CLEAR CELL SARCOMA - REAL WORLD DATA ANALYSIS

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Objective

Clear Cell Sarcoma (CCS) is an ultra-rare and aggressive soft tissue sarcoma which typically develops in tendons or aponeuroses and affects mostly teens and young adults. In most cases CCS is caused by a translocation resulting in fusion of the genes for Ewing Sarcoma breakpoint region 1 (EWSR1) and activating transcription factor 1 (ATF1), resulting in the EWSR1-ATF1 fusion protein. Since CCS is so rare, there is a paucity of research, leading to few treatment options that are generally based on weak scientific evidence. The CCS patient community is eager to share real world evidence (RWE) data extracted from a proprietary platform that collects and de-identifies electronic health records (EHRs). This partnership with xCures is establishing an ongoing natural history study funded by the Clear Cell Sarcoma Foundation (CCSF). Through this study the CCSF will continue to work with clinicians, researchers and patients for the purpose of discovering the most effective ways to treat CCS patients and thereby improve patient outcomes.

Methods

CCS Natural History Study based on EHRs: Following an IRB approved process, CCS patients registered and consented to have their EHRs extracted, annotated, and placed in a searchable platform by xCures. An announcement was released to the private CCS facebook family and also on CCSF social media. Patient responses to the request were captured through a registration page. Once patients were consented, EHRs were collected and annotated by xCures biostatisticians and then de-identified data sets were coded and supplied to CCSF through a searchable link. The information obtained from the EHRs was analyzed to establish cancer related records and normalize terms, etc. across all health records. To date, 53 CCS patients have registered to participate, 22 have been fully consented and data for 15 participants has been annotated and released to CCSF. Patterns in efficacy of various treatment regimens, and other patterns of CCS disease progression were captured and analyzed.

Results

To date, EHRs for 15 CCS subjects have been annotated and released to CCSF for analysis. Demographics: The median age at diagnosis is 28 yrs (range 12-56 yrs); median overall survival is 5 yrs (range 0.42-30.5 yrs); 73% of respondents are female (11/15); 60% are caucasian, 7% are asian, and 33% were not reported. Primary tumor location: 53% lower extremity, 7% upper extremity, 13% chest, 13% head/neck, and 13% GI system. Number of patients alive to date: 73%. Treatment type: surgery 93%, cytotoxic chemotherapy 27%, radiation 47%, Tyrosine Kinase Inhibitor (TKI) 20%, and immunotherapy 40%. Biomarkers: EWSR1-ATF1 93%, histology confirmation of CCS 7%. In Figure 1, data are presented for survival time compared to treatment type. Figure 2 shows survival time versus use of adjuvant or neoadjuvant therapy. In Figure 3, data are presented for patients diagnosed with CCS positive lymph nodes showing the relationship of survival time versus removal decision. Figure 4 shows data for survival time of long term CCS survivors (>5 yrs) versus treatment type.

Preliminary results indicate automated EHR collections are incomplete and require human intervention to locate and extract missing data for a complete understanding of the natural history of the disease. In some cases, patients with similar therapeutic treatment history share similar outcomes. Results indicate that pediatric patients are often prescribed different treatment regimens than adult patients with CCS.

Patient Demographics N = 15

Median Age at Dx	Race	Location of Primary Tumor	Treatment Type
28 years (12-56)	Asian 7% (1/15)	Lower Extremity 53% (8/15)	Surgery 93% (14/15)
Sex at Birth	White 60% (9/15)	Upper Extremity 7% (1/15)	Cytotoxic 27% (4/15)
Female 73% (11/15)	Not Reported 33% (5/15)	Chest 13% (2/15)	Radiation 47% (7/15)
Male 27% (4/15)	**Biomarkers**	Head/Neck 13% (2/15)	Tyrosine Kinase Inhibitor (TKI) 20% (3/15)
Median Overall Survival	EWSR1-ATF1 93% (14/15)	Gi System 13% (2/15)	Immunotherapy 40% (6/15)
5 years (.42-30.5)	CCS by Histology 7% (1/15)	**Alive to Date 73% (11/15)**	

Figure 1.

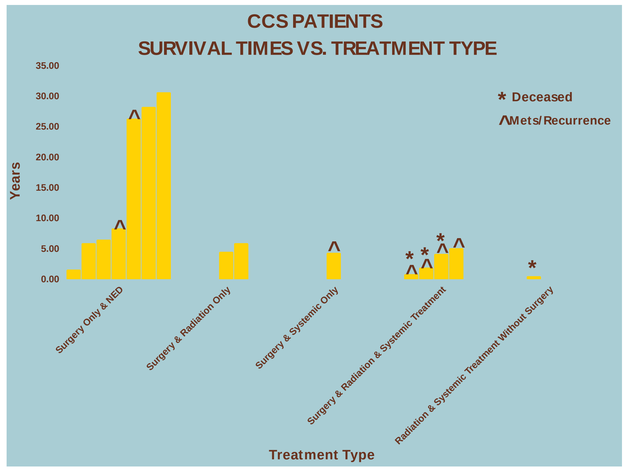


Figure 2.

