Updated Real-World Insights into Clear Cell Sarcoma from a Patient-Led Electronic Health Record Registry

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Objective

Clear cell sarcoma (CCS) is an ultra-rare, aggressive soft tissue sarcoma characterized most commonly by an EWSR1::ATF1 gene fusion. It typically affects adolescents and young adults, has a propensity to metastasize, and responds poorly to conventional systemic therapies. Effective systemic treatment options remain a critical unmet need, and clinical trial data are limited. To address this evidence gap, the Clear Cell Sarcoma Foundation established a patient-led electronic health record registry capturing treatment histories and outcomes across institutions. Building on previously reported findings, this study describes an expanded cohort, examining patient characteristics, treatment patterns, and observed time from diagnosis to death or last follow-up by disease status at diagnosis.

Methods

Patients with confirmed clear cell sarcoma (CCS), or their caregivers, voluntarily enroll in the Clear Cell Sarcoma Foundation registry and authorize collection of medical records from their treating institutions. Electronic health records are aggregated and standardized through xCures, LLC. Data abstracted include demographics, diagnostic findings, primary tumor location, disease status at diagnosis, treatment history, and outcomes. Historical records are supplemented as additional records become available, capturing care across academic and community settings. This update describes 32 patients. Observed time was measured from diagnosis to death or last follow-up, and treatment exposure reflects documented receipt at any point during the disease course. Analyses were descriptive; formal statistical comparisons were not performed because of the small cohort, limited number of deaths, variable follow-up, and heterogeneous treatment histories.

Patient Demographics and Clinical Characteristics, N=32

Median Age at Dx

30 years (10-57)

Sex at Birth

- Female: 59.4% (19/32)
- Male: 40.6% (13/32)

Race/Ethnicity

- Asian: 6.3% (2/32)
- White: 65.6% (21/32)
- Middle Eastern/North African: 3.1% (1/32)
- Hispanic/Latino: 3.1% (1/32)
- Not Reported: 21.9% (7/32)

Biomarkers

- EWSR1::ATF1: 84.4% (27/32)
- EWSR1 rearrangement (fusion partner unspecified), with histologic confirmation: 6.3% (2/32)
- CCS diagnosed by Histology only: 9.4% (3/32)

Disease Status at Diagnosis

- Localized: 65.6% (21/32)
- Metastatic: 34.4% (11/32)

Location of Primary Tumor

- Lower Extremity 50.0% (16/32)
- Upper Extremity 15.6% (5/32)
- Trunk 15.6% (5/32)
- Head/Neck 9.4% (3/32)
- GI System 9.4% (3/32)

