Ann Surg Oncol (2020) 27:623–624
https://doi.org/10.1245/s10434-019-08185-y

Annals of
SURGICAL ONCOLOGY
OFFICIAL JOURNAL OF THE SOCIETY OF SURGICAL ONCOLOGY

EDITORIAL – THORACIC ONCOLOGY

Those Who Cannot Remember the Past are Condemned to Repeat It

Daniel P. Raymond, MD

Cleveland Clinic Foundation, Cleveland, OH

In the late 20th century, competing cancer theories struggled to explain the fact that long-term survival was achievable for a limited set of patients with a low burden of metastatic disease. In 1995, Hellman and Weichselbaum[1] proposed the concept of the oligometastatic state as a component of the spectrum theory of cancer. Formerly, two theories dominated the field. The one was the Halsted theory, which described cancer as an orderly inexorable progression from primary site to lymphatic system to systemic metastases and explained the locoregional approach to oncologic surgery. The other was the more contemporary systemic theory, which suggested that any clinically evident cancer is a systemic process.

The spectrum theory suggests that cancer can present in a variety of ways, including the oligometastatic state. The current literature abounds with predominately retrospective studies that affirm the notion of the oligometastatic state. This literature, however, is challenged by several common themes. The most obvious are patient selection bias and biologic selection bias. These studies are potentially selecting the healthiest patients with more indolent disease. Thus, the question remains, is the treatment responsible for any improvement in survival? Additional challenges include the notion of immortal time bias[2] and the simple variability in the definition of the "oligometastatic state." Does this include synchronous and metachronous oligometastases, oligoprogression, and oligorecurrence?

Ohkura et al.[3] present their data on the treatment of oligometastatic esophageal cancer. They demonstrate the ability of patients with oligometastatic disease and find the oligometastatic presentation to be a statistically significant predictor of survival. The standard challenges mentioned earlier, however, remain with these data. Biologic selection is quite obvious because these patients with stage 4 cancer have a 5-year survival rate of 51.7%, much higher than the standard survival for stage 2 or 3 populations in general. Furthermore, the patients in the study were only those who could tolerate a major operation for treatment of disease, thus contributing significantly to selection bias. Moreover, the patients were treated by various means including endoscopic definitive chemotherapy and radiation therapy, as well as surgery, thus introducing some question of how local control and oligometastases are defined.

Regardless, what the authors have challenged is the nihilism often encountered in dealing with stage 4 disease. Currently, a method to identify those patients with a true oligometastatic presentation versus those presenting the mere tip of the iceberg is needed to avoid the overuse of local therapies in scenarios that will not benefit from them.[4] Mutational analysis may some day offer the answer to this challenge, which then can be verified only with a rigorous randomized trial.

We must be conscious of the lessons from history, including that of stem cell transplantation for breast cancer. An estimated 40,000 women were subjected to a costly and morbid therapy that ultimately was demonstrated in well-conducted randomized trials to offer no benefit. In hindsight, many of the same challenges faced in the oligometastatic scenario, including patient selection and biologic selection, led 80% of oncologists to believe incorrectly that this morbid therapy was the standard of care.[2] We must therefore combat nihilism, yet balance

First Received: 19 December 2019;
Published Online: 7 January 2020

D. P. Raymond, MD
e-mail: Raymond3@ccf.org

enthusiasm and hope with a healthy dose of skepticism until an appropriate randomized trial can answer this challenging question.

DISCLOSURES Daniel P. Raymond, MD, has stock ownership in Bristol Myers Squibb.

REFERENCES

1. Hellman S, Weichselbaum RR. Oligometastases. *J Clin Oncol.* 1995;13:8–10. https://doi.org/10.1200/jco.1995.13.1.8.
2. Palma DA, et al. The oligometastatic state: separating truth from wishful thinking. *Nat Rev Clin Oncol.* 2014;11:549–57. https://doi.org/10.1038/nrclinonc.2014.96.
3. Ohkura Y, Shindoh J, Ueno M, Iizuka T, Udagawa H. Clinicopathologic characteristics of oligometastases from esophageal cancer and long-term outcomes of resection. *Ann Surg Oncol.* 2020. https://doi.org/10.1245/s10434-019-08175-0.
4. Kaneda H, Saito Y. Oligometastases: defined by prognosis and evaluated by cure. *Cancer Treat Commun.* 2015;3:1–6.