Treatment Patterns of Patients with Soft Tissue Sarcoma Progressing to Third Line of Therapy

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BACKGROUND

- Soft tissue sarcomas (STS) are a group of rare and heterogeneous tumors, accounting for <1% of all neoplasms in the United States (US), with an incidence rate of 3.5 new cases per 100,000 persons.[1,2]
- Treatment options for STS include surgery, radiotherapy, and systemic agents[2] and treatment recommendations vary by subtype, location of the tumor, and stage.[3]
- For patients with unresectable or metastatic STS, after first-line (1L) therapy with anthracyclines, few agents have shown survival benefits.[4]
- In the real world, patients with advanced STS have used docetaxel and gemcitabine combination therapy as 1L and second line (2L) regimen, and pazopanib was commonly used as a 2L agent. Real world studies observed no third line (3L) regimen in the STS patients.[5,6]

OBJECTIVE

- The objective of this retrospective analysis was to characterize treatment patterns, including types and duration of treatments, in patients with STS who have received at least three lines (3Ls) of therapy.

STUDY DESIGN

Data Source

- This retrospective database study used electronic medical records (EMR) provided by Guardian Research Network (GRN), which has access to the complete EMR (progress notes, imaging results, pathology reports, etc.) for every cancer patient treated in their partner facilities.

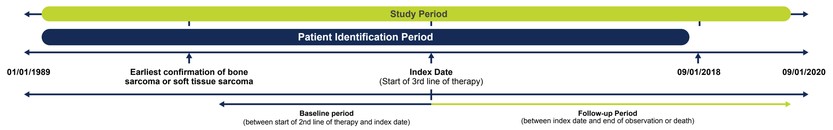
Study Population

- Patients with STS who received a 3L were identified between Jan 1, 1989 and Sep 1, 2018 - **patient identification period**. All patient data between Jan 1, 1989 and Sep 1, 2020, was evaluated in this analysis - **study period** (**Fig. 1**).
  - This approach allowed all included patients to have an opportunity of at least two years of follow-up, although no minimum follow-up was required.
- The **index date** was defined as the date of initiation of 3L following the first observed STS histology confirmation.
- The **baseline period** was defined as the time between the start of 2L and the index date.
- Patients were followed from the index date until death or the end of follow-up, whichever came first (**follow-up period**).
- Patients were required to be ≥ 18 years of age at the time of diagnosis or date of histology confirmation, whichever came first.
- Patients were excluded from the analysis if they had evidence of death occurring prior to the index date or earliest of first observed diagnosis date or date of histology confirmation occurred after the index date.
- Line of Therapy (LoT) Definition
  - Lines of therapy were defined using drug names, route of administration, and days' supply.
  - Days' supply:
    - Injectable and infusible drugs: The largest recommended time gap between two consecutive administrations on the drug label.
    - Oral drugs: A fixed 30-day days' supply was assumed for all oral medications.
- Lines were assumed to have initiated on the first observed administration and ended if there was a treatment gap of >60 days, a new agent was added >28 days after initiation of the line, or the end of patient follow-up was reached.
  - All agents initiated within 28 days after the initiation of the line were considered as part of the line.
  - If the subsequent line had the same agents as the previous line and was started within 90 days of the end of the previous line, then the line was considered to have continued.

Baseline Patient Characteristics and Outcomes

- Demographic (age at index date, gender, race), clinical characteristics (comorbidities and comorbidity burden), and treatment patterns (treatment regimens, duration of treatment, and time between treatments for 1L, 2L, and 3L) during the baseline period were assessed.
- The treatment patterns during the follow-up period were assessed, including treatment regimens, duration of treatment, and time between treatments for the 3L and 4L.
- Duration of treatment for 3L and 4L was described using the Kaplan-Meier method to account for censoring and death. The time between 3L and 4L was described using the Kaplan-Meier method with death as a competing risk.

