Co-inhibition of IL-2, IL-9 and IL-15 by the novel immunomodulator, BNZ-1, provides clinical efficacy in patients with refractory cutaneous T cell lymphoma in a phase 1/2 clinical trial

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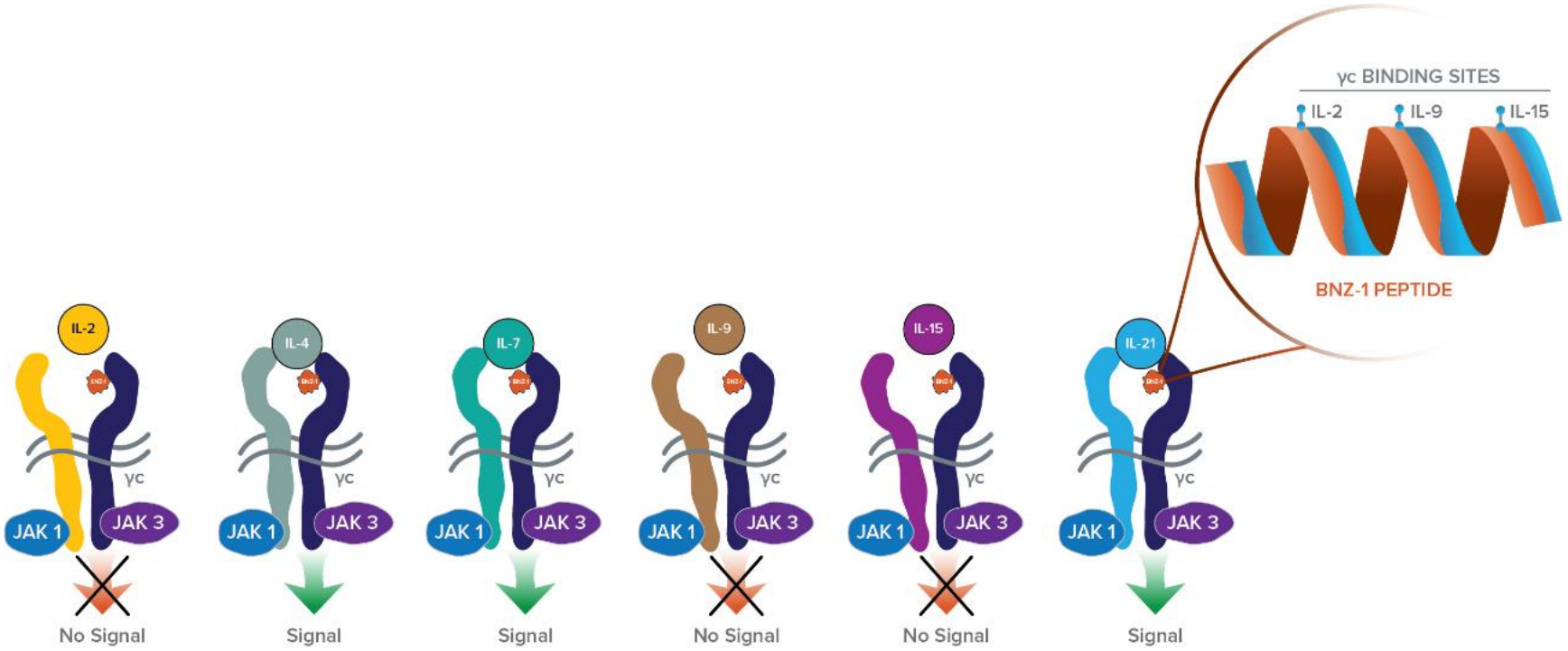
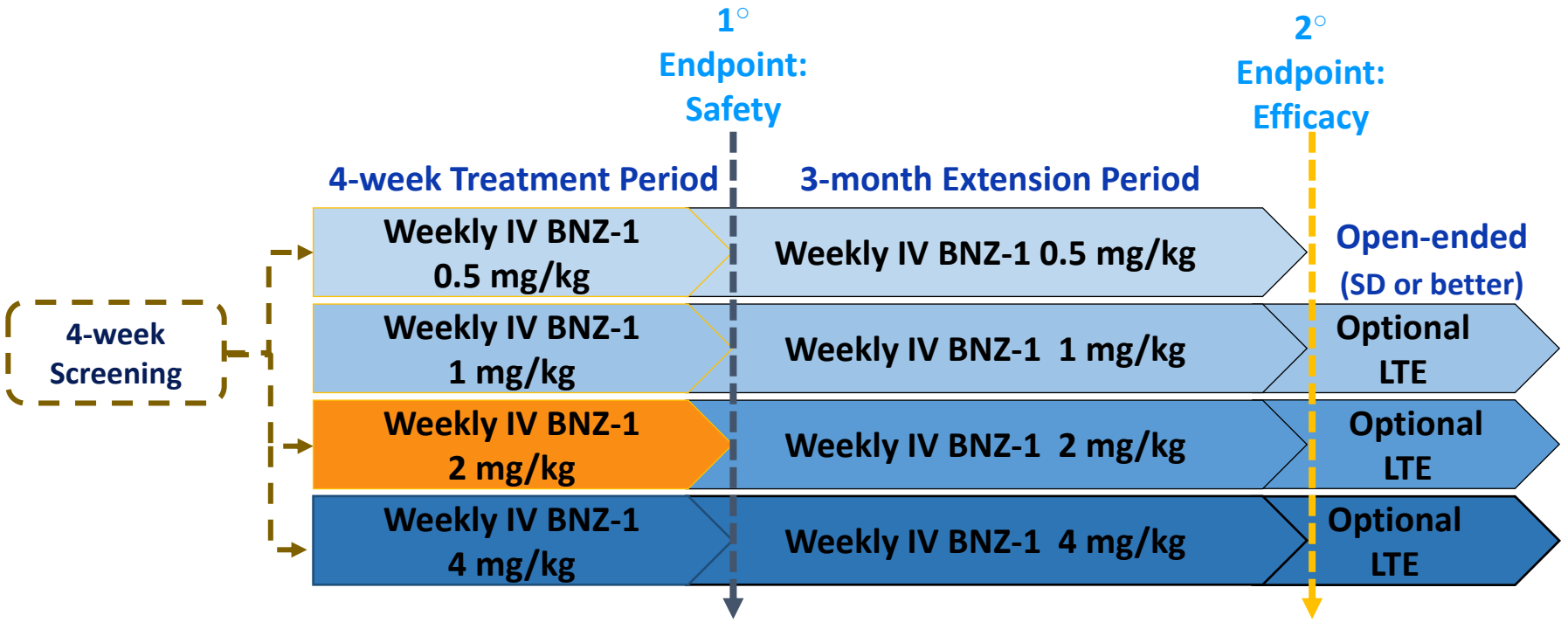
2018…2022
T-Cell Lymphomas: finally vision and mission!
Bologna, October 25-26, 2022
Royal Hotel Carlton

