Results of Pivotal Phase 2 Trial of Tagraxofusp (SL-401) in Patients with Blastic Plasmacytoid Dendritic Cell Neoplasm (BPDCN)

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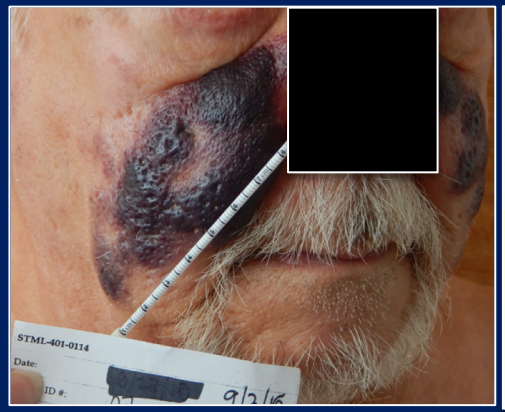
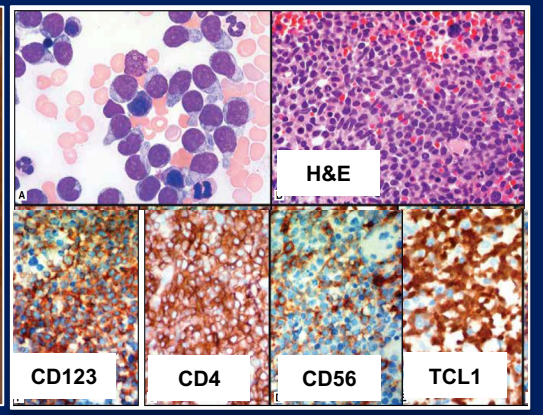
BPDCN: Aggressive Malignancy of Unmet Medical Need

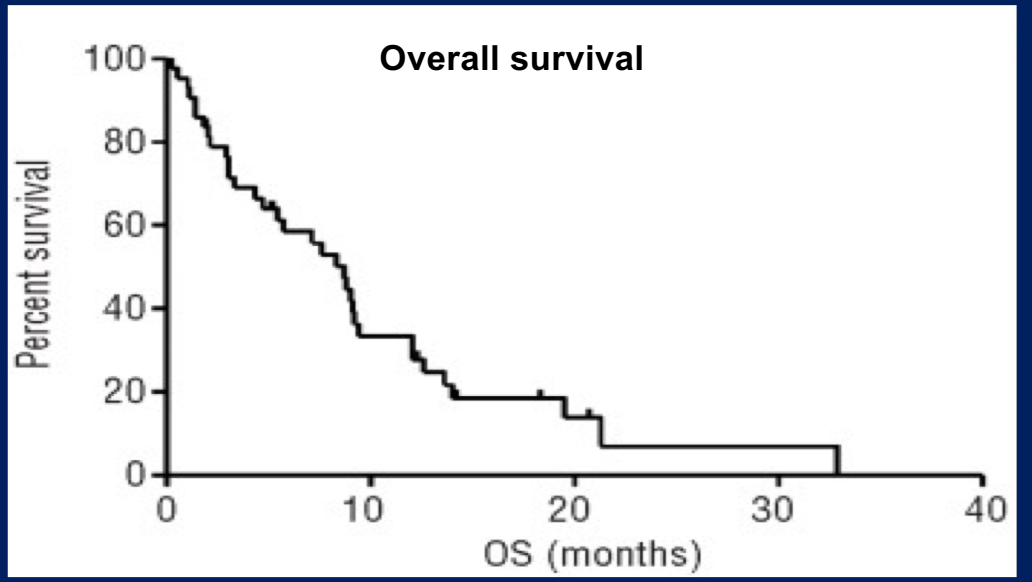
- Primary sites: skin, bone marrow
- Secondary sites: LN, CNS, visceral
- CD123, CD4, CD56 - "Think 123456"
- TCL-1, CD303, TCF-4
- *TET2, ASXL1, RAS, TP53*
- No approved therapies
- Outcomes poor; med OS ~8-14 mos
- SCT promising for select/fit patients

