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Clinical Factors That Affect the Establishment of Soft Tissue Sarcoma Patient-Derived Orthotopic Xenografts: A University of California, Los Angeles, Sarcoma Program Prospective Clinical Trial

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Abstract

Purpose: Given the diverse and aggressive nature of soft tissue sarcomas (STSs), a need exists for more-precise therapy. Patient-derived orthotopic xenografts (PDOXs) provide a unique platform for personalized treatment. Thus, identification of patient and treatment factors that predict PDOX establishment is important. This study assessed the feasibility of incorporating PDOXs into the clinical setting and identifying factors associated with PDOX establishment.

Patients and methods: From May 2015 to May 2016, 107 patients with biopsy-proven or potential STS were enrolled. Tumor samples were obtained intraoperatively and orthotopically implanted into nude mice in the corresponding anatomic location. PDOXs were considered established after engraftment and serial passage. Factors associated with establishment were analyzed by logistic regression and time to establishment by time-to-event analysis.

Results: Only high-grade tumors established (32 of 72 [44.4%]). The establishment rate (ER) varied by neoadjuvant therapy and treatment response, with the highest ER among untreated high-grade tumors (26 of 42 [61.9%]). Tumors exposed to radiation preoperatively did not establish (zero of 11 [0%]), and tumors exposed to neoadjuvant chemotherapy had a lower ER(31.9%) than untreated tumors. Only STSs with minimal pathologic response to neoadjuvant treatment (≤ 30%) established a PDOX (six of 18 [33.3%]). Median establishment time was 54 days, which varied by neoadjuvant therapy but was not statistically significant (P = .180).

Conclusion: To our knowledge, in the largest STS PDOX study to date, we demonstrate a 62% ER among untreated high-grade tumors with a median establishment time of 54 days. Neoadjuvant therapy, particularly radiation, and pathologic response to treatment were associated with a reduced rate of PDOX establishment.

Conflict of interest statement

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST The following represents disclosure information provided by authors of this manuscript. All relationships are considered compensated. Relationships are self-held unless noted. I = Immediate Family Member, Inst = My Institution. Relationships may not relate to the subject matter of this manuscript. For more information about ASCO's conflict of interest policy, please refer to www.asco.org/rwc or po.ascopubs.org/site/ifc. Tara A. Russell No relationship to disclose Mark A. Eckardt No relationship to disclose Takashi Murakami No relationship to disclose Irmina A. Elliott No relationship to disclose Kei Kawaguchi No relationship to

disclose Tasuku Kiyuna No relationship to disclose Kentaro Igarashi No relationship to disclose Yungfeng Li No relationship to disclose Joseph G. Crompton No relationship to disclose Danielle S. Graham Stock and Other Ownership Interests: DaVita (I) Sarah M. Dry No relationship to disclose Nicholas Bernthal Honoraria: Daiichi Sankyo Consulting or Advisory Role: Onkos Surgical, Bonesupport Research Funding: Onkos Surgical Jane Yanagawa No relationship to disclose Anusha Kalbasi No relationship to disclose Noah Federman Stock and Other Ownership Interests: Genmab, Kite Pharma Consulting or Advisory Role: Zelda Therapeutics Bartosz Chmielowski Consulting or Advisory Role: Amgen, Bristol-Myers Squibb, Merck, Genentech, Roche, Eisai, Immunocore Speakers' Bureau: Genentech, Roche, Janssen Pharmaceuticals Travel, Accommodations, Expenses: Genentech, Roche, Bristol-Myers Squibb, Janssen Pharmaceuticals, Merck Arun S. Singh Consulting or Advisory Role: Eli Lilly, Daiichi Sankyo Speakers' Bureau: Eli Lilly, Eisai Travel, Accommodations, Expenses: Eli Lilly, Daiichi Sankyo, Eisai Stock and Other Ownership Interests: AntiCancer-PDOX Robert M. Hoffman Stock and Other Ownership Interests: AntiCancer-PDOX Fritz C. Eilber Stock and Other Ownership Interests: AntiCancer-PDOX

Figures

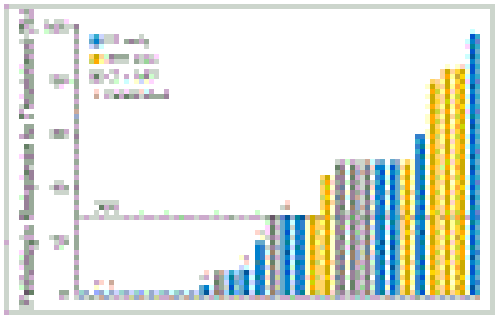

Fig 1.

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Pathologic response is associated with…

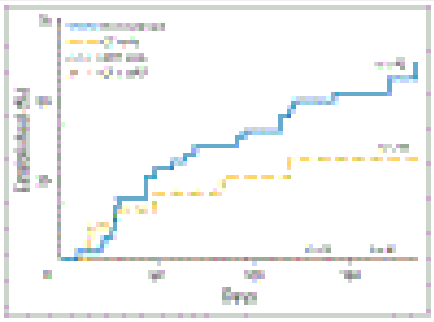

Fig 2.

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Time to establishment varied by…