BNZ-1 is a selective inhibitor of IL-2, IL-9, and IL-15

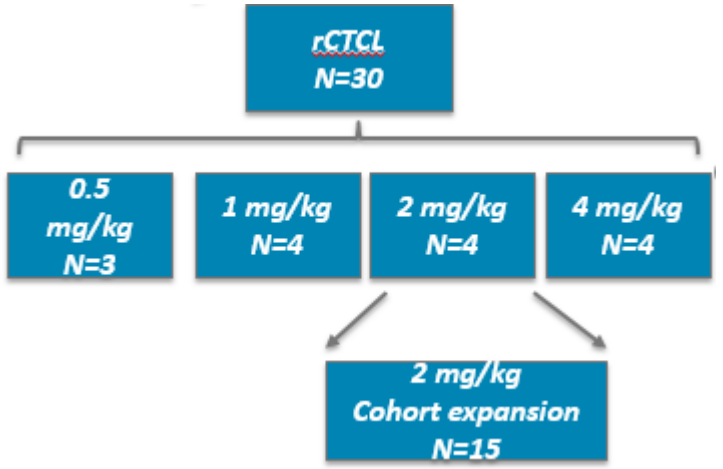
- These cytokines belong to the IL-2 family of cytokines that includes IL-2, IL-4, IL-7, IL-9, IL-15, and IL-21
- They all share the common γ (γc) receptor
- BNZ-1 is a peptide that blocks the interaction of IL-2, IL-9 and IL-15 to the γc receptor but does not interrupt the binding of IL-4, IL-7, and IL-21



Phase 1/2 open label study of BNZ-1 in patients with refractory CTCL



Based on PK/PD data and early clinical efficacy, the 2 mg/kg cohort was expanded



Patient Demographics in the Phase 1/2 trial of BNZ-1 in rCTCL

Median age (years) (range)	61 (32-87)
Gender	
Male	21
Female	9
Clinical stage	
IB	12
IIA	1
IIB	14
IVA1	2
IVB	1
Race/ethnicity	
Caucasian	25
African American	2
Asian	3

CTCL subtype	
MF, classic	12
MF, folliculotropic type	7
MF, Large cell transformation	4
MF syringotropic	1
Sezary Syndrome	3
Prior treatment (median)	
Systemic	5
Skin-directed	2

Safety results from Phase 1/2 study demonstrated a favorable profile

	BNZ-1 0.5 mg/kg (N=3) n (%)	BNZ-1 1 mg/kg (N=4) n (%)	BNZ-1 2 mg/kg (N=19) n (%)	BNZ-1 4 mg/kg (N=4) n (%)	All Patients (N=30) n (%)
Patients with any AEs	3 (100.0)	4 (100.0)	15 (78.9)	4 (100.0)	26 (86.7)
Patients with any TEAEs	3 (100.0)	4 (100.0)	15 (78.9)	4 (100.0)	26 (86.7)
TEAEs by highest severity [1]					
Grade 1	2 (66.7)	2 (50.0)	9 (47.4)	1 (25.0)	14 (46.7)
Grade 2	0 (0.0)	0 (0.0)	4 (21.1)	3 (75.0)	7 (23.3)
Grade 3	1 (33.3)	2 (50.0)	2 (10.5)	0 (0.0)	5 (16.7)
Grade 4	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Grade 5	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
TEAEs by closest relationship to study drug [2]					
Unrelated	0 (0.0)	2 (50.0)	9 (47.4)	2 (50.0)	13 (43.3)
Unlikely	2 (66.7)	2 (50.0)	1 (5.3)	0 (0.0)	5 (16.7)
Possible	1 (33.3)	0 (0.0)	4 (21.1)	2 (50.0)	7 (23.3)
Probable	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Related	0 (0.0)	0 (0.0)	1 (5.3)	0 (0.0)	1 (3.3)
Patients with a TEAE with action of study drug withdrawal	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Patients with a serious TEAE	0 (0.0)	1 (25.0)	3 (15.8)	1 (25.0)	5 (16.7)

AE = adverse event; rCTCL = refractory cutaneous T-cell lymphoma; TEAE = treatment-emergent adverse event.