BPDCN skin lesions



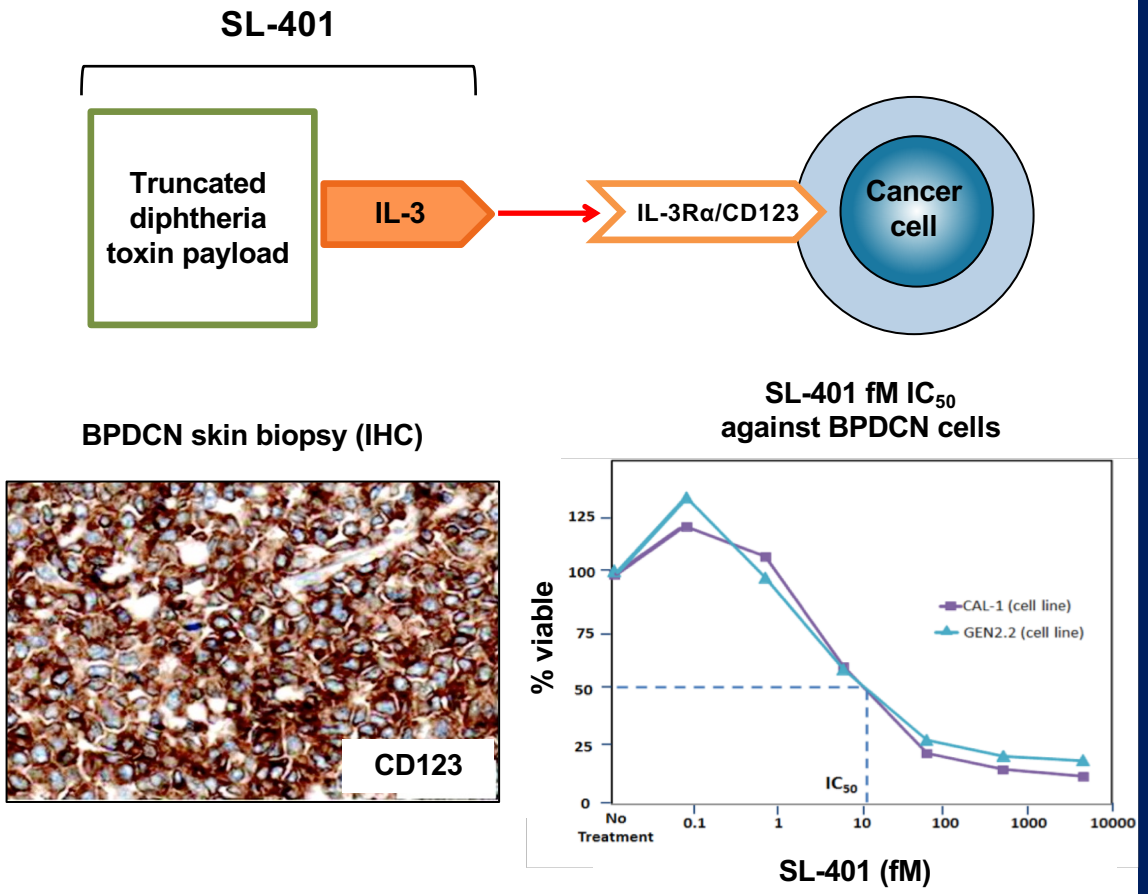
BPDCN bone marrow





Riaz et al. Cancer Control, 2014; Pagano et al. Haematologica, 2013; Pemmaraju N. Clin Adv Hematol Oncol, 2016; Gilliet,Cao &Liu; *Nature Reviews Immunology* 8, 594-606;2008, Pemmaraju&Konopleva The Hematologist Sept/Oct 2018 Vol 15 Issue 5

Tagraxofusp (SL-401): Novel Targeted Therapy Directed to the IL-3 Receptor (IL-3Rα / CD123)



- IL-3Rα/CD123 overexpressed on BPDCN and many other hematologic cancers
- Tagraxofusp (SL-401) is a targeted therapy directed to CD123
- Tagraxofusp potent *vs* BPDCN cells *in vitro* and *in vivo*
- Previous Phase 1 study
  - Major responses in 7/9 patients (78%):

    5 CR, 2 PR (*Frankel et al. Blood, 2014*)

Tagraxofusp: Study Design and Inclusion / Exclusion

Stage 1 (Lead-in, dose escalation)	Stage 2 (Expansion)	Stage 3 (Pivotal, confirmatory)
• BPDCN (1L and R/R) • Tagraxofusp (7, 9, 12, or 16 μg/kg) via IV infusion, days 1-5 of a 21-day cycle • Key objectives: To determine optimal dose and regimen for Stage 2	• BPDCN (1L and R/R) • Tagraxofusp (12 μg/kg) via IV infusion, days 1-5 of a 21-day cycle • Key objectives: To further define safety and efficacy	• BPDCN (1L) • Tagraxofusp (12 μg/kg) via IV infusion, days 1-5 of a 21-day cycle • Key objective: To confirm efficacy for registration

