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See Article page 1549.

Commentary: Evidence over dogma: Lung transplant for posthematopoietic stem cell transplant related pulmonary failure

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Recent malignancy within 2 years has been deemed an absolute contraindication to lung transplant listing ever since the first edition of the recipient selection guidelines put forth by the International Society for Heart and Lung Transplantation in 1998.¹ In their most recent consensus from 2014, hematologic malignancies are specified among others in whom a disease-free interval (DFI) of 5 years is recommended.² Noguchi and colleagues³ in their recent study sought to demonstrate that, with appropriate selection based on estimated recurrence rates, patients with previous hematologic malignancies treated with hematopoietic stem cell transplant (HSCT) can safely undergo lung transplant without reaching a 5-year DFI.

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CENTRAL MESSAGE

Five-year disease free-interval, while safe, may not be necessary in well-selected hematopoietic stem cell transplant patients who develop early pulmonary complications and failure.

The study presented included all lung transplants at their institution for pulmonary complications after HSCT but placed focus on 2 distinct aspects of these complicated patients: a disease process that does not allow for an extended DFI and the alteration of blood type after HSCT. In response to the early onset of post-HSCT lung failure, their protocol allows for lung transplant candidacy after 2 years for cadaveric lung transplant and earlier for living-donor lung transplant if the risk of recurrence of primary malignancy is considered less than 30%. While the authors do not clearly outline the methods of determining anticipated recurrence rates, it is important to note that the rate of primary malignancy relapse is greatest within the first 5 years following HSCT.⁴ A stratification to “standard risk” versus “high risk” based on malignancy characterization at time of

HSCT may be the difference between a 20% recurrence rate and a 40% to 80% recurrence rate, respectively.⁵ Regardless of their patient selection criteria, the authors did not find any disease recurrence following lung transplant during their study period. If sufficient stratification to high or low risk of recurrence is truly feasible, then an overarching rule of 5-year DFI for all hematologic malignancies may be an overreach. This provides hope for patients whose estimated life expectancy is less than 5 years secondary to severe pulmonary illness.

The second dogma that the authors have challenged is the use of ABO-incompatible donors, given the patient's lack of antibodies to donor antigens. Regardless of current ABO blood type after HGCT, the testing of anti-A/B antibodies in their study demonstrated varied findings or lack of any anti-A/B antibodies. Using living ABO-incompatible donors, the authors were able to expand the donor pool for 5 patients who successfully underwent mismatched transplant without further intervention. With all 5 patients alive and a follow-up of 1.5 to 8 years, initial results suggest good outcomes.

Understanding the disease biology of primary malignancy is key in offering these patients organ transplant. The 5-year DFI rule has served us well for the most part and remains the standard of care. This new evidence not only provides hope but also highlights our understanding

or lack thereof in cancer biology. In practice, patients who receive HSCT are a small portion of patients with cancer who need lung transplant. More commonly, we find ourselves unable to offer potentially lifesaving transplant to patients with recent breast, colon, lung, prostate cancers, and melanoma. A better handle on predicting recurrence based on tumor biology may allow us to better select some such patients who may not need to wait for 5 years. More importantly, modulating the iatrogenic immune deficiency and preventing tumor immune-evasion is key in prolonging survival after solid-organ transplant.

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