[a] Patients are counted only once, under the highest severity (as per CTCAE 4.03 toxicity grade) TEAE experienced during the study.

[b] Patients are counted only once, under the closest study drug relationship TEAE experienced during the study.

Source: Table 14.3.1.1

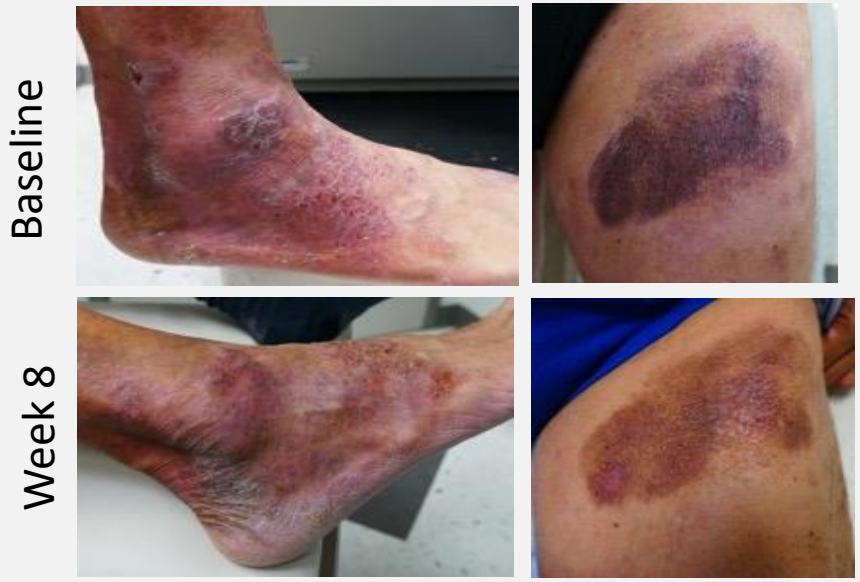
- No DLT was observed and no MTD was achieved
- All patients (n=30) completed the 4-week safety period.
- No patients discontinued study drug due to SAE
- 1 patient discontinued study drug due to AE
- AE was deemed moderate in severity and not related to study drug.
- No apparent dose-AE relationship
- No SAE deemed to be related to BNZ-1
- No remarkable changes in vital signs, clinical laboratory, ECG etc

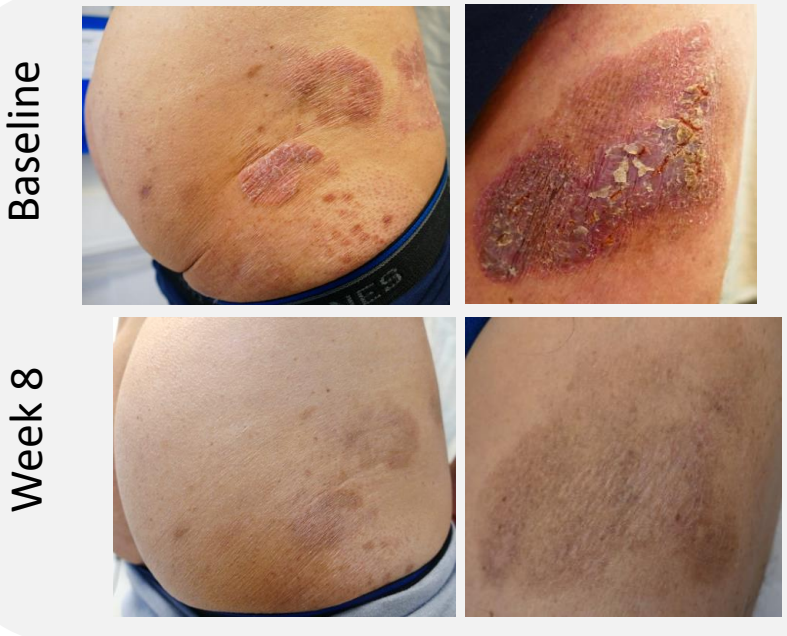
Most frequently reported TEAE (none deemed related to BNZ-1):