Select inclusion criteria

- Patient Population:
  - Stage 1: BPDCN (1L or R/R)
  - Stage 2: BPDCN (1L or R/R)
  - Stage 3: BPDCN (1L)
- Age ≥ 18; ECOG PS 0-2
- Adequate organ function including: LVEF ≥ lower limit of normal, creatinine ≤ 1.5mg/dL, albumin ≥ 3.2 g/dL, bilirubin ≤ 1.5 mg/dL, AST/ALT ≤ 2.5x ULN

Select exclusion criteria

- Persistent clinically significant toxicities from prior chemotherapy
- Received chemotherapy or other investigational therapy within the prior 14 days
- Clinically significant cardiopulmonary disease
- Receiving immunosuppressive therapy

➢ *To ensure ongoing access to tagraxofusp, BPDCN patients are being enrolled in an additional cohort, Stage 4*

Tagraxofusp: Demographics

Demographics	Stages 1 & 2	Stage 3	Stages 1, 2 & 3
n	32	13	45
Age: years median [range]	72 [28-84]	65 [22-84]	70 [22-84]
Gender: male [n, (%)]	26 (81)	11 (85)	37 (82)
First-line (1L) [n, (%)]	19 (59)	13 (100)	32 (71)
Relapsed / Refractory (R/R) [n, (%)]	13 (41)	--	13 (29)
Baseline sites of disease [n, (%)]			
Cutaneous	30 (94)	13 (100)	43 (96)
Bone Marrow	16 (50)	7 (54)	23 (51)
Extramedullary (non-cutaneous)	18 (56)	6 (46)	24 (53)
Dose [n]			
7 μg/kg/day	3	--	3
12 μg/kg/day	29	13	42

BPDCN Disease Measurements

Site of disease	Assessment tool	Criteria	Key Reference
Primary			
• Skin	mSWAT/ biopsy	mSWAT calculation and pathology[1]	Olsen, 2011
• Bone Marrow (BM)	BM aspirate/biopsy, peripheral blood counts	AML	Cheson, 2003
Secondary[2]			
• Lymph nodes, viscera	CT or PET/CT	NHL	Cheson, 2014

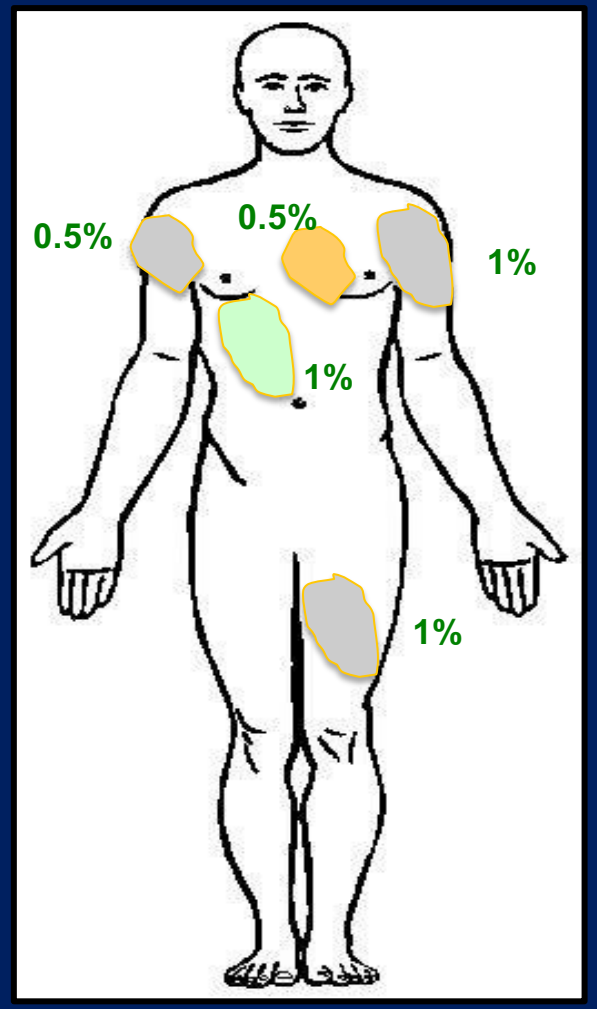


Illustration of mSWAT surface area assessment

[1]CR includes Clinical CR (CRc) = complete response in all non-skin disease sites, marked clearance of all skin lesions from baseline but with residual skin abnormalities not indicating active BPDCN

