Outcomes of Tagraxofusp (SL-401) in Older Patients with Blastic Plasmacytoid Dendritic Cell Neoplasm (BPDCN)

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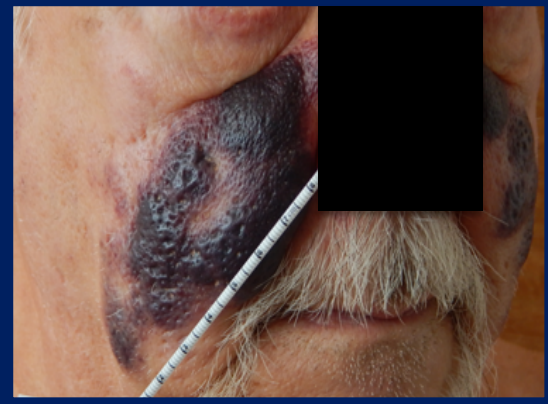
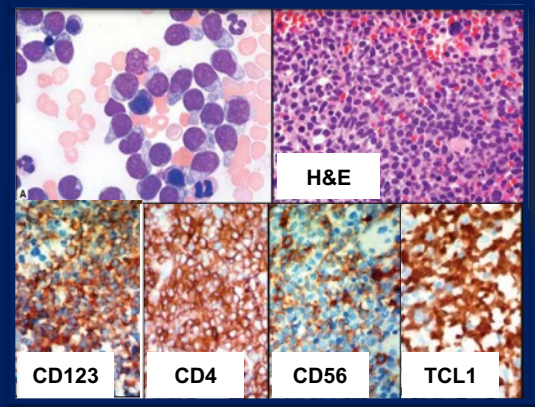
BPDCN: Aggressive Hematologic Malignancy

- Rare, aggressive hematologic malignancy often with cutaneous manifestations (~80% of patients present with skin lesions)
  - Lymph nodes and viscera may also be involved
- Cell of origin: plasmacytoid dendritic cell (pDC)
- Historically, has been misdiagnosed as AML, NHL, and other heme malignancies
- **Diagnostic signature triad: CD123 / CD4 / CD56.** ***Think "123456" - aids in the correct diagnosis***
- Historically poor prognosis - median overall survival of 8-12 months with chemotherapy