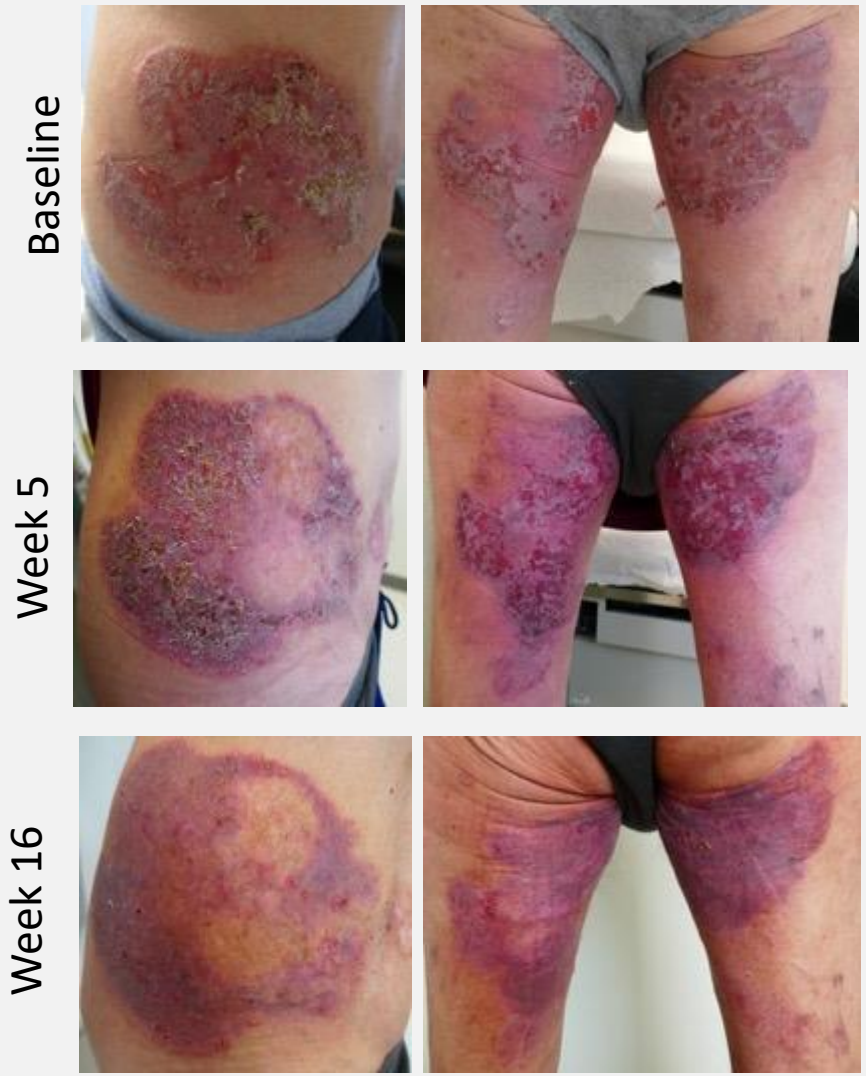
- Fatigue (7 out of 30 patients, 23.3 %)
- Upper respiratory tract infection (7 out of 30 patients, 23.3 %)
- Diarrhea (6 out of 30 patients, 20%)
- Anemia (6 out of 30 patients, 20%)
- Pruritus (5 out of 30 patients, 16.7%)
- Dizziness (5 out of 30 patients, 16.7%)

Number of upper respiratory infections similar to expected in general Adult population

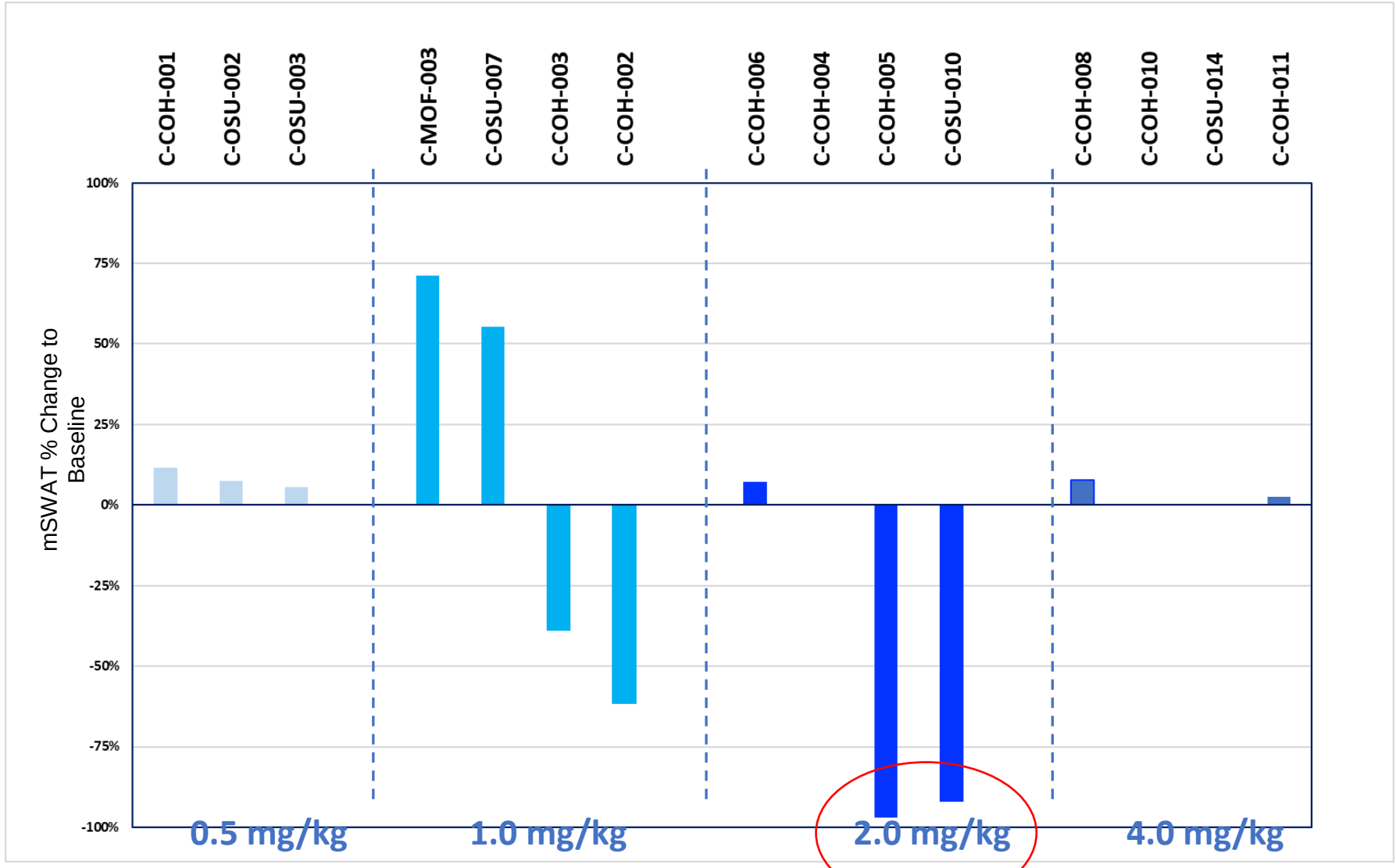
Examples of clinical efficacy in rCTCL patients treated with BNZ-1