[2]Assessed at baseline and thereafter as necessary

Tagraxofusp: Safety and Tolerability

All Tagraxofusp Clinical Trials (12 μg/kg/day) (n=148)

Most Common Adverse Events (AEs) (>15% Treatment-Related AEs, TRAEs)[1]						
Preferred Term	All Grades n (%)		TRAEs n (%)			
	TRAEs	All AEs	Gr 1-2	Gr 3	Gr 4	Gr 5
ALT increased	65 (43.9%)	80 (54.1%)	31 (20.9%)	34 (23.0%)	0 (0.0%)	0 (0.0%)
AST increased	65 (43.9%)	74 (50.0%)	30 (20.3%)	31 (20.9%)	4 (2.7%)	0 (0.0%)
Hypoalbuminaemia	65 (43.9%)	73 (49.3%)	64 (43.2%)	1 (0.7%)	0 (0.0%)	0 (0.0%)
Thrombocytopenia	39 (26.4%)	48 (32.4%)	7 (4.7%)	8 (5.4%)	24 (16.2%)	0 (0.0%)
Nausea	38 (25.7%)	70 (47.3%)	37 (25.0%)	1 (0.7%)	0 (0.0%)	0 (0.0%)
Pyrexia	33 (22.3%)	60 (40.5%)	33 (22.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Fatigue	30 (20.3%)	67 (45.3%)	26 (17.6%)	4 (2.7%)	0 (0.0%)	0 (0.0%)
Weight increased	28 (18.9%)	42 (28.4%)	28 (18.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Chills	26 (17.6%)	40 (27.0%)	25 (16.9%)	1 (0.7%)	0 (0.0%)	0 (0.0%)
Capillary leak syndrome (CLS)[2]	25 (16.9%)	25 (16.9%)	16 (10.8%)	5 (3.4%)	3 (2.0%)	1 (0.7%)
Hypotension	23 (15.5%)	36 (24.3%)	17 (11.5%)	5 (3.4%)	1 (0.7%)	0 (0.0%)
Oedema peripheral	22 (14.9%)	57 (38.5%)	21 (14.2%)	1 (0.7%)	0 (0.0%)	0 (0.0%)

- No apparent cumulative AEs, including in the bone marrow, over multiple cycles
- CLS largely cycle 1-related and manageable with monitoring and pre-emptive measures

[1]As of August 2018

[2]0.6% (1/166) for all trials (12 μg/kg/day) and 1.5% (3/202) for all trials (all doses) were grade 5. A myocardial infarction, grade 5, was also reported in a patient who experienced a grade 4 CLS

Tagraxofusp: Clinical Activity – All Stages (1, 2, and 3)

Stages 1, 2, and 3: BPDCN (12 µg/kg/day) (n=42)

Line of Therapy	1L	R/R	1L & R/R
n	29	13	42
ORR, n (%)	**26 (90%)**	**9 (69%)**	**35 (83%)**
CR + CRc + CRi, n (%)	**21 (72%)**	**5 (38%)**	**26 (62%)**
CR	14	1	15
CRc	7	1	8
CRi	0	3	3
PR, n (%)	**5 (17%)**	**4 (31%)**	**9 (21%)**
Bridged to SCT, *n* (%)	**13 (45%)**	**1 (8%)**	**14 (33%)**
Allo	10	1	11
Auto	3	0	3

Tagraxofusp: Clinical Activity – Stage 3

Stage 3: BPDCN (12 μg/kg/day) (n=13)

- Pivotal, confirmatory cohort met primary endpoint
- 54% rate of CR + CRc (7/13) [95% CI: 25.1, 80.8]; exceeded pre-specified rate

