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EDITORIAL – SARCOMA

Assessment of the PARITY Sub-Analysis "Neoadjuvant Chemotherapy and Endoprosthetic Reconstruction for Lower Extremity Sarcomas: Does Timing Impact Complication Rates?"

Lauren Zeitlinger, DO, and R. Lor Randall, MD

Department of Orthopaedic Surgery, University of California Davis School of Medicine, University of California, Sacramento, CA

The Prophylactic Antibiotic Regimens in Tumor Surgery (PARITY) study is a landmark study not only for musculoskeletal oncology patients but also for orthopedic oncologists as an academic community. The global study attempts to rigorously address a fundamental question of optimal duration of perioperative antibiotics to minimize postoperative surgical site infections (SSIs) in this high-risk group of patients undergoing endoprosthetic reconstruction for bone cancers.[1] Given the risk of infection approaches 10–20% in this cohort, it is important to further risk stratify these patients to gain a deeper understanding of factors affecting infection rates.[2] Furthermore, the consequences of infection after endoprosthetic reconstruction can be devastating, increasing the risk for subsequent amputation, and portends increased health care costs.[3–5] Antibiotic prophylaxis in other orthopedic surgical procedures has been studied extensively; however in orthopedic tumor patients, variations in chemotherapy, radiation, length of resection, immune status, need for soft tissue resection and coverage as well as other confounding variables make this difficult to provide evidence-based recommendations for prophylaxis. The PARITY study identified that 24 h of antibiotics was not inferior to a 5-day course of prophylactic antibiotics and was associated with less antibiotic-associated adverse effects and complications.[1] In efforts to further assess the impact of these findings, multiple subanalyses have been conducted to further expand on prophylactic antibiotic recommendations.

In their work entitled "Neoadjuvant chemotherapy and endoprosthetic reconstruction for lower extremity sarcomas: does timing impact complication rates?", Gazenda et al. propose that the timing between neoadjuvant chemotherapy and surgical intervention may impact infection rates.[6] Patients who received neoadjuvant chemotherapy were subdivided by duration between chemotherapy and surgery at <3 weeks, 3–6 weeks, and >6 weeks. Within the PARITY cohort, 216 patients received neoadjuvant chemotherapy and most of these patients had osteosarcoma. The authors found there was no statistically significant increased risk for SSI in any time point after chemotherapy (differing from the results reported by Sutton et al.) and that neutropenia did not affect SSI infection rates.[2,6] They did however identify that duration of surgical procedure was an independent risk for SSI, with a hazard ratio of 1.21 per hour.[6]

While informative to comment on duration between chemotherapy and surgical intervention, the authors did not subdivide this category into those patients randomized by PARITY into 24 h of antibiotics versus a 5-day course. It is possible that these groups could have demonstrated differences that were unidentified. It is also unknown how the effect of surgical time impacts SSI rates in patients who did not receive neoadjuvant chemotherapy, and the results for this cohort may differ. Lastly, additional considerations such as need for soft tissue coverage for wound closure could likely impact both surgical time and also risk for infection, which was not addressed in this subanalysis. Ideally, the results of these subanalyses will allow for a risk stratification, where those with increased risk for SSI may

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L. Zeitlinger, DO
e-mail: Lauren.zeitlinger@gmail.com

benefit from an extended course of prophylactic antibiotic therapy while minimizing risk for antibiotic-related complications for those at lower risk.

A very important additional consideration is that it has been demonstrated that an overall delay in resumption of chemotherapy of more than 3 weeks from definitive surgical local control for non-metastatic osteosarcoma has been shown to be a poor prognosticator in terms of overall survival.[7] Accordingly, it is important that surgeons do all that they can to effect local control as soon as it is safe to do so during the local control window.

Ultimately, we are grateful for the efforts of the PARITY study team and subcategory investigators. This work is a paradigm setting for more questions yet to be answered. We are eager to see the results of several subanalyses that are forthcoming. These studies will impact care tremendously for these high-risk patients and will hopefully result in a stratification model to prevent SSI and subsequent complications, all while minimizing complications from antibiotic prophylaxis.

DISCLOSURE Lauren Zeitlinger and R. Lor Randall have no disclosures to declare.

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