LEVINE CANCER INSTITUTE

Atrium Health

A pilot study evaluating the safety, tolerability, and efficacy of doxorubicin and pembrolizumab in patients with metastatic or unresectable soft tissue sarcoma

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BACKGROUND

- Doxorubicin is the traditional standard therapy for treatment of advanced soft tissue sarcoma (STS). Pembrolizumab monotherapy has demonstrated activity and tolerability in a previous study of advanced STS (SARC028).
- **AIM:** this study assessed the **safety and efficacy profile of combination pembrolizumab and doxorubicin in the frontline and relapsed setting.**
- **STUDY DESIGN:**
  - **30 histologically confirmed unresectable or metastatic STS with no prior anthracycline therapy subjects were enrolled in this single-center, single arm study**
  - Treatment: Pembrolizumab 200 mg IV and doxorubicin 60 mg/m2 (75 mg/m2 dose escalation per investigator discretion) IV every 3 weeks. Growth factor support was also given per investigator discretion.
- **ENDPOINTS:**
  - **Primary** : Safety stopping rule, evaluating if severe or life-threatening treatment emergent adverse event (TEAE) rate exceeded 0.55 (based on CTCAE v 4.0)
  - **Secondary** : Overall survival (OS), objective response rate (ORR), duration of response (DOR), and progression free survival (PFS) based on RECIST 1.1

Table 1 & 2 : Patient Demographics and Tumor Characteristics

	N	%
Gender		
Female	16	53.3%
Male	14	46.7%
Ethnicity		
Hispanic or Latino	3	10.0%
Not Hispanic or Latino	26	86.7%
Unknown or Not Reported	1	3.3%
Race		
White	23	76.7%
Black or African American	4	13.3%
Unknown or Not Reported	3	10.0%
Age		
18 – 29 years	2	6.7%
30 – 49 years	4	13.3%
50 – 69 years	14	46.7%
70+ years	10	33.3%

	N	%
Primary Tumor Site		
Extremity – arm	2	6.7%
Extremity – leg	8	26.7%
Retroperitoneal/Abdomen	12	40.0%
Other	8	26.7%
Histology		
Liposarcoma	7	23.3%
Leiomyosarcoma	10	33.3%
Synovial sarcoma	1	3.3%
Undifferentiated pleomorphic sarcoma	3	10.0%
Other	9	30.0%
Stage		
IB	2	6.7%
IIB	4	13.3%
III	8	26.7%
IV	12	40.0%
Unknown	4	13.3%
Histologic Grade		
G1 (low, well differentiated)	3	10.0%
G2 (int., moderately differentiated)	5	16.7%
G3 (high, poorly differentiated)	18	60.0%
Unknown/cannot be assessed	4	13.3%
Metastatic Site		
Liver	6	20.0%
Lung	6	20.0%
Lymph Node	2	6.7%
Other	15	50.0%
Unknown	1	3.3%

*Note, at the time of data export (4/21/2020), not all data elements were fully validated.

RESULTS

- **Incidence of serious adverse events (SAE)**: 53.3% (95% CI: 34.3% - 71.7%)
- At the time of analysis: 23 of 30 subjects (76.7%) had at least one grade 3+ AE
- Majority of grade 3+ AEs were **hematologic in nature**

Table 3. Most common grade 3+ AEs experienced by 3 or more subjects

Adverse Event	N	%
Neutropenia	13	43.3%
White blood cell decreased	11	36.7%
Febrile neutropenia	5	16.7%
Anemia	5	16.7%
Nausea	4	13.3%
Fatigue	3	10.0%
Hyponatremia	3	10.0%
Lymphopenia	3	10.0%
Vomiting	3	10.0%
Lung infection	3	10.0%
Generalized muscle weakness	3	10.0%
Arthralgia	3	10.0%

Disease Control Rate: 80.0% (95% CI: 61.4% - 92.3%)

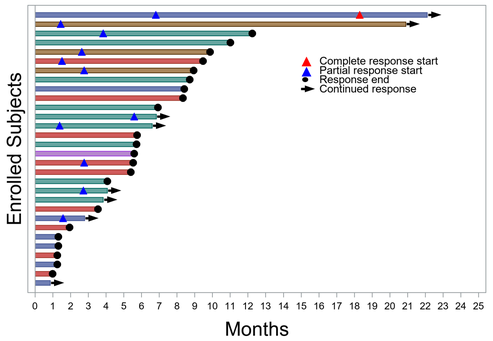


Figure 2: Swimmers plot of duration of response / disease control

Objective Response Rate: 36.7% (95% CI: 19.9% - 56.1%)

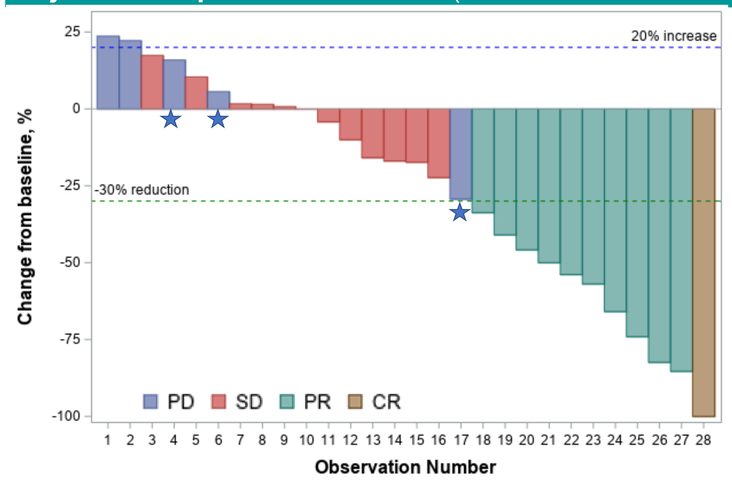
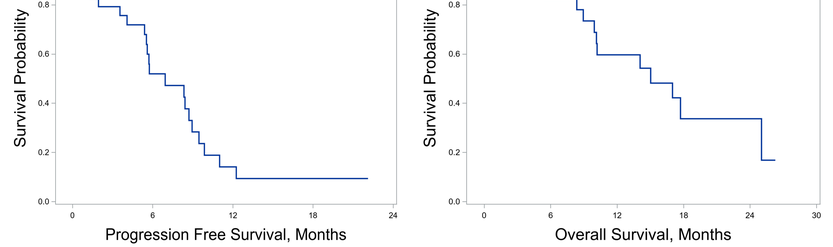


Figure 1: Waterfall plot of best change in target-lesion size from baseline

n = 28 subjects, post-baseline scans were not available for 2 subjects;
★ subjects progressed due to new lesions, not by target lesion size increase

Table 4: ORR by Sarcoma Histologic Subtype

Histology	ORR N (%)
Liposarcoma (n = 7)	2 (28.6%)
Leiomyosarcoma (n = 10)	4 (40.0%)
Synovial sarcoma (n = 1)	0 (0.0%)
UPS (n = 3)	3 (100.0%)
Other (n = 9)	2 (22.2%)



Median PFS (95% CI)	6 Month PFS	Median OS (95% CI)	6 Month OS
6.9 (5.4-8.9)	51.9% (31.7-68.8%)	15 (9.9-25)	82.4% (62.6-92.3%)

Figure 3 & 4: Progression free survival and overall survival

The combination of pembrolizumab with doxorubicin has manageable toxicity and preliminary data demonstrates promising efficacy in the treatment of anthracycline-naive advanced soft tissue sarcomas.

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CONTACT INFORMATION

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