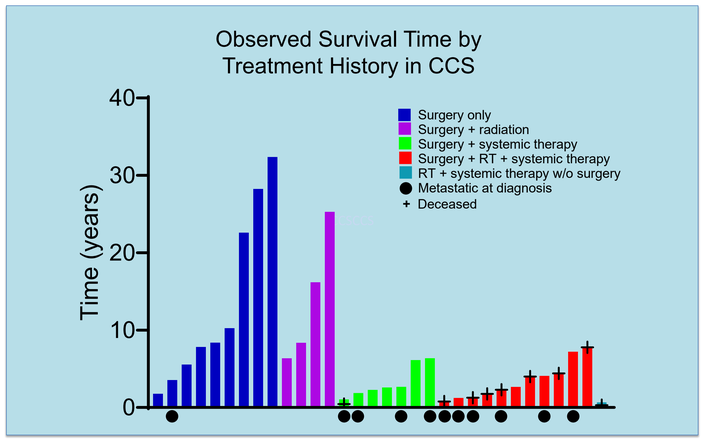
Treatment Type

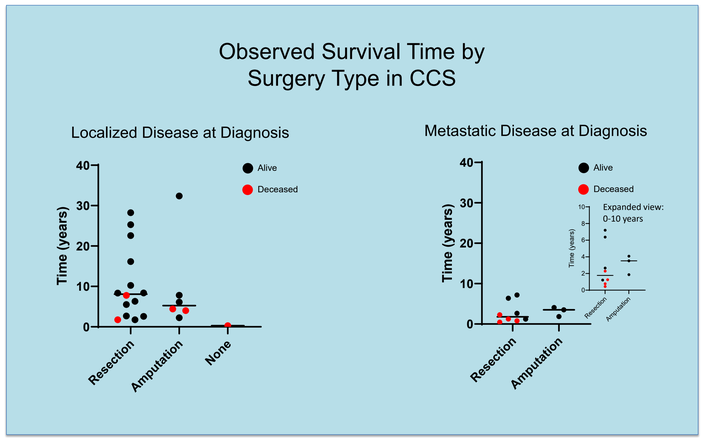
- Surgery: 96.9% (31/32)
- Cytotoxic Chemotherapy: 21.9% (7/32)
- Radiation: 50.0% (16/32)
- Tyrosine Kinase Inhibitors: 37.5% (12/32)
- Immune Checkpoint Inhibitors: 40.6% (13/32)
- Care Oncology Protocol: 15.6% (5/32)

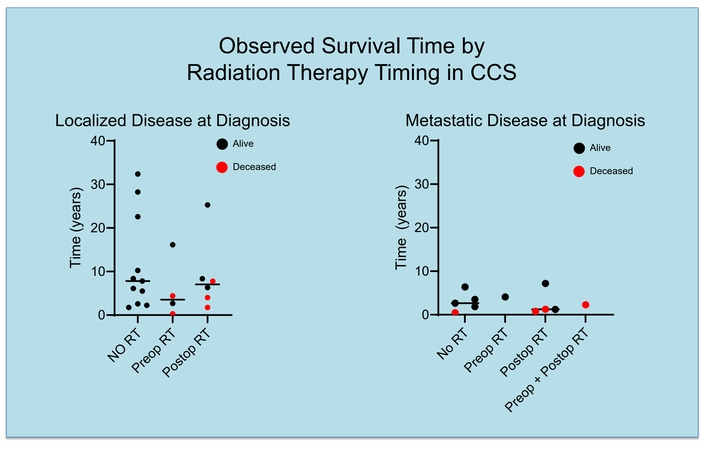
Alive at last follow-up: 71.9% (23/32); data cutoff: 10.29.2026