BPDCN Skin Lesions

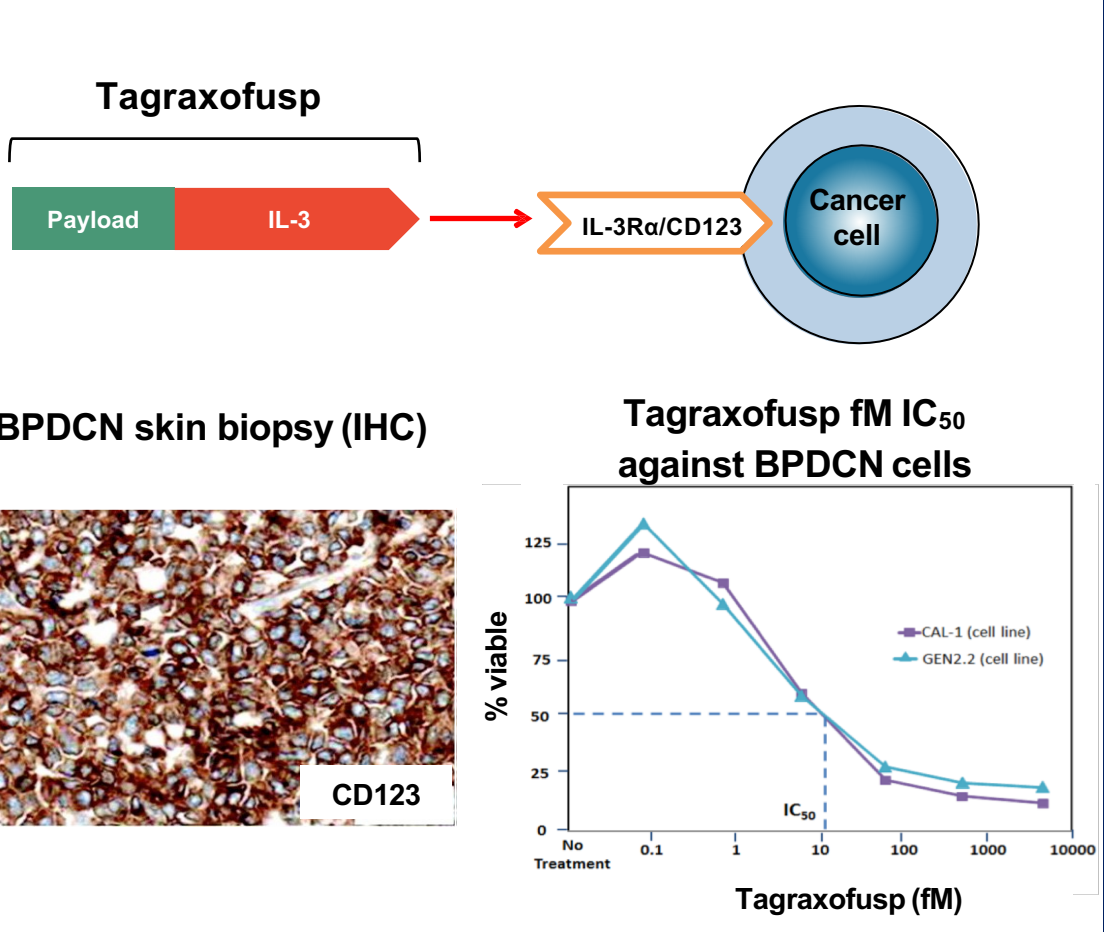


BPDCN Bone Marrow



Riaz W, et al. *Cancer Control*. 2014;21(4):279-289; Pagano L, et al. *Haematologica*. 2013;98(2):239-246; Pemmaraju N. *Curr Hematol Malig Rep*. 2017;12(6):510-512.; Gilliet M, et al. *Nat Rev Immuno*l. 2008;8(8):594-606; Pemmaraju N, Konopleva M. *Ask the Hematologist*. September-October 2018;15(5); National Comprehensive Cancer Network. Acute Myeloid Leukemia (Version 2. 2020); **https://www.nccn.org/professionals/physician_gls/pdf/aml.pdf** Accessed Sept. 16th 2019.

Tagraxofusp: First Drug Approved in BPDCN



- Tagraxofusp is a targeted therapy directed to CD123
- CD123 overexpressed on BPDCN and other hematologic cancers
- Tagraxofusp potent against BPDCN *in vitro* and *in vivo*
- Tagraxofusp FDA-approved in December 2018 for treatment of adult and pediatric patients, 2 years and older, with BPDCN
- MAA under review in Europe

Payload = truncated diphtheria toxin
FDA, Food and Drug Administration; MAA, Marketing Authorization Application
Frankel AE, et al. Activity of SL-401, a targeted therapy directed to interleukin-3 receptor, in Blastic Plasmacytoid Dendritic Cell Neoplasm Patients. Blood. 2014;124(3):385-392. ELZONRIS® (tagraxofusp). Prescribing information 12/2018. Stemline Therapeutics, Inc. New York, NY.

Tagraxofusp: Study Design and Inclusion / Exclusion

Stage 1 (Dose Escalation)

- BPDCN (treatment-naïve and previously-treated)
- Tagraxofusp (7 or 12 mcg/kg) via IV infusion, days 1-5 of a 21-day cycle*
- Key objectives: To determine the recommended phase 2 dose (RP2D)

Stage 2 (Expansion)

- BPDCN (treatment-naïve and previously-treated)
- Tagraxofusp (12 mcg/kg) via IV infusion, days 1-5 of a 21-day cycle*
- Key objectives: To further define safety and efficacy of the RP2D

Stage 3 (Pivotal, Confirmatory)

- BPDCN (treatment-naïve)
- Tagraxofusp (12 mcg/kg) via IV infusion, days 1-5 of a 21-day cycle*
- Key objective: To confirm efficacy for regulatory decision making

› *BPDCN patients were enrolled in an additional cohort, Stage 4, to ensure continued access during regulatory review*

Select inclusion criteria

- Patient population: treatment-naïve or previously-treated
- Age ≥18
- ECOG PS 0-2
- Adequate organ function including: LVEF ≥ lower limit of normal, creatinine ≤1.5 mg/dL, albumin ≥3.2 g/dL, bilirubin ≤1.5 mg/dL, AST/ALT ≤2.5×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

ALT, alanine aminotransferase; AST, aspartate aminotransferase; BPDCN, blastic plasmacytoid dendritic cell neoplasm; ECOG PS, Eastern Cooperative Oncology Group performance status; LVEF, left ventricular ejection fraction; ULN, upper limit of normal; FDA, Food and Drug Administration

*The study design allowed for a 10-day treatment window in which patients could receive the total of five drug infusions, to allow for dose interruptions, if needed.

