MADRID 2023 ESMO congress

Efficacy and safety of botensilimab plus balstilimab in patients with refractory metastatic sarcoma

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DISCLOSURES

Breelyn A. Wilky, MD

Consultant/Advisory Role: Adaptimmune, Adcendo, Daiichi Sankyo, Deciphera, Epizyme, Polaris, Springworks

Institutional Research Funding: Exelixis

Institutional Coordinating PI: Agenus

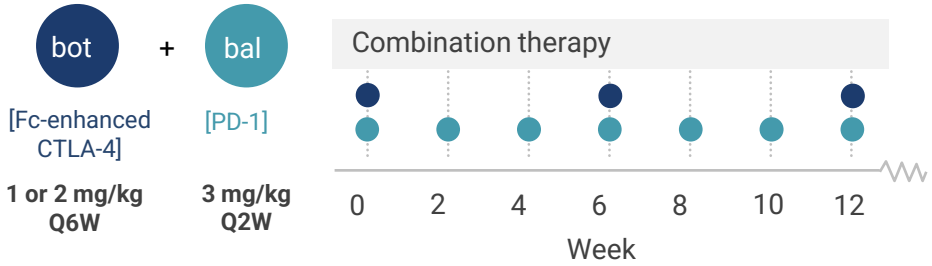
C-800-01 STUDY: SARCOMA COHORT

NCT03860272: First-in-human trial of **botensilimab (bot)** ± **balstilimab (bal)** in patients with advanced cancer[1]

Evaluable Study Population*

- **41** treated with 1 or 2 mg/kg bot + bal as of 06 April 2023 with ≥1 Q6W imaging assessment

Treatment (*up to 2 years*)



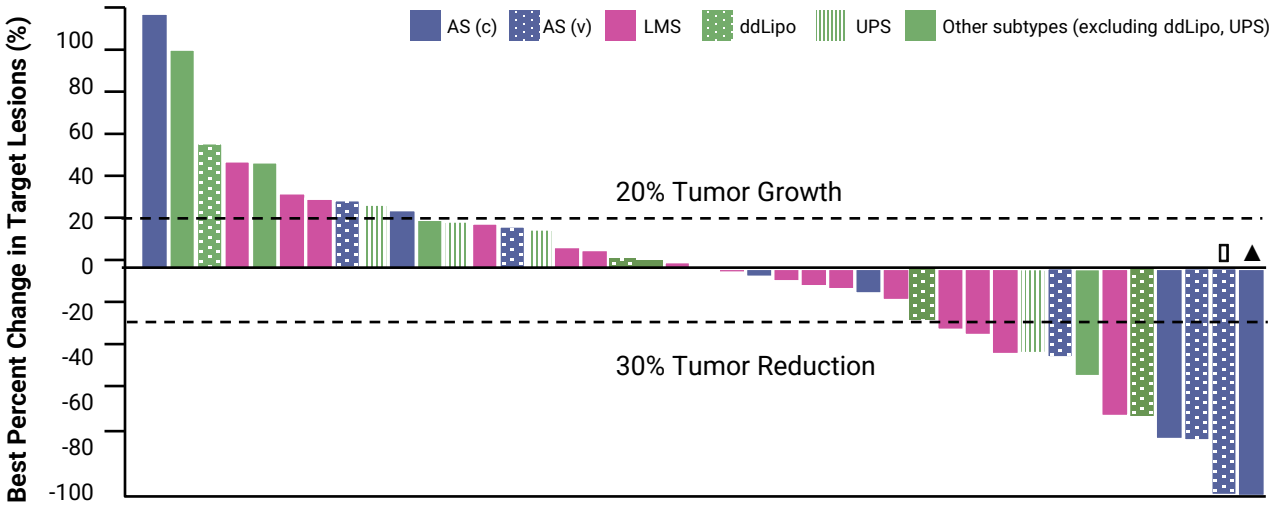
[1]https://clinicaltrials.gov/ct2/show/NCT03860272.
*Nine additional patients were treated as of 06 April 2023 but had not received the first 6-week tumor assessment (ITT/Safety population=50).
Data cutoff: 17-Aug-2023.