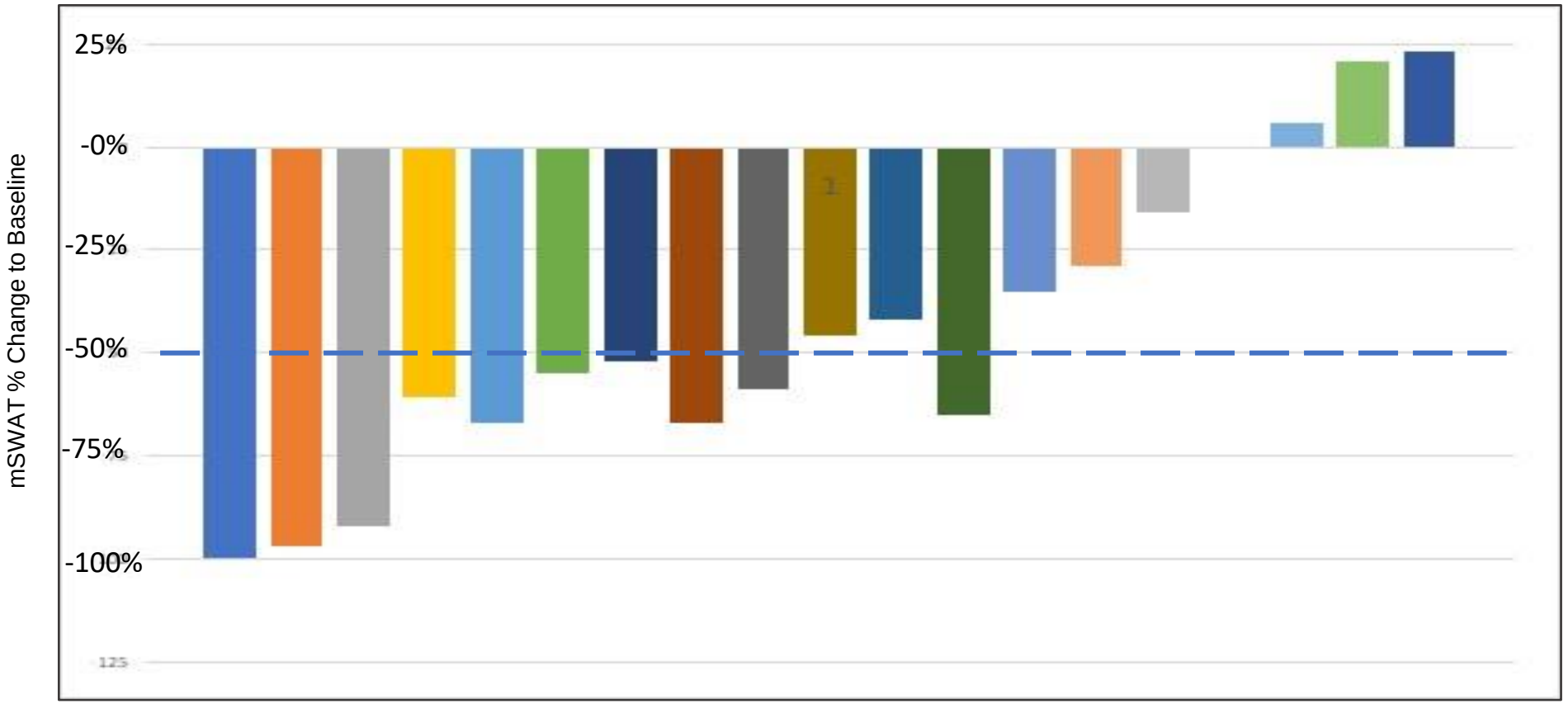


Waterfall plot of mSWAT scores as percent change over baseline across 4 different cohorts