Tagraxofusp: Demographics By Age Group

Parameter	All Patients N=44	Age ≥ 70 years N=20	Age < 70 years N=24
Gender, N (%)			
Male	36 (82)	18 (90)	18 (75)
Female	8 (18)	2 (10)	6 (25)
Race, N (%)			
Asian	2 (5)	1 (5)	1 (4)
American Indian/Alaska Native	1 (2)	0 (0)	1 (4)
White	40 (91)	19 (95)	21 (88)
Other	1 (2)	0 (0)	1 (4)
Age (years)			
Median	68.5	75	61.5
Minimum, Maximum	(22, 84)	(70, 84)	(22, 69)
ECOG, N (%)			
0	20 (46)	7 (35)	13 (54)
1	24 (54)	13 (65)	11 (46)

BPDCN, blastic plasmacytoid dendritic cell neoplasm; ECOG, Eastern Cooperative Oncology Group.
Performance-status scores on the ECOG scale range from 0 to 5, with 0 indicating no symptoms and higher scores indicating an increasing severity of symptoms.
Per inclusion criteria, can range from 0-2.

Tagraxofusp: Safety and Tolerability in Older Patients

- **No apparent cumulative AEs, including in the bone marrow, over multiple cycles**
- **CLS most serious adverse reaction**
  - CLS largely cycle 1-related and manageable with monitoring and pre-emptive measures
  - Across all patients treated at prescribed dose, 55% of patients experienced CLS[1], including Grades 1-2 in 46% (43/94), Grade 3 in 6% (6/94), Grade 4 in 1% (1/94), and 2 fatal events (2%; 2/94)

Adverse Reactions in ≥ 30% of Patients ≥ 70 years		
	N=39	
	All Grades (%)	Grade ≥ 3 (%)
ALT Increase	69	51
AST Increase	67	46
Hypoalbuminemia	62	3
Peripheral edema	54	3
Nausea	49	0
Fatigue	41	10
Thrombocytopenia	41	36
Pyrexia	36	0
Weight Increase	36	0
Anemia	33	23
Hyperglycemia	33	18
Hypotension	33	5
Chills	31	3
Decreased Appetite	31	0

Analysis includes patients treated with AML and BPDCN treated with tagraxofusp at 12 µg/kg

[1]Defined as any event reported as CLS during treatment with tagraxofusp or the occurrence of at least 2 of the following CLS manifestations within 7 days of each other: hypoalbuminemia, edema, hypotension.

AE, Adverse Events; CLS, Capillary leak syndrome; ALT, Alanine aminotransferase; AST, Aspartate aminotransferase.

Tagraxofusp: Clinical Activity Across Age Groups

Response Rates in BPDCN Patients (Tagraxofusp at 12 mcg/kg)

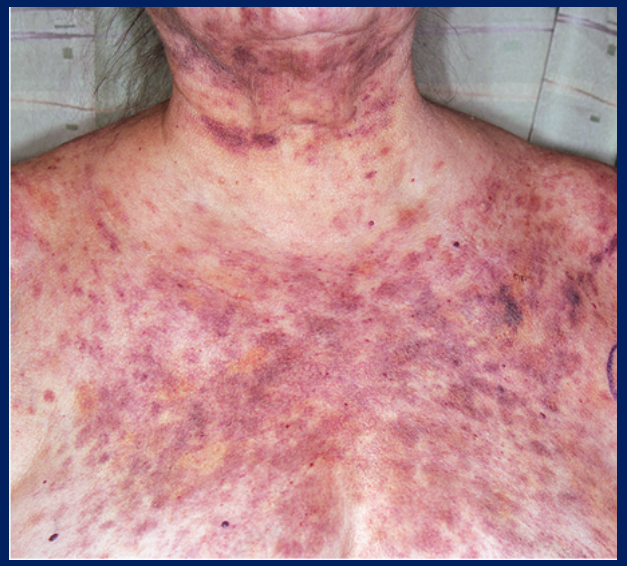
Efficacy Measures	Treatment-Naïve Patients			Previously-Treated Patients		
	All ages N=29	Age ≥ 70 years N=10	Age < 70 years N=19	All ages N=15	Age ≥ 70 years N=10	Age < 70 years N=5
ORR, % (n)	90% (26)	100% (10)	84% (16)	67% (10)	70% (7)	60% (3)
CR/CRc rate, % (n)	72% (21)	70% (7)	74% (14)	13% (2)	10% (1)	20% (1)
Bridged to SCT, % (n)	45% (13)	20% (2)	58% (11)	7% (1)	0	20% (1)