Stage 3 responders

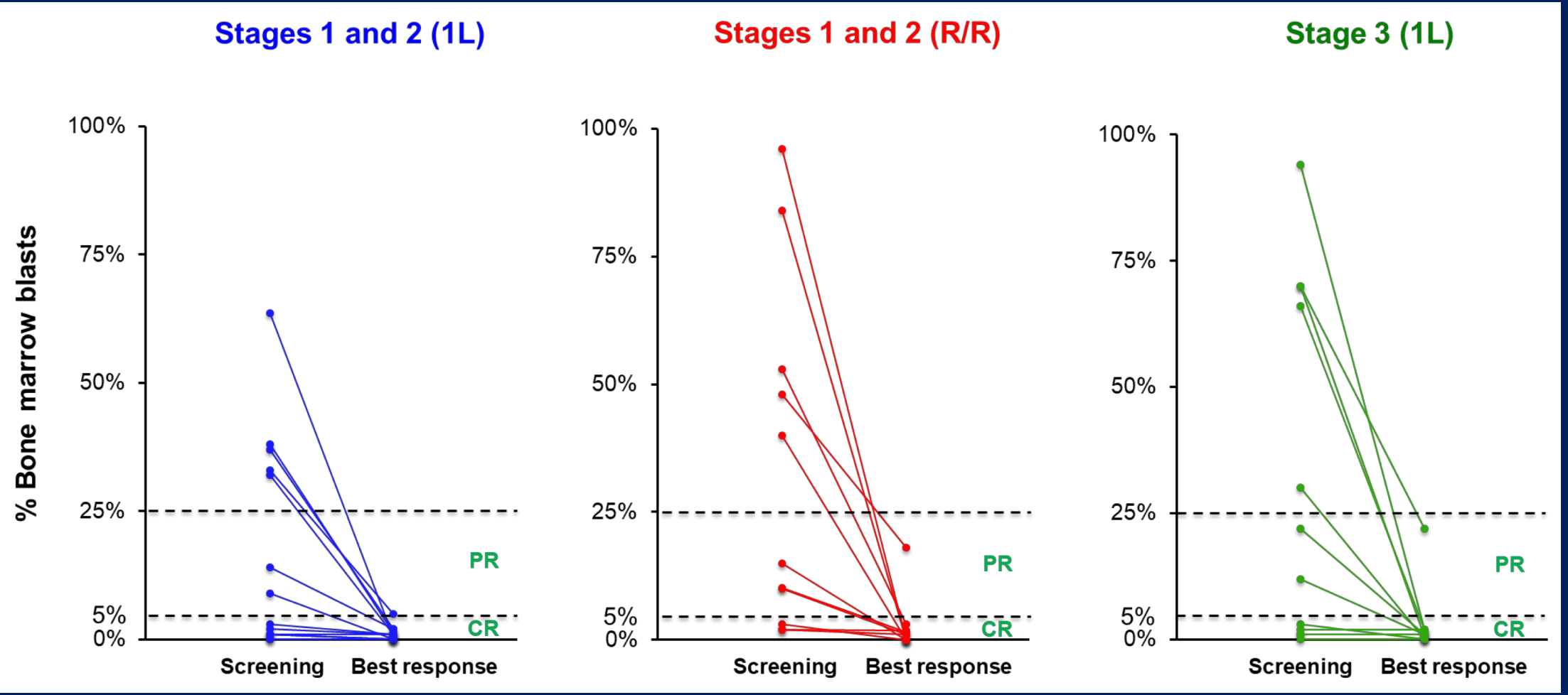
Line of Therapy Dose Level	First-line 12 μg/kg
n	13
ORR, n (%)	10 (77%)
CR + CRc + CRi, n (%) CR CRc CRi	7 (54%) 3 4 0
PR, n (%)	3 (23%)
Bridged to SCT, n (%) Allo Auto	6 (46%) 6 0