Fig. 1: Study Time Period



The three most common regimens (Trabectedin, Docetaxel + Gemcitabine, Pazopanib) accounted for less than one-third of patients, suggesting an absence of a standardized approach. These results may reflect rapid later-stage disease progression or low durability of response and indicate an unmet need for more effective treatment for patients with advanced STS.

Tab. 1: Patient Demographic and Baseline Clinical Characteristics Prior to Start of 3rd Line of Therapy

	Total[1] N=55	
Age at index date (years)		
Mean (SD)	60.85	(11.96)
Median	64	
Gender (n, %)		
Female	37	67.3%
Male	18	32.7%
Race (n, %)		
White	47	85.5%
Black or African American	4	7.3%
Other[2] or Unknown/Missing	4	7.3%
Ethnicity (n, %)		
Not Hispanic or Latino	47	85.5%
Hispanic or Latino	4	7.3%
Unknown/Missing	**	**
Baseline period (months)		
Mean (SD)	7.19	(6.4)
Median	4.9	

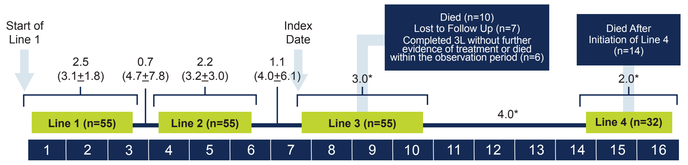
	Total[1] N=55	
Baseline Quan Charlson Comorbidity Index (QCI) score[3]		
n (%)	55	100.0%
Mean (SD)	0.98	(1.24)
Median	1	
Baseline Comorbidities		
Presence of comorbidity (n, %)		
Diabetes without chronic complication	15	27.3%
Chronic pulmonary disease	9	16.4%
Congestive heart failure	7	12.7%
Mild liver disease	6	10.9%
Peripheral vascular disease	3	5.5%
Rheumatic disease	2	3.6%
Diabetes with chronic complication	2	3.6%

	Total[1] N=55	
Follow-up period (years)		
Mean (SD)	1.57	(1.51)
Median	1.11	
Time since diagnosis (years)		
Mean (SD)	3.39	(4.68)
Median	1.34	
Soft Tissue Sarcoma Subtype		
Leiomyosarcoma	30	54.5%
Liposarcoma	9	16.4%
Synovial Sarcoma	4	7.3%
Rhabdomyosarcoma	4	7.3%
STS Not Otherwise Specified	3	5.5%
Angiosarcoma	2	3.6%
Fibroblastic Sarcoma	1	1.8%
Gynaecological Sarcoma	1	1.8%
Retroperitoneal Sarcoma	1	1.8%

1. Includes Leiomyosarcoma, Liposarcoma, Other Soft Tissue Sarcoma, Synovial Sarcoma
2. Includes Native Hawaiian or Other Pacific Islander, Asian, and American Indian or Alaska Native
3. Excludes cancer

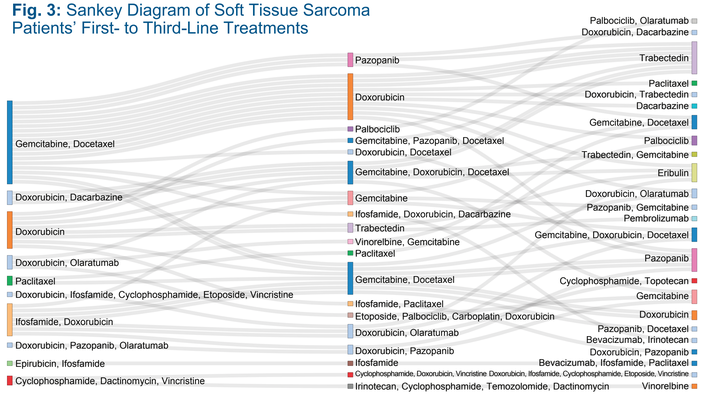
** Represents results that cannot be reported due to a sample size <4

Fig. 2: Duration of Therapy and Time Between Lines for Patients with Soft Tissue Sarcoma*