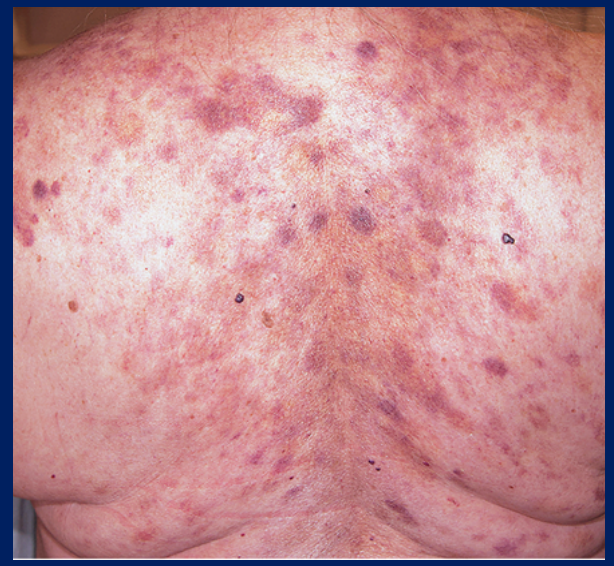
CR, complete response; CRc (clinical CR), complete response with minimal residual skin abnormalities not indicative of active disease; ORR, overall response rate; SCT, stem cell transplant

Tagraxofusp: Representative Skin Response

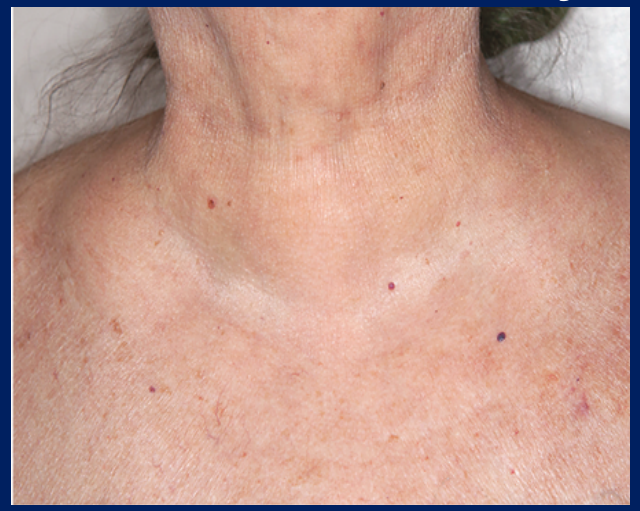
- 71 year old female with BPDCN
- Treatment-naïve; extensive skin and bone marrow (BM) involvement
- Received six cycles of tagraxofusp at 12 mcg/kg
- Bridged to stem-cell transplantation after CR and 6 cycles of tagraxofusp