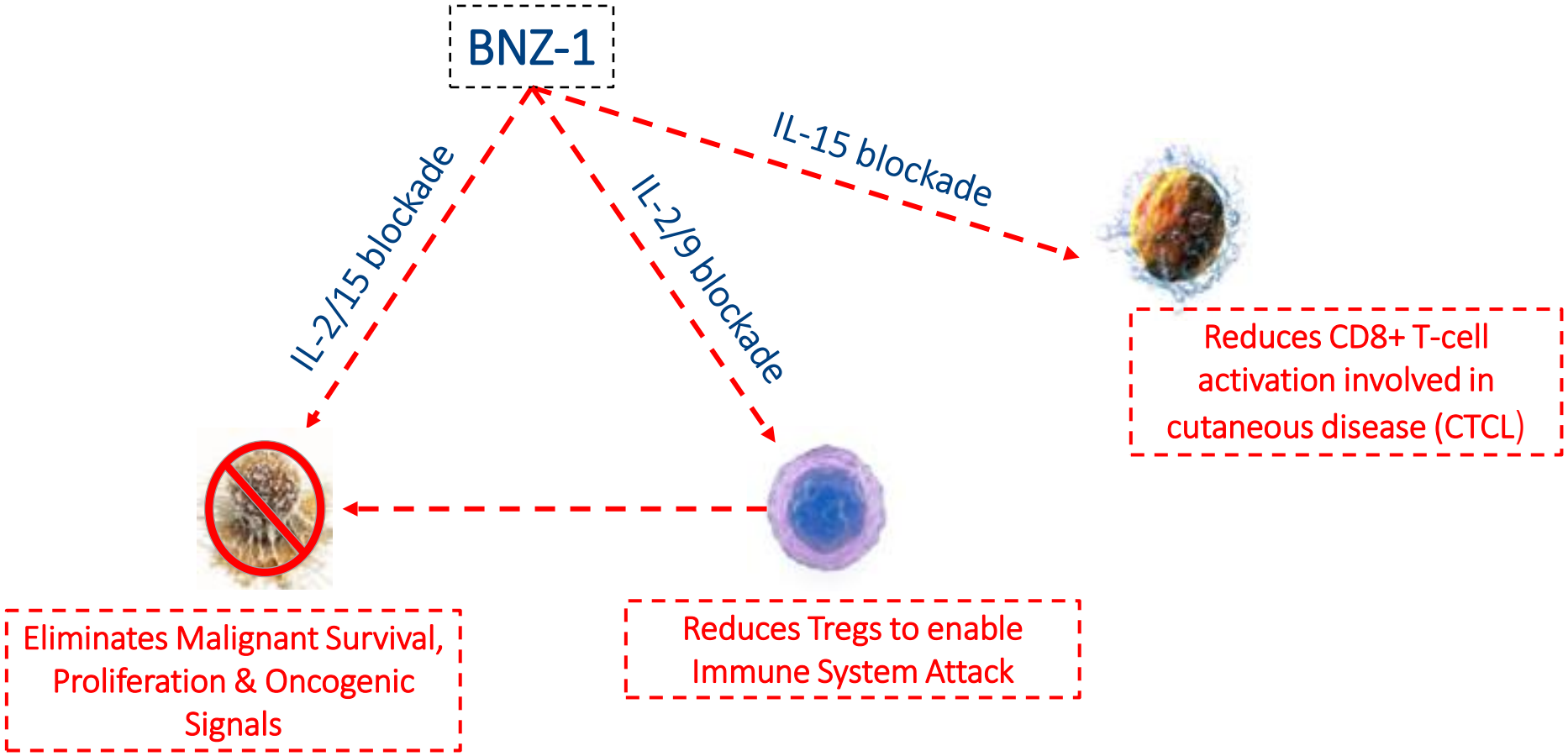
Expanded cohort based on PK/PD and clinical efficacy

Waterfall plot of mSWAT scores as percent change over baseline for the expanded cohort of 2 mg/kg (n=19)



- 1 CR and 10 PR = 11/19 → **ORR = 52.6%**
- 1 CR at week 13 → response lasted until week 30
- 2 subjects reached a PR as early as 4 weeks after initiating the BNZ-1 treatment
- Duration of treatment for initial patients across 4 cohorts: up to 73 weeks, duration of response: 64 weeks
- Duration of treatment for expanded cohort: 4-30 weeks, duration of response: 4 – 26 weeks (median 12 weeks)
- Time to PR/CR response: median 14 weeks

