Melanoma Surveillance Strategies: Different Approaches to a Shared Goal

Keisuke Shirai, MD, MSc¹ and Sandra L. Wong, MD, MS²

¹Department of Medicine, The Geisel School of Medicine at Dartmouth and Dartmouth-Hitchcock Medical Center, Lebanon, NH; ²Department of Surgery, The Geisel School of Medicine at Dartmouth and Dartmouth-Hitchcock Medical Center, Lebanon, NH

In this issue of *Annals of Surgical Oncology*, Read et al. describe the patterns of follow-up for a cohort of clinical stage I and II melanoma patients diagnosed between 2006 and 2007 in New South Wales, Australia.¹ Major findings are that nearly all of these early-stage patients were recommended to have some type of post-treatment follow-up, and most patients were provided with skin self-examination techniques and education about skin changes that might indicate melanoma. Many of the findings reported by Read et al. are not surprising but highlight the need for more nuanced discussions around surveillance strategies.

We have seen the landscape of melanoma treatment for advanced disease change completely since 2011, starting with the US FDA approval of the immune checkpoint inhibitor ipilimumab, an anti CTLA-4 antibody. This was followed in rapid succession by six other agents, including anti-PD1 antibodies (pembrolizumab and nivolumab), BRAF inhibitors (dabrafenib and vemurafenib), and MEK inhibitors (trametinib and cobimetinib).

These major advances in melanoma treatment have established the availability of effective treatment for advanced disease. As such, melanoma surveillance strategies deserve assessment and re-evaluation. On one hand, a relatively higher intensity surveillance strategy (e.g. shorter intervals between prescribed follow-up) could be leveraged to take advantage of earlier detection to allow for earlier treatment. Conversely, relatively lower-intensity

surveillance could be justified because there are, in fact, available and effective treatments.

Read et al. have addressed many of the important tenets of melanoma surveillance and survivorship care, including an emphasis on opportunities for patient education and a focus on treatment-related morbidity and psychosocial distress.¹ We take this opportunity to highlight the principles of evidence-based, goal-directed, and individualized surveillance recommendations. These principles should help inform what the most effective follow-up regimens for early-stage melanoma are, given the currently available treatment options for detected recurrences.

Guidelines for surveillance should be evidence-based Comprehensive evaluation of the existing