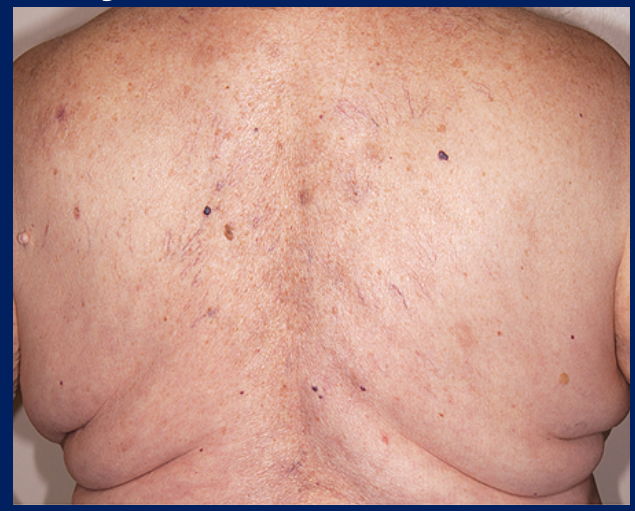
Baseline





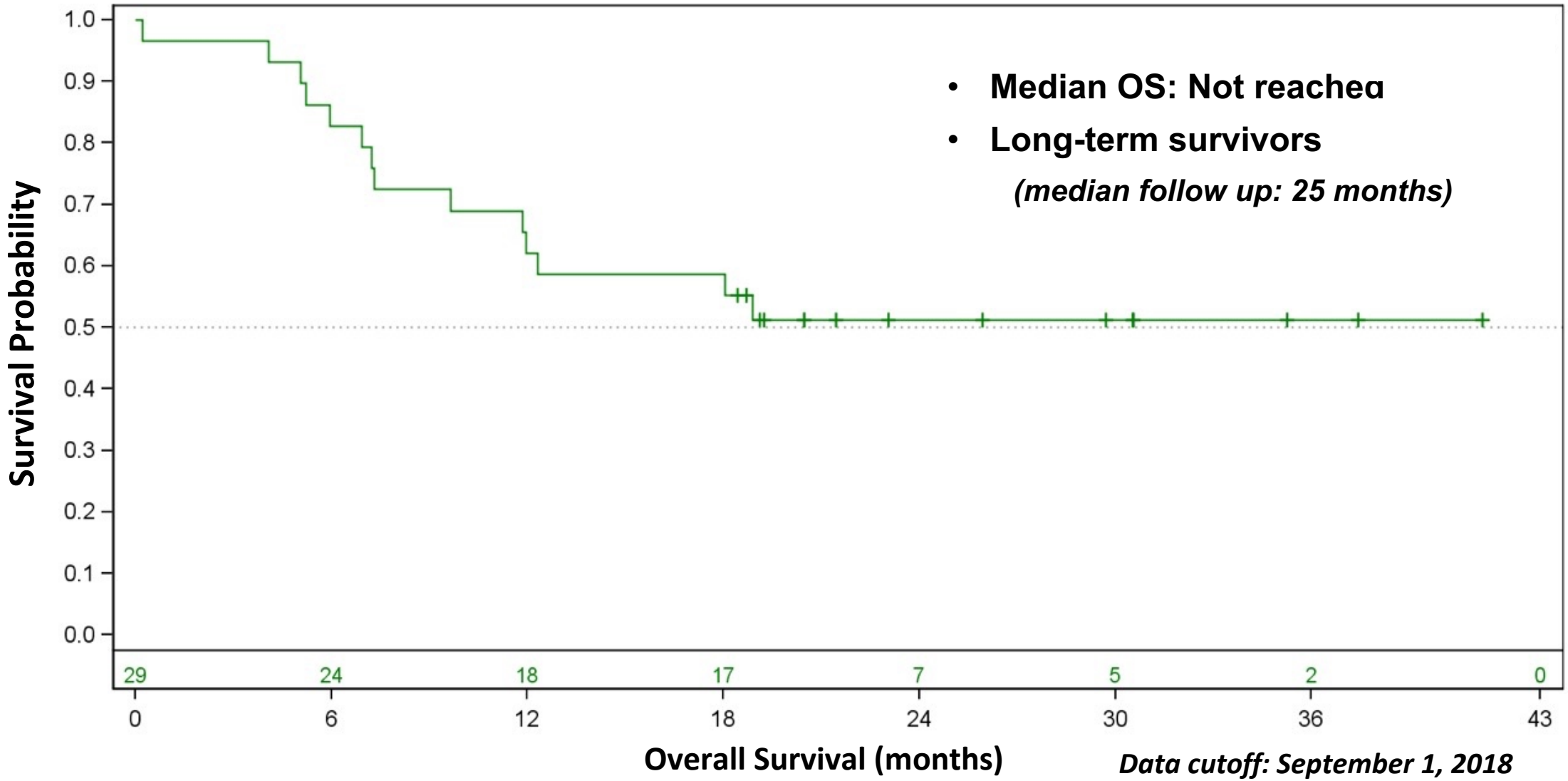
Cycle 1 Day 21





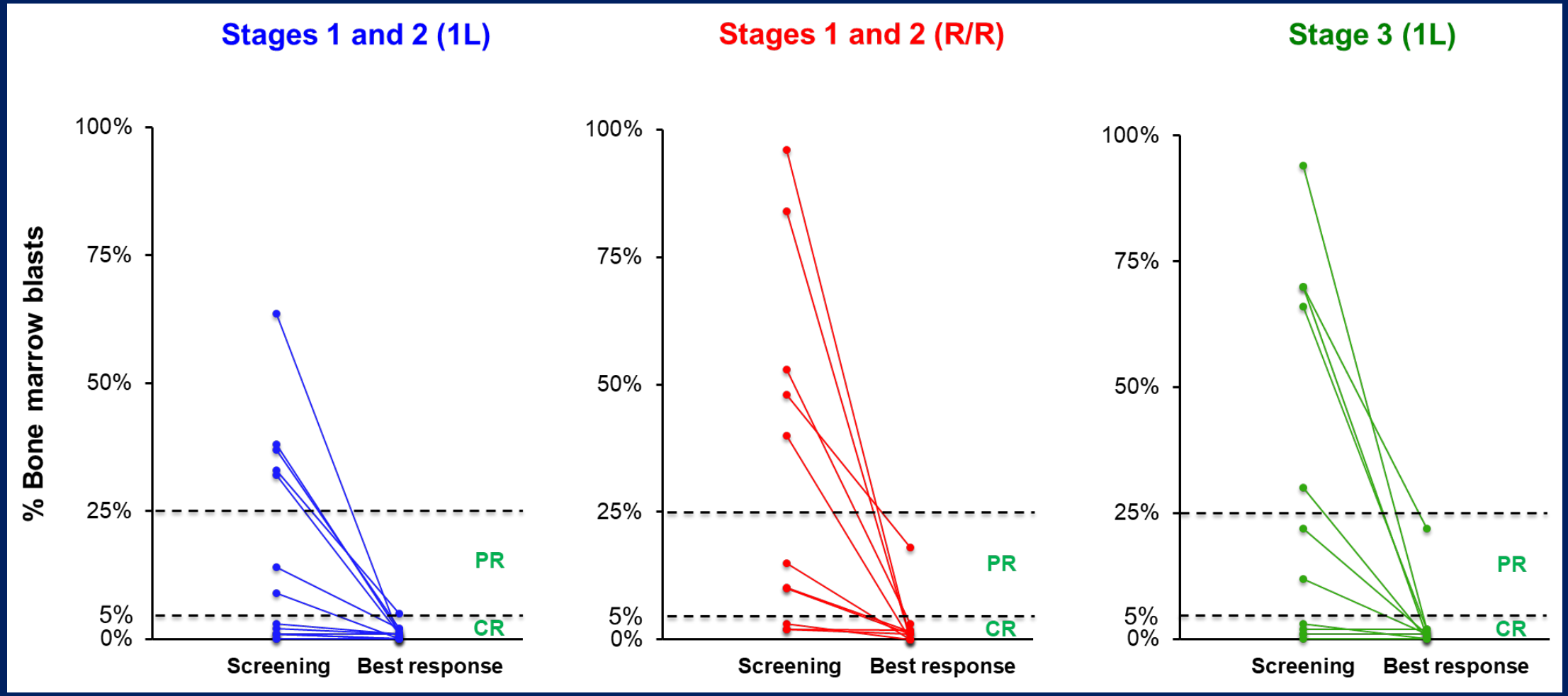
Tagraxofusp: Overall Survival (OS)

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



Tagraxofusp: Bone Marrow Responses

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



Tagraxofusp: Summary and Conclusions

- BPDCN: historically poor outcomes
- Tagraxofusp, a novel targeted therapy directed to CD123, demonstrated high levels of clinical activity across age cohorts in patients with BPDCN
  - Treatment-naïve patients, age ≥ 70 years (N=10)
    - 100% ORR; 70% CR/CRc; 20% bridged to receive SCT
  - Previously-treated patients, age ≥ 70 years (N=10)
    - 70% ORR; 10% CR/CRc
- Tagraxofusp has a predictable and manageable safety profile in patients with BPDCN
  - Most serious adverse reaction is CLS
  - Most common adverse reactions in patients ≥ 70 years are AST/ALT increase, hypoalbuminemia and peripheral edema
- First medication approved for BPDCN
  - U.S. FDA approved for adult and pediatric patients with BPDCN on December 21, 2018
  - Marketing Authorization Application (MAA) for BPDCN under review by the European Medicines Agency (EMA)

CR, complete response; CRc (clinical CR), complete response with minimal residual skin abnormalities not indicative of active disease; ORR, overall response rate; SCT, stem cell transplant; CLS, Capillary leak syndrome; ALT, Alanine aminotransferase; AST, Aspartate aminotransferase.

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