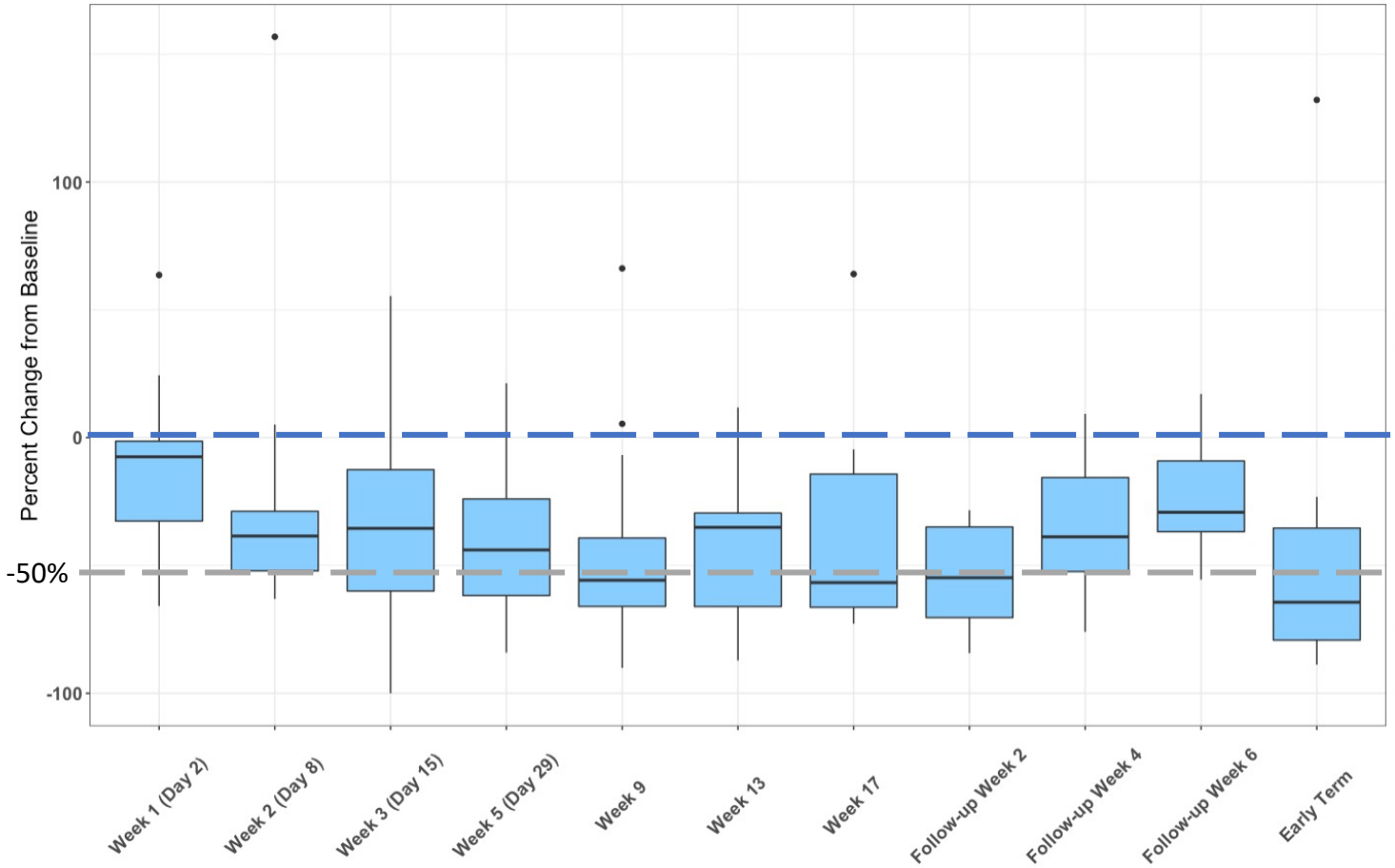
BNZ-1 has multi-modal properties in CTCL



BNZ-1 reduces the number of Treg cells

acting as an immuno-oncology agent that activates anti-tumor response

- Peripheral blood was used to monitor the lymphocyte populations such as CD4, CD8, B, NK and Treg cell population
- A targeted reduction in Treg cell population in the CD4 cells was observed due to IL-2 inhibition by BNZ-1
- No meaningful change was observed during the treatment in total CD4, CD8, B cells and monocytes

