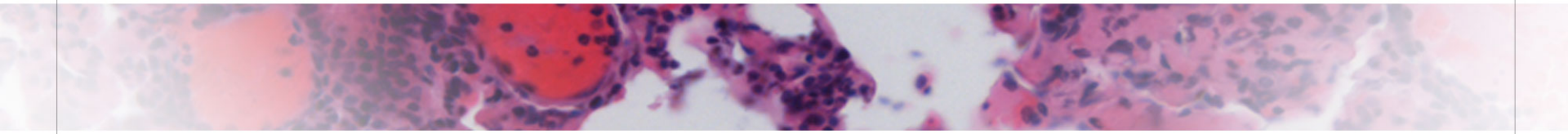

A Multicenter Phase 1/2 Clinical Trial of Tagraxofusp, a CD123-Targeted Therapy, in Patients with Poor-Risk Primary and Secondary Myelofibrosis

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Disclosures

I have the following conflicts of interests to disclose:

- **Consultant: Pacylex Pharmaceuticals**
- **Honoraria: AbbVie, Blueprint Medicines, Celgene, DAVA Oncology, Incyte, LFB Biotechnologies, MustangBio, Novartis, Roche Diagnostics, Stemline Therapeutics**
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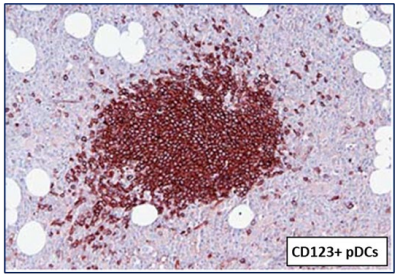
Introduction

- **Prognosis of patients with myelofibrosis (MF) who are R/R is poor, with a median survival of ~24 months**
- **Prognosis for patients with MF and thrombocytopenia at baseline or during JAK inhibitor therapy, monocytosis, accelerated phase, or who develop clonal evolution is also poor and these patients often have limited treatment options**
- **CD123 (IL3Rα) is aberrantly expressed on leukemia stem cells and aberrant/malignant microenvironmental plasmacytoid dendritic cells (pDC) in certain myeloid cancers including MF**
- **Tagraxofusp (TAG), a CD123-targeted therapy FDA approved for patients with blastic plasmacytoid dendritic cell neoplasm, has demonstrated preclinical proof-of-concept in MF**

CD123 expression in MF

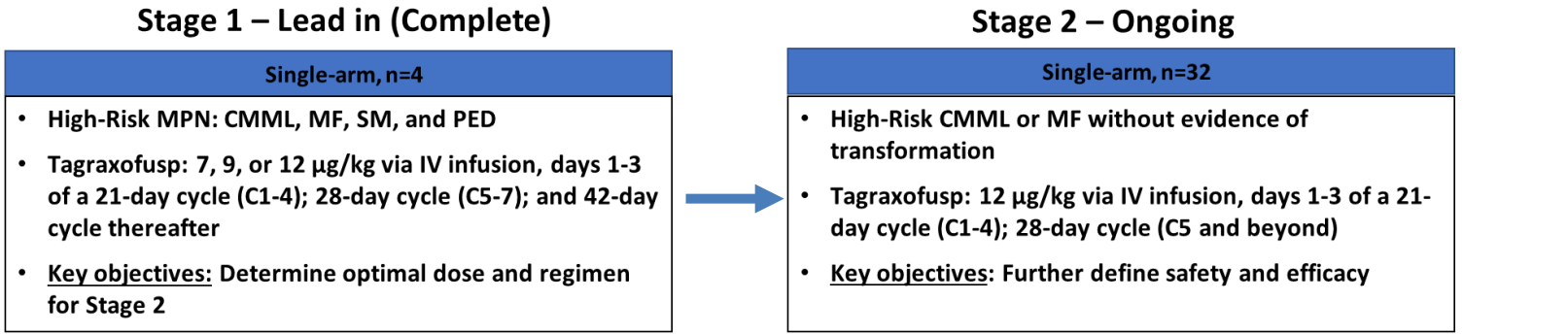


CMML-like features in MF

- **Monocytosis (>1x10^9/L monocytes) associated with accelerated disease phase and poor prognosis**
- **Monocytes and CD123+ pDCs share common progenitor**

Mcloran DP, Harrison CN. *Br J Haematol* 2020; doi:1111/bjh.16573; Newberry KJ et al. *Blood* 2017; Gangat N, Tefferi A. *Br J Haematol* 2020; doi:10.1111/bjh.16576; Kuykendall AT et al. *Ann Hematol* 2018; Palandri F et al. *Cancer* 2019; Facchetti et al. *Mod Pathol*.2016Feb;29(2):98-11; Solary et al. *Leukemia* 2019Oct;33(10):2466-2480.