Stage 3 complete responders

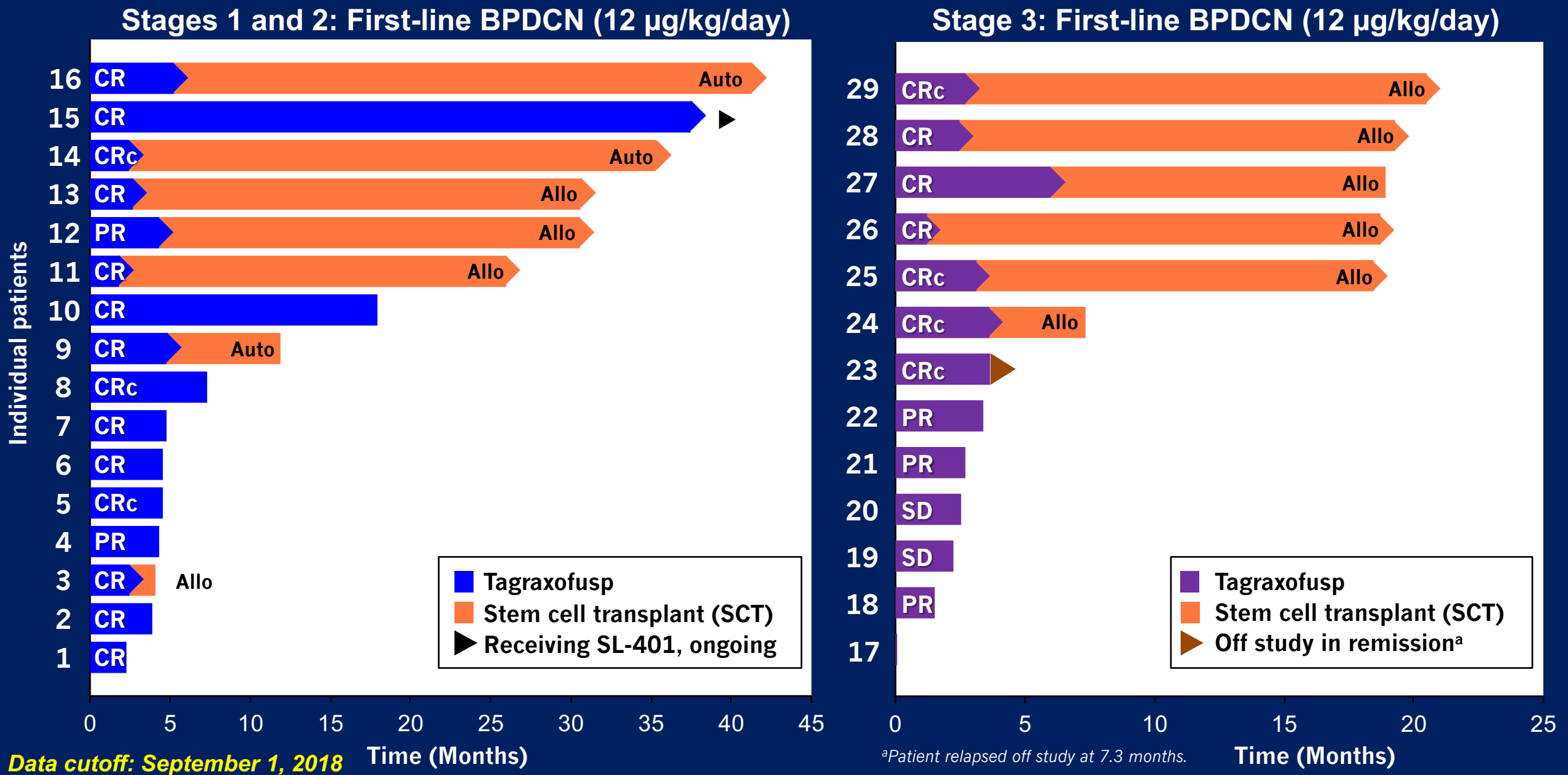
Age (years)	Best Response	Bone Marrow (% Blasts)		Skin (mSWAT)		SCT
		Baseline	Best response	Baseline	Best response	
69	CR	94%	2%	1.2%	0.0%	Allo
68	CRc	70%	2%	72.0%	0.0%	Allo
57	CR	66%	2%	35.0%	0.0%	Allo
74	CRc	22%	1%	54.0%	4.0%	-
65	CR	12%	1%	70.0%	0.0%	Allo
32	CRc	2%	2%	18.0%	0.3%	Allo
22	CRc	1%	1%	22.0%	0.4%	Allo