PATIENT CHARACTERISTICS

	All Sarcoma N=41
Age, median (range)	61 (31–80)
Sex, n (%)	
Male	13 (32)
Female	28 (68)
ECOG PS at baseline, n (%)	
0	16 (39)
1	25 (61)
Prior lines of therapy, n/N (%)	
Median (range)	3 (1–10)
≥3	20/38 (53)
Botensilimab dose, n (%)	
1 mg/kg	27 (66)
2 mg/kg	14 (34)
Prior PD-(L)1 therapy, n/N (%)	6/38 (16)
TMB >10, mut/Mb, n/N (%)	2/16 (13)
PD-L1 (≥1% positive), n/N (%)	7/27 (26)

	All Sarcoma N=41
Sarcoma subtype, n (%)	
Angiosarcoma (AS)	12 (29)
Cutaneous	7 (17)
Visceral	5 (12)
Leiomyosarcoma (LMS)	16 (39)
Soft tissue	13 (32)
Uterine	3 (7)
Other	13 (32)
Dedifferentiated liposarcoma (ddLipo)	4 (10)
Undifferentiated pleiomorphic (UPS)	4 (10)
Undifferentiated spindle cell	2 (5)
Myxofibrosarcoma	1 (2)
Osteosarcoma/spindle cell	1 (2)
Myxoid liposarcoma	1 (2)

BROAD ACTIVITY IN HETEROGENOUS POPULATION



Two additional patients showed significant clinical response (NOT INCLUDED in RECIST v1.1 response rate):

▯ 1 deep PR in AS (v) by iRECIST; patient had minor early progression at 6 weeks followed by a deep response in target lesion (-98%) that is durable at 102+ weeks.

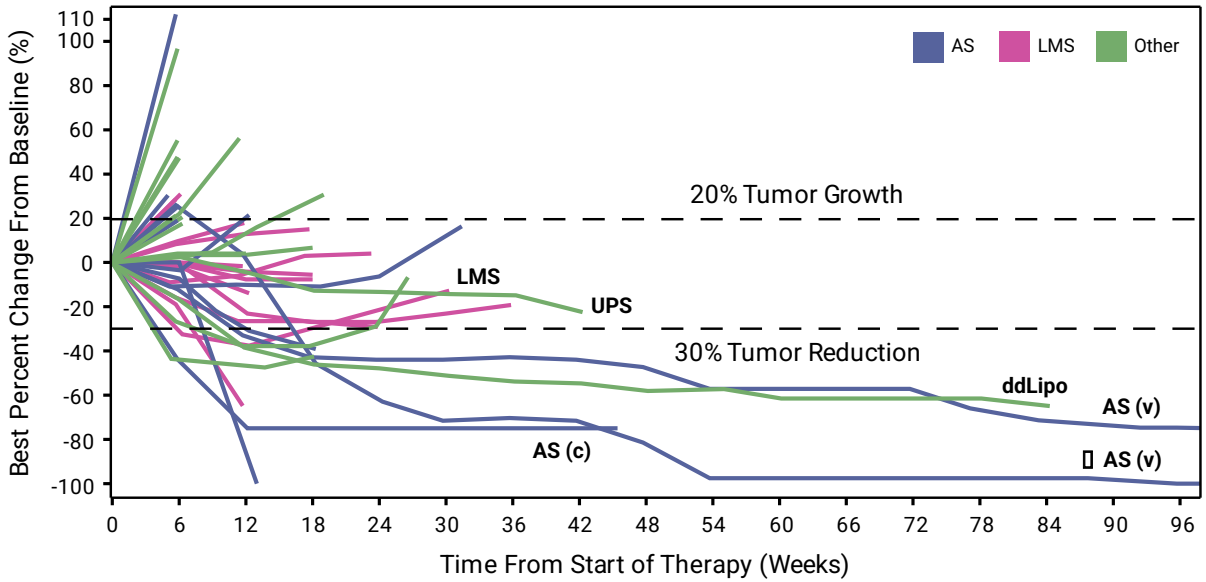
▲ 1 unconfirmed CR in AS (c); patient had a visible skin lesion that disappeared on exam, images on file.