Tagraxofusp in MF: Study Design (N=36)



Select Inclusion Criteria

- 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)
- Efficacy: First assessment performed at the end of cycle 4

Tefferi A., et al. *Am J Hematol* 2013A; 88:142-150.

Patient Characteristics

CHARACTERISTICS	
Median Age, years [range]	70 [54-87]
Female, n (%)	17 (47)
Median ECOG PS [range]	1 [0-2]
Baseline Splenomegaly/Hepatomegaly, n (%)	
Spleen	27 (75)
Liver	5 (14)
Baseline Blood Counts*	
Platelets (10^9/L), median [range]	59 [5-579]
>100, n (%)	11 (31)
>50-100, n (%)	11 (31)
≥20-50, n (%)	8 (22)
<20, n (%)	6 (17)
Hemoglobin (g/dL), median [range]	8.6 [6.0-15.2]
WBC (x10^9/L), median [range]	11.9 [1.4-86.9]

CHARACTERISTICS	
Prior Systemic Therapy for MF, n (%)	
JAK 1/2 inhibitor	24 (67)
Allogeneic stem cell transplant	2 (6)
Median # of prior tx [range]	2 [1-4]
Myelofibrosis Subtype, n (%)	
Primary Myelofibrosis (PMF)	25 (69)
Post-Polycythemia Vera (Post-PV MF)	8 (22)
Post-Essential Thrombocythemia (Post-ET MF)	3 (8)
DIPSS-plus risk score, n (%)**	
High	10 (28)
Intermediate-2	20 (55)
Intermediate-1	6 (17)

CHARACTERISTICS	
Cytogenetics (n=9)	
20q-	3
-7/7q-	3
-5/5q-	2
12p-	2
13q-	1
i(17q)	1
Molecular mutations (n=36)	
JAK2V617F	23
CALR	3
MPL	2
ASXL1	9
U2AF1	6

*3 patients had WHO-defined accelerated phase MF (Arber DA, et al. *Blood* 2016); **1 patient did not have data available.

Safety Analysis

Common (≥10%) Treatment-Related Adverse Events (TRAEs) (N=36)

Adverse Event	All Grades, n (%)		TRAEs, n (%)			
	TRAEs	All AEs	G1 & 2	G3	G4	G5
Hypoalbuminemia	8 (22)	14 (39)	7 (19)	1 (3)	--	--
Headache	6 (17)	11 (31)	6 (17)	--	--	--
Alanine aminotransferase increased	6 (17)	7 (19)	6 (17)	--	--	--
Anemia	4 (11)	12 (33)	--	4 (11)	--	--
Thrombocytopenia	6 (17)	9 (25)	2 (6)	2 (6)	2 (6)	--
Aspartate aminotransferase increased	3 (8)	3 (8)	2 (6)	1 (3)	--	--
Capillary leak syndrome (CLS)	3 (8)	3 (8)	1 (3)	1 (3)	1 (3)	--
Dizziness	3 (8)	11 (31)	3 (8)	--	--	--
Fatigue	3 (8)	9 (25)	2 (6)	1 (3)	--	--
Nausea	3 (8)	3 (8)	3 (8)	--	--	--

Analysis includes all doses (1 patient treated, 7mcg/kg; 1 patient treated, 9mcg/kg; and remaining patients treated, 12mcg/kg).

Spleen Size Reductions

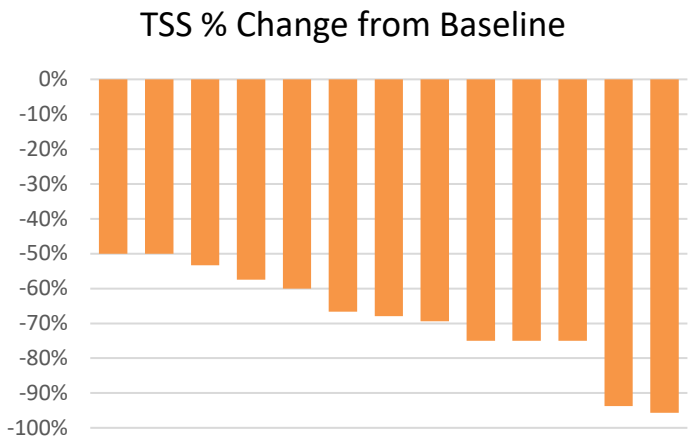
Spleen Size Reductions	Patients with splenomegaly ≥5 cm BCM at baseline	Patients with Thrombocytopenia		Patients with Monocytosis
		Platelets <100x10^9/L	Platelets <50x10^9/L	Monocytes ≥1x10^9/L
Baseline Splenomegaly	21	16	8	5
All Spleen Size Reductions	11 (56%)	8 (50%)	4 (50%)	4 (80%)
≥50% Size Reduction	2	1	1	0