*Median (Mean +/- SD); Median calculated using Kaplan Meier method

Fig. 3: Sankey Diagram of Soft Tissue Sarcoma Patients' First- to Third-Line Treatments



RESULTS

Baseline Demographic and Clinical Characteristics

- A total of 55 patients who initiated 3L were included in the analysis (age [mean±SD; median: 60.9±12.0; 64.0] years, 67% female, 86% white, **Tab. 1**).
  - Leiomyosarcoma was the most common histologic subtype (55%), followed by liposarcoma (16%), synovial sarcoma (7%), and other STS (22%) (**Tab. 1**).
- Average baseline period, defined as the time between the start of 2L and the day before the start of the 3L, was [7.2±6.4; 4.9] months, and patients were followed for an average of [1.6±1.5; 1.1] years.
- Average time from first observed diagnosis of STS to 3L initiation was [3.4±4.7; 1.3] years.
- Average Quan's modification of the Charlson Comorbidity Index (QCI) (excluding cancer) was [0.98±1.24; 1.0].

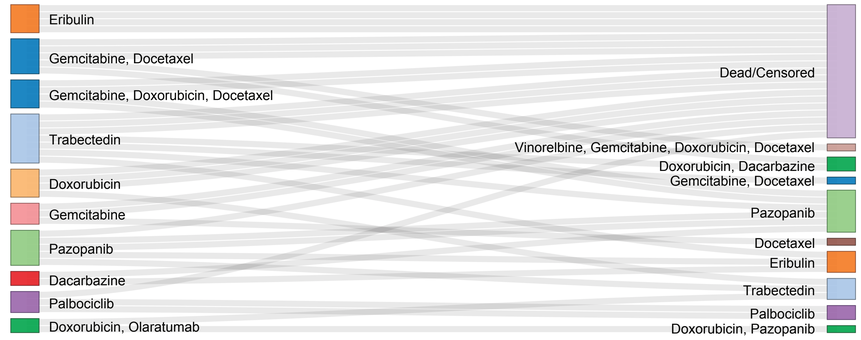
Treatment Patterns prior to initiation of 3L

- A greater percentage of patients had monotherapy at 2L (49%) relative to 1L (33%).
- The top 1L therapies were docetaxel + gemcitabine (33%), doxorubicin (15%), and doxorubicin + ifosfamide (13%).
- The top 2L treatments were doxorubicin (18%), docetaxel + gemcitabine (15%), and docetaxel + gemcitabine + doxorubicin (9%).
- Median durations of treatment were 2.5 (1L) and 2.2 (2L) months. The median times between therapies were 0.7 (1L to 2L), and 1.1 (2L to 3L) months (**Fig. 2**).

Treatment Patterns During Follow-up

- A greater percentage of patients had monotherapy at 4L (66%) relative to 3L (60%).
- The top 3L regimens were trabectedin (13%), docetaxel + gemcitabine (9%), and pazopanib (9%), accounting for 31% of patients (**Fig. 3**).
- Median duration of treatment for 3L was 3.0 months (**Fig. 2**).
  - Of 3L patients, 32 (58%) patients initiated 4L, 10 (18%) died, 7 (13%) were lost to follow up, 6 (11%) did not initiate 4L.
- The median time between 3L and 4L was 4 months (**Fig. 2**).
- The top 4L regimens were pazopanib (19%), eribulin (16%), and trabectedin (16%), accounting for 50% of 4L patients (**Fig. 4**).

Fig. 4: Sankey Diagram of Soft Tissue Sarcoma Patients' Third-and Fourth-Line Treatments



CONCLUSIONS

- Prior real-world studies of patients with STS focused on initial treatment following diagnosis, while this analysis focused on patients who received 3L treatment.
- Third-line treatments administered included a wide range of regimens. The three most common regimens accounted for less than one-third of patients, suggesting an absence of a standardized approach.
- These results may reflect rapid later-stage disease progression or low durability of response and indicate an unmet need for more effective treatment for patients with advanced STS.

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Presented at the NCCN 2022 Annual Conference (March 31 – April 2, 2022) Live Virtual Event