Twenty Years of CTOS: The Transdisciplinary Society Dedicated to Studying the Rare and Helping the Underserved

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Since its inception in 1995, the international Connective Tissue Oncology Society (CTOS) has been dedicated to improving the clinical outcomes for patients with a rare but often aggressive form of mesenchymal neoplasia, collectively known as sarcomas. Physicians and scientists from around the world have come together once a year to share their latest data, imparting wisdom but also taking critical feedback from the membership. Every medical discipline is represented in the Society as well as on the board of directors and presidential line. Over the span of 20 years, we have grown from an initial meeting of ten experts gathering in the basement of Massachusetts General Hospital to over 1100 members from 29 countries. The last meeting, held in Salt Lake City, Utah, hosted 354 abstracts covering all aspects of sarcomatology and honored our founding father, Herman Suit, MD. Our featured speakers included two world-renowned clinical and molecular pathologists, Christopher Fletcher, MD, and Julia Bridge, MD, respectively. Symposia included models and approaches to the study of sarcoma, genetic risk, and adolescent and young adult oncology. We also had a special session dedicated to circulating tumor DNA. Each year has seen a growth in the quantity and quality of intellectual effort. Much thanks must be given to our immediate past president, Paolo Dei Tos, MD, our program co-chair, Matt van de Rijn, MD, PhD, and the program committee. Because the majority of the sarcoma professional community travels to CTOS, the American Association for Cancer Research (AACR) holds their sarcoma basic biology meeting

adjacent to CTOS when in the United States. Furthermore, SARC, the clinical trials organization, also holds one of their semiannual meetings at CTOS (the other being ASCO). This coming fall, we travel to Lisbon under the auspices of the *Annals'* own Alessandro Gronchi, who currently serves as our president. It is sure to be a magnificent program, with the latest and most relevant research in sarcomatology presented by our committed international membership.

In this month's issue of the *Annals*, two articles have been chosen to celebrate and reflect our commitment and passion to studying the rare and helping the underserved. The first, by colleagues in the Netherlands, investigates cell cycle activity in synovial sarcoma (SS), the most common soft tissue sarcoma in adolescents and young adults.¹ Although it is a connective tissue cancer whose cell of origin remains obfuscating (although it may be the myoblast), its relatively well-defined molecular chimeric pathogenic signature (SS18, –SSX1,2,4) makes it an attractive sarcoma to investigate for molecular targeting.^{2,3} SS can be quite aggressive, often consuming its host from metastatic propagation, and accordingly more refined biotargeting is needed. Specifically, Vletterie et al. looked at in vitro cyclin-dependent kinase activity but also assay expression of several key cell cycle regulators to determine its prognostic significance in over 40 human specimens. They also suggested that pablociclib may have a therapeutic role in a subset of SSs. While these data requires further preclinical support, perhaps in patient-derived xenographs or genetically engineered mouse models, it lays a foundation for further inquiry where therapeutic options remain quite limited.

The second article, by an Italian group, looked at response rates of the exceptionally rare epithelioid hemangioendothelioma (EHE) to sirolimus, a mammalian target of rapamycin (mTOR) inhibitor.⁴ By combining the

experience across their major centers since 2005, they were able to treat 17 patients with advanced or metastatic EHE and one case of retiform hemangioendothelioma. In addition to being a vanishingly rare cancer, the clinical behavior for EHE is hard to predict. Even when the disease is metastatic, the clinical course is not always fulminant, but it can be. Accordingly, therapeutic efficacy of a given drug or modality can be hard to prove for EHE. As cited by the authors, case reports suggest that antiangiogenics such as pazopanib may be a possible treatment option.^{5,6} This study, however, appears to be the largest in the literature, and the first to investigate an mTOR inhibitor. Accordingly, Stacchiotti et al. have set a baseline for comparison moving forward.

In closing, I want to thank the members of CTOS, past, present and future. It is the collective vision and drive of this society that enables us to learn from one another and collaborate across the world and disciplines. Because sarcomas are rare and heterogenous, finding sources of support and garnering the energy to tackle the challenges that face our patients are fleeting at best. As the torch

bearer, CTOS is striving to address the needs of an underserved global group of cancer patients in such dire need of medical breakthroughs.

DISCLOSURE The author is a Past President for CTOS and served as Program Chair for the 2015 meeting.

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