To slay a dragon: Timing of chemotherapy in resectable pleural mesothelioma

Bryan M. Burt, MD, R. Taylor Ripley, MD, and Shawn S. Groth, MD, MS

From the Division of General Thoracic Surgery, The Michael E. DeBakey Department of Surgery, Baylor College of Medicine, Houston, Tex.

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Address for reprints: Bryan M. Burt, MD, Division of General Thoracic Surgery, Department of Surgery, Baylor College of Medicine, One Baylor Plaza, BCM 390, Houston, TX 77030 (E-mail: bryan.burt@bcm.edu).

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Central Message
Innovative treatment approaches to MPM are required to meaningfully affect survival for those with this disease.

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Only the surgeon knows the completeness of resection at the time of pleurectomy/decortication (P/D) or extrapleural pneumonectomy (EPP) for malignant pleural mesothelioma (MPM). MPM is a tumor that develops along pleural surfaces; therefore, resection margins cannot be assessed by conventional methods. A true microscopic complete (R0) resection in MPM is not possible or measurable. Rather, the goal is complete “cytoreduction” through a macroscopic complete (R1) resection, although this model has recently been challenged by retrospective evidence supporting a survival benefit of less complete (R2) resections.

Because of the inability of surgery alone to effectively treat microscopic disease, resection should be performed only in a multimodality treatment setting, which often includes chemotherapy. In fact, the survival benefit of surgery alone is inferior compared with surgery as part of a multimodal treatment strategy. However, the optimal sequence of chemotherapy and surgery is unknown and is currently being evaluated in a randomized phase II trial (NCT02436733).

In their thoughtful analysis of the National Cancer Database, Verma and colleagues compared induction and adjuvant chemotherapy for patients undergoing resection for node-negative epithelial/biphasic MPM in propensity-matched groups. Overall survival was similar in each group. However, postoperative morbidity and mortality were higher in the induction group. Although these results seem to favor adjuvant chemotherapy, many patients are unable to receive chemotherapy in the postoperative setting, likely secondary to the extended recovery that patients require to overcome the significant physiologic impact of a P/D or EPP. Unfortunately, these data were not available in this study.

Despite a number of controversies in the multimodal treatment of MPM, such as the use of chemotherapy in the neoadjuvant versus adjuvant setting, the use of EPP versus P/D, the use of intraoperative adjuvant therapies (heated chemotherapy, Betadine, photodynamic therapy), and the inclusion of radiation therapy (and what modality), the steep descent of modern-day survival curves for MPM is sobering. Although large dataset studies have demonstrated a statistically improved survival for patients undergoing surgery as a component of their treatment regimen, at times, the survival benefit appears marginal. Offsetting this nihilistic view of the current state of MPM treatment for patients with MPM, there is a growing number of randomized trials in other malignancies demonstrating improved efficacy of immunotherapy in the form of checkpoint blockade, alone and in combination with chemotherapy, compared with standard chemotherapy. Although the published data for checkpoint blockade in MPM are from patients with unresectable disease in phase I and II trials and retrospective analyses, the results are encouraging. Although rates of objective response are approximately 20%, rates of durable clinical response are approximately 50%. It is reasonable to anticipate that incorporating checkpoint blockade into the multimodal approach to MPM including resection may impart a favorable impact on the ominous survival statistics that we have become accustomed to citing.

References