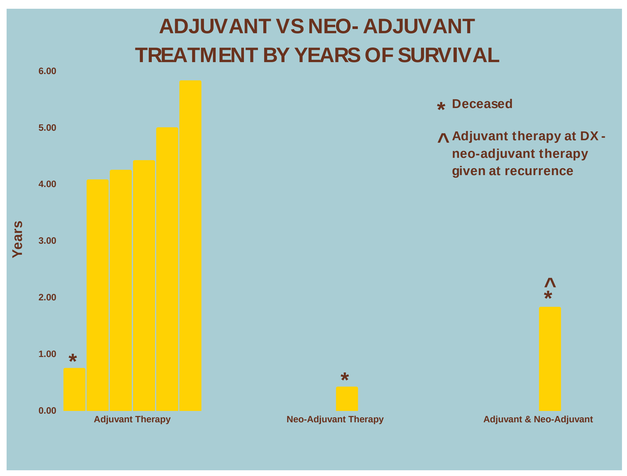


Figure 3.

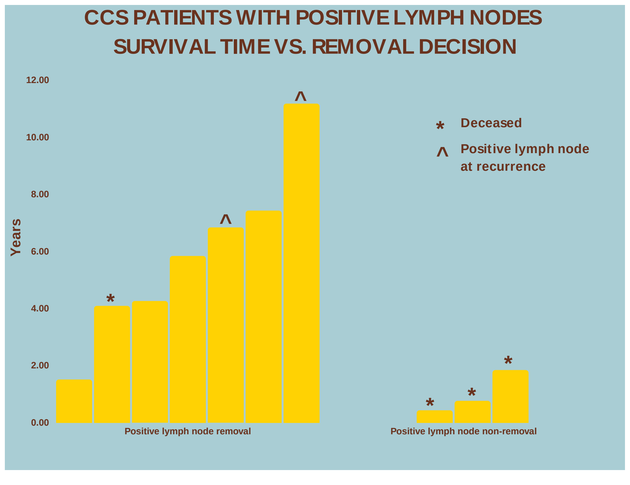
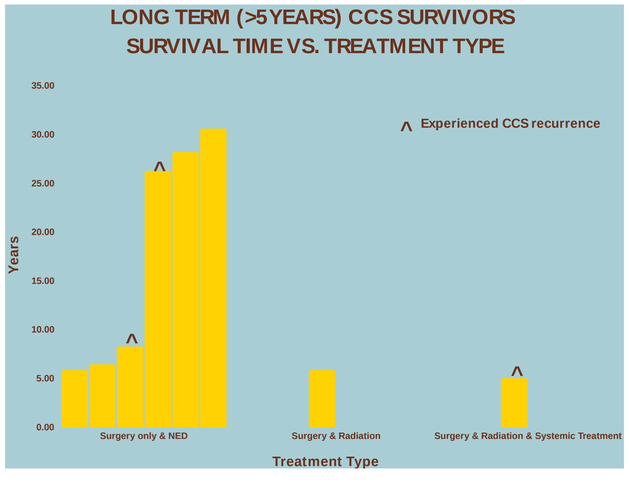


Figure 4.



Discussion

This is the first of many reports and updates from CCSF about the analysis of RWE collected for the purpose of studying CCS treatment and outcomes. At this time, only 15 patient records could be thoroughly vetted for accuracy and completeness. Vetting was in many cases done with the patient or primary caregiver involved through interviews and written reports that could be cross referenced with the xCures EHRs for accuracy. In any case involving a discrepancy in data that could not be verified, the patient's data was excluded. Rare sarcoma patients often find inaccurate data in their records therefore having patients partnered with the project ensures the highest level of accuracy in the data collected.

Conclusion

The collection of data for this effort is still in progress. Early analysis supports reported evidence that aggressive surgical removal of all evidence of CCS including lymph nodes is the best treatment option. When complete surgical resection is not possible then Sunitinib has shown the best albeit poor response rate (partial response rate 30%/mPFS 4 months) of systemic treatments options compared in a recent retrospective study.[1] Published studies are also generally in agreement that cytotoxic chemotherapy is not beneficial for CCS treatment.[2]

Future Directions

The research team at CCSF along with clinicians and researchers are working together to publish a paper on the findings of CCS patients' RWE collected in this EHRs effort. The intent is to help guide treatment for CCS patients toward promising options and away from options that RWE shows to be ineffective or even detrimental. The intent is also to expose the areas of the greatest need to focus future research. Going forward efforts will be made to analyze the EHRs and determine if particular systemic treatments or radiation or their combinations contribute to hyper-progressive disease in CCS as seen in other cancers.[3] Patient's themselves are often a rich source of data to improve diagnoses and to understanding the biology and the effect of treatments in ultra rare cancers like clear cell sarcoma.[4] CCSF held the first annual symposium on CCS to discuss the current state of CCS and a consensus paper is in preparation. Going forward, there will be workshops and symposiums held with CCS patients and caregivers along with clinicians and researchers focused on CCS to further efforts to improve patient outcomes.

References

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