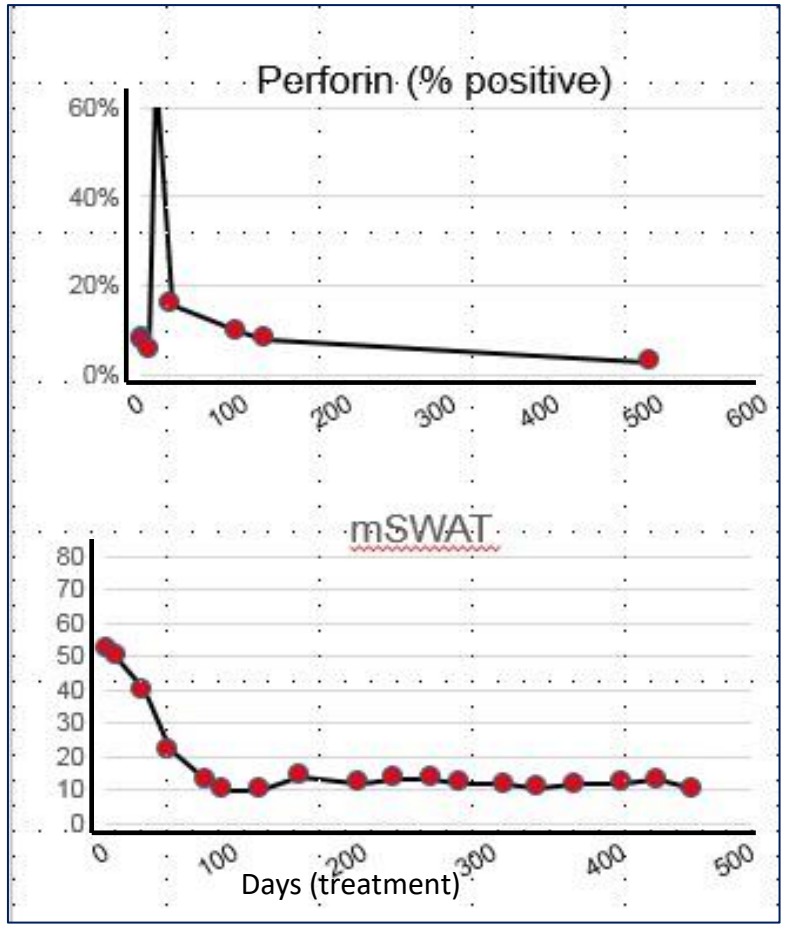


Data from the expanded cohort, N=19

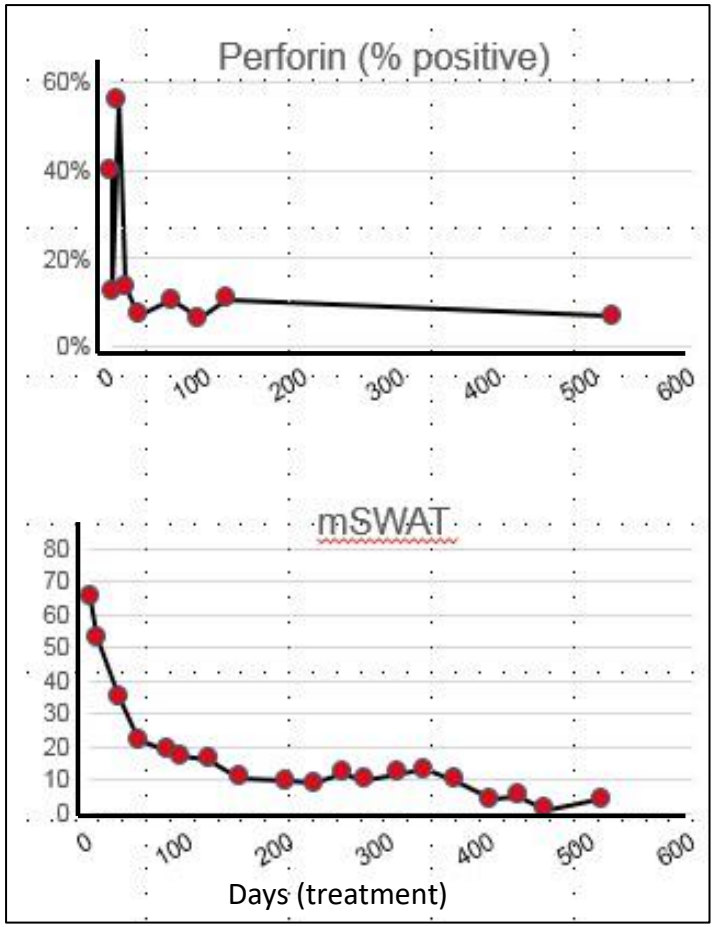
BNZ-1 reduces the activation markers in CD8 cells
supports its anti-inflammatory effect

- Peripheral blood was used to monitor the expression of CD8 activation markers (perforin) in CTCL during BNZ-1 treatment
- A reduction of CD8 activation marker was observed in some patients who showed mSWAT response to BNZ-1 treatment

OSU-010 (responder)



COH-005 (responder)



Conclusion

- BNZ-1:
  - is a selective inhibitor of IL-2, IL-9, and IL-15
  - is well tolerated with no AE-trend, or laboratory abnormalities
  - exhibited efficacy (ORR of 52.6%) in rCTCL patients who have failed a median of 5 prior systemic treatments
  - Has a multi-prong modality
    - direct inhibition of malignant cells,
    - activation of tumor immunity,
    - suppression of inflammation.
  - BNZ-1 favorable safety and efficacy in rCTCL patient population supports further development in a phase 2 trial

Investigators:

- City of Hope
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- University of Pittsburgh
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  - Brian Poligone, MD

- University of Maryland; Yutaka Tagaya, PhD,
- Bioniz Therapeutics (Equillium); Nazi Azimi, PhD

Extra slides

Efficacy results from Phase 1/2 study (2mg/kg)

Responses at primary efficacy analysis (Week 17) Before or After

Timepoint applicable for Phase 3 study

Response based on mSWAT	N	CR	PR	ORR	SD	PrD	Response (ORR) N=19
Response at Week 17	12	1 (8.3%)	4 (33.3%)	5 (41.7%)	7 (58.3%)	0	26.3%
Response during the initial 17 weeks of treatment	19	1 (5.3%)	5 (26.3%)	6 (31.6%)	13 (68.4%)	0	31.6%
Response during only the LTE + FU	13	1 (7.7%)	8 (61.5%)	9 (69.2%)	4 (30.8%)	0	47.3%
Response during the entire study (including the FU)	19	1 (5.3%)	9 (47.4%)	10 (52.6%)	9 (47.4%)	0	52.6%
Response based on GRS							
Response at Week 17	12	1 (8.3%)	4 (33.3%)	5 (41.7%)	7 (58.3%)	0	26.3%
Response during the initial 17 weeks of treatment	19	1 (5.3%)	5 (26.3%)	6 (31.6%)	13 (68.4%)	0	31.6%
Response during only the LTE + FU	12	1 (8.3%)	10 (83.3%)	11 (91.7%)	1 (8.3%)	0	57.8%
Response during the entire study (including the FU)	19	1 (5.3%)	11 (57.9%)	12 (63.2%)	7 (36.8%)	0	63.2%

Time to PR/CR: median 14 weeks

DoR is calculated for the initial cohort (4 patients as part of the dose ranging study) and the expanded cohort of 15 patients.

- **Two out of 4 initial patients remained in the study until its completion (total of 73 weeks), DoR for 2 responders were 64 weeks.**
- **Patients who enrolled as part of the cohort expansion had a shorter time for the treatment since the study needed to be completed and closed out for data analysis. This cohort had maximum of 42 weeks of treatment and showed DoR of median of 12 weeks.**

CR = complete response; FU = follow up period; GRS = global response score; LTE = long-term extension; mSWAT = modified severity weighted assessment tool; ORR = overall response rate (CR + PR); PrD = progressive disease; PR = partial response; SD = stable disease.
Percentages given in parentheses are based on a denominator from assessed patients (column N).