All Sarcoma (N=41)*	iRECIST	RECIST v1.1
ORR†, % (95% CI)	20% (9–35)	17% (7–32)
ORR at 1mg/kg (%) n=27	15%	11%
ORR at 2mg/kg (%) n=14	29%	29%
BOR, n (%)		
CR	0	0
PR	8 (20)	7 (17)
SD	18 (44)	18 (44)
PD	15 (37)	16 (39)
Median DOR, months (95% CI)	19.4 (1.9–NR)	11.8 (1.9–NR)
DCR (CR + PR + SD), % (95% CI)	63% (47–78)	61% (45–76)
CBR (CR + PR + SD at 6 months), % (95% CI)	27% (14–43)	24% (12–40)
6-month PFS, % (95% CI)	40% (23–57)	37% (20–54)

* Median f/u: 5.7 months (range: 1.4–28.4).

† One response confirmed after data cutoff.

DURABILITY OF BENEFIT IN HETEROGENOUS POPULATION



One additional patient showed significant durability (NOT INCLUDED in RECIST v1.1 response rate):

1 deep PR in AS (v) by iRECIST; patient had minor early progression at 6 weeks followed by a deep response (-98%) that is durable at 102+ weeks.

All Sarcoma (N=41)*	iRECIST	RECIST v1.1
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SAFETY

TRAEs in ≥10% of All Sarcoma Patients in the ITT/Safety Population (N=50)

	All Grades	Grade 3	Grade 4
Any*	39 (78)	6 (12)	0
Gastrointestinal			
Immune-mediated diarrhea/colitis†	17 (34)	4 (8)	0
Nausea	7 (14)	1 (2)	0
Vomiting	6 (12)	1 (2)	0
Constitutional			
Fatigue	12 (24)	1 (2)	0
Pyrexia	9 (18)	0	0
Chills	7 (14)	0	0
Endocrine			
Hypothyroidism	5 (10)	0	0
Musculoskeletal			
Myalgia	6 (12)	1 (2)	0
Skin			
Rash	7 (14)	1 (2)	0
Rash maculo-papular	6 (12)	0	0

* Note: A higher frequency of any TRAEs was observed in patients receiving 2 mg/kg of botensilimab (93%) relative to the 1 mg/kg dose (70%).
† Patient received immunosuppressants (eg, steroids and/or a TNF-α inhibitor).

- No new safety signals
- Safety consistent across tumor types
- No cases of related hypophysitis, pneumonitis, hepatitis or myocarditis
- 8% discontinued due to a TRAE
- No grade 4 or 5 TRAEs

CONCLUSIONS & FUTURE DIRECTIONS

- Botensilimab and balstilimab demonstrates objective responses, durability, and disease stabilization in poorly immunogenic or “cold” sarcoma subtypes
- Durable and broad clinical benefit observed in visceral and cutaneous angiosarcoma, leiomyosarcoma, dedifferentiated liposarcoma, and undifferentiated pleomorphic sarcoma
- Relapsed/refractory sarcoma represents an unmet medical need where previous immunotherapies have shown limited activity
- Safety profile is manageable, and reversible with diarrhea/colitis the most clinically significant immune-mediated adverse event
- The current phase 1 study (C-800-01) is actively enrolling patients in an expansion sarcoma cohort (NCT03860272)

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ABBREVIATIONS

AE, adverse event
APC, antigen presenting cell
bal, balstilimab
BOR, best overall response
bot, botensilimab
CBR, clinical benefit rate
CI, confidence interval
CR, complete response
CTLA-4, cytotoxic T-lymphocyte antigen-4
DCR, disease control rate
DOR, duration of response
ECOG, Eastern Cooperative Oncology Group
Fc, fragment crystallizable
F/U, follow-up
I-O, immunotherapy
ITT, intent-to-treat
NSCLC, non-small cell lung cancer
NR, not reached
ORR, objective response rate
PD, progressive disease
PD-1, programmed death receptor-1
PD-L1, programmed death-ligand 1
PFS, progression-free survival
PR, partial response
PS, performance status
QXW, every X weeks
R/R, relapsed/refractory
SD, stable disease
TMB, tumor mutational burden
TRAE, treatment-related adverse event

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