Patients with palpable spleen (by physical exam) at baseline. Imaging was not available for evaluation in these patients.

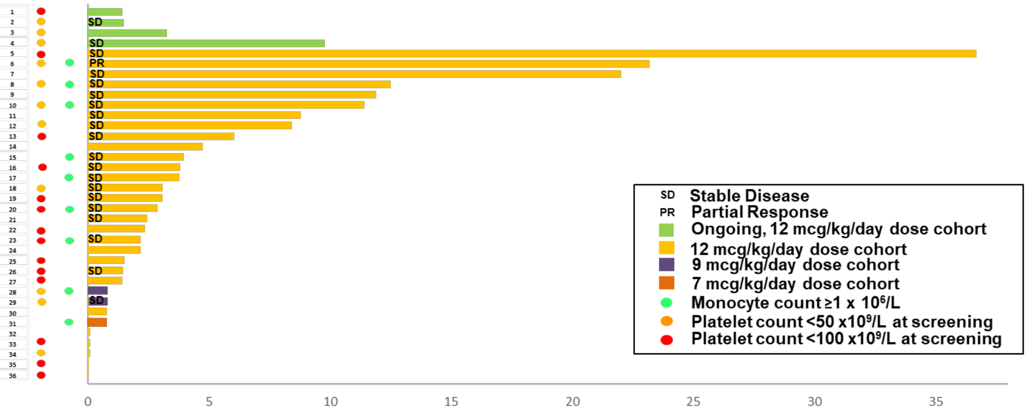
Spleen Size Reduction & Improvement in TSS

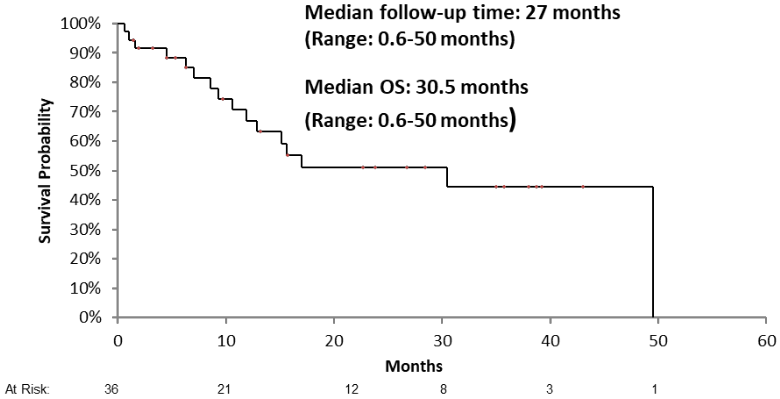
- **48% (13/27) of evaluable patients had symptom burden reduction, including 3 with total symptom score (TSS) reduction per IWG-MRT 2013 MF response criteria**
- **20 out of 36 (56%) patients were assessed as Stable Disease per IWG 2013 criteria**

	Total Symptom Score (TSS)			Spleen Size at TSS Best Response		
Pt	Baseline	Best Response	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	1	96%	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%
10	8	4	50%	-	-	N/E
11	15	6	60%	-	-	N/E
12	48	12	75%	-	-	N/E
13	30	15	50%	19	19	0%



Treatment Duration & OS





Tagraxofusp in MF: Conclusions

- **Tagraxofusp has demonstrated clinical efficacy with a predictable safety profile including in patients with recognized poor prognostic features, including thrombocytopenia, monocytosis, accelerated phase, and clonal evolution**
- **Current, ongoing cohort is being expanded to continue to evaluate tagraxofusp in patients with R/R MF**
- **Currently evaluating additional areas for further development including patients with MF subsets exhibiting:**
  - **Thrombocytopenia**
  - **Monocytosis (CD123-expressing subsets)**
  - **Accelerated phase**