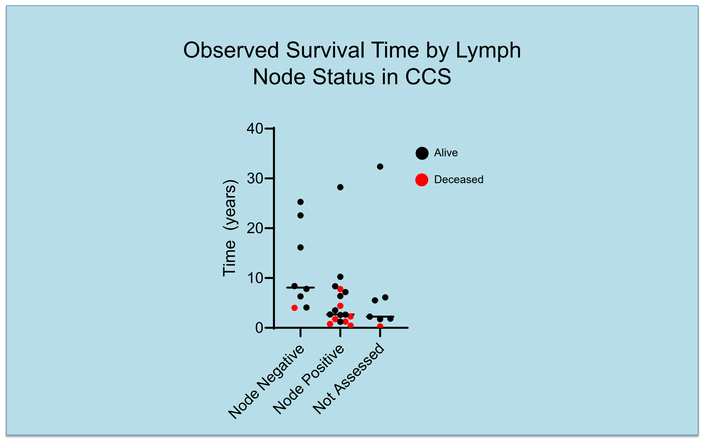
Results

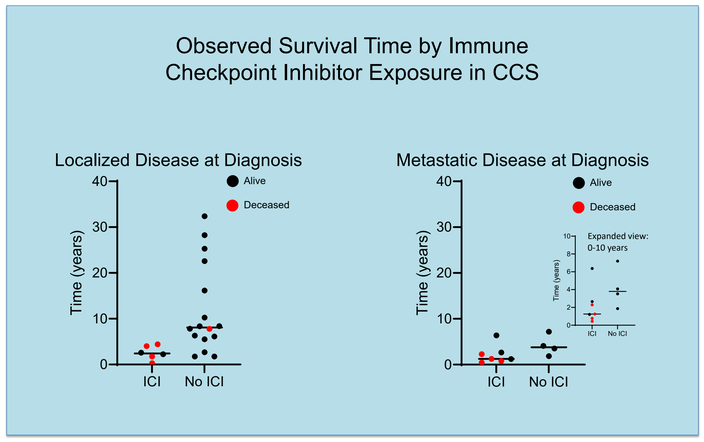
A total of 32 patients with clear cell sarcoma (CCS) were included. Median age at diagnosis was 30 years (range 10–57), and 59.4% were female. At diagnosis, 21 patients (65.6%) had localized disease and 11 (34.4%) had metastatic disease. EWSR1::ATF1 fusions were documented in 27 patients (84.4%); two (6.3%) had an EWSR1 rearrangement with an unspecified partner, with additional histologic confirmation; the remaining three patients (9.4%) were diagnosed by histology to confirm CCS and exclude melanoma. The lower extremity was the most common primary tumor location (50.0%). Documented treatment histories included surgery (96.9%), radiation therapy (50.0%), immune checkpoint inhibitors (40.6%), tyrosine kinase inhibitors (37.5%), cytotoxic chemotherapy (21.9%), and the Care Oncology protocol (15.6%). Some patients received more than one treatment type during their disease course. At last follow-up, 23 patients (71.9%) were alive and nine (28.1%) were deceased.

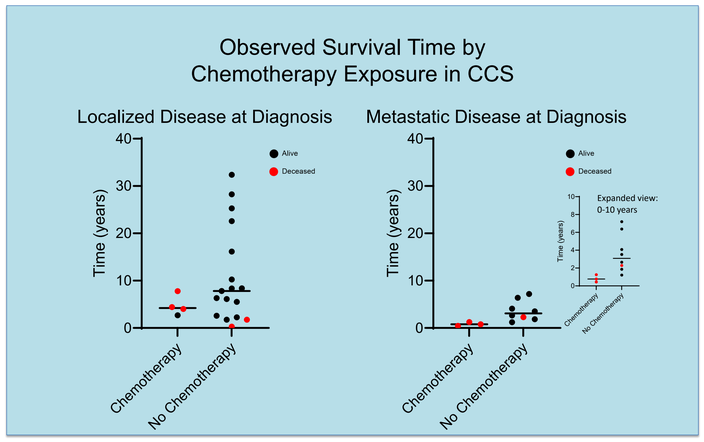












Results (Continued)

Treatment histories ranged from surgery alone to surgery, radiation, and systemic therapies. The longest observed times from diagnosis exceeded 20 years and occurred among patients treated with surgery alone or surgery plus radiation. Among patients with localized disease at diagnosis, the resection group showed a wider range of observed times than the amputation group. Observed times were shorter overall among patients with metastatic disease at diagnosis. Among patients with localized disease at diagnosis, observed times from diagnosis to death or last follow-up were generally shorter in the preoperative radiation group than in the postoperative or no-radiation groups; however, the small number of patients limits interpretation. Node-negative patients generally had longer observed times than node-positive patients, although both groups included patients followed for more than 20 years. Patients with immune checkpoint inhibitor or chemotherapy exposure generally had shorter observed times than those without these exposures in both diagnosis groups. These findings are descriptive. Formal statistical comparisons were not performed because of small subgroup sizes, few deaths, variable follow-up, and heterogeneous treatment histories. Times for patients alive at last follow-up represent incomplete survival observations. Treatment exposure and lymph node involvement could occur after diagnosis, and treatment selection may reflect disease progression or severity. These plots therefore do not establish treatment benefit or harm; horizontal lines represent medians of observed times, not estimates of median overall survival.

Conclusions and Future Directions

The expanded CCSF–xCures registry captures diverse treatment histories and outcomes in ultra-rare CCS. Patients help identify gaps in their records, and xCures works with treating institutions to obtain missing documentation, linking patient knowledge with electronic health records. Findings are descriptive and do not establish treatment effects. Priorities include expanded enrollment, longer follow-up, and assessment of radiation timing, surgical margins, systemic therapy sequencing, and treatment tolerability. A long-term goal is to develop sufficiently robust registry data to support external control groups for future CCS clinical trials and regulatory evaluation.

Acknowledgements

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