Tagraxofusp: Bone Marrow Responses

BPDCN (12 μg/kg/day); Stages 1, 2, and 3



Tagraxofusp: Best Response and Treatment Duration

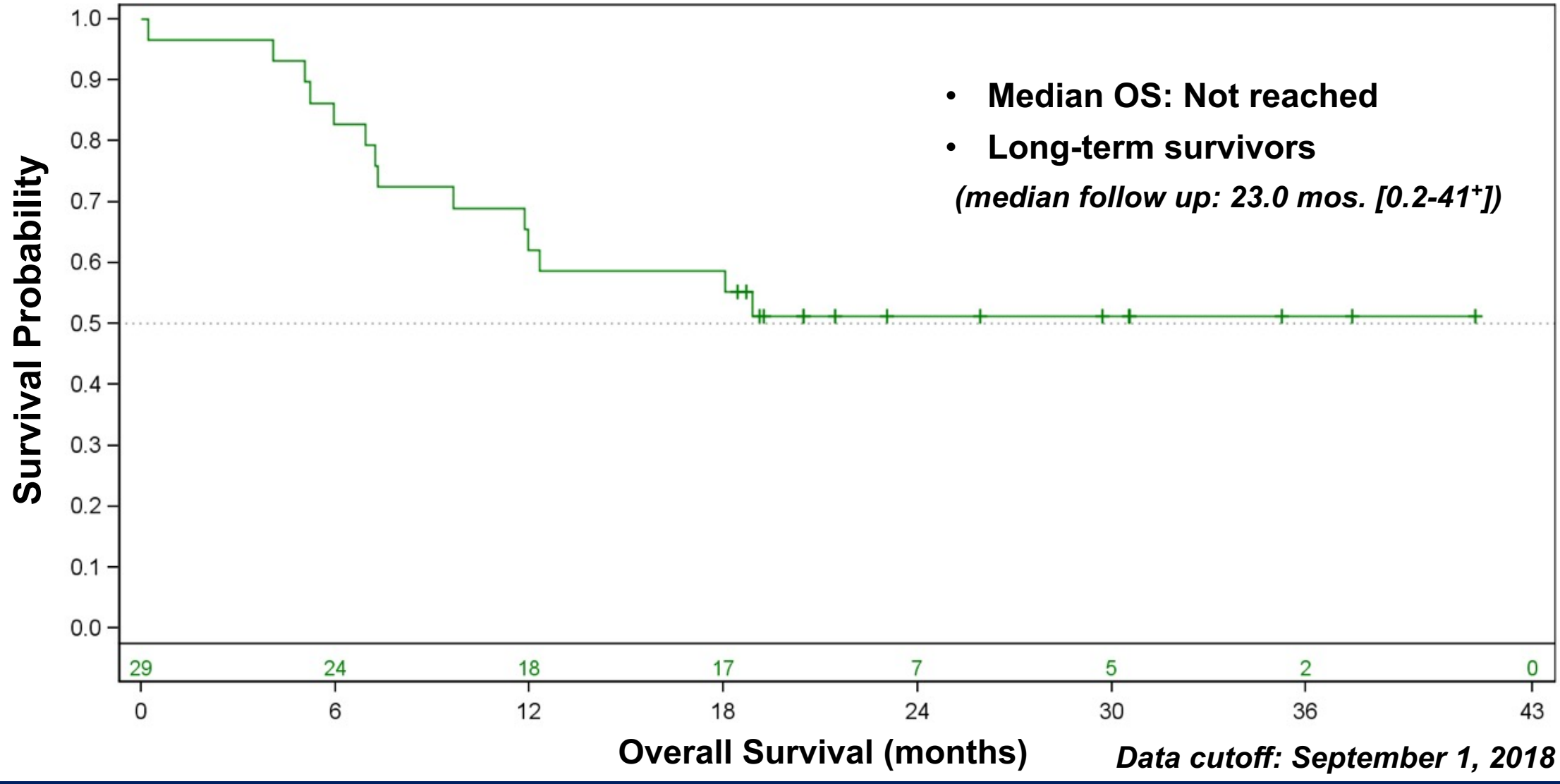


Data cutoff: September 1, 2018

[a]Patient relapsed off study at 7.3 months.

Tagraxofusp: Overall Survival (OS)

First-line BPDCN (12 μg/kg/day) - Stages 1, 2, and 3 (n=29)



Tagraxofusp: Summary and Conclusions

- BPDCN: historically poor outcomes; no standard of care
- High response rates in BPDCN
  - 90% ORR in first-line (12 μg/kg; n=29); 69% ORR in R/R (n=13)
  - Majority of responses are CR/CRc
- 45% of patients treated with tagraxofusp in first-line setting (12 μg/kg) were bridged to SCT in remission (n=13)
- Tagraxofusp for BPDCN:
  - Breakthrough Therapy Designation (BTD) granted by FDA
  - BLA under Priority Review; February 21, 2019 PDUFA action date
- Tagraxofusp is also being clinically evaluated in additional malignancies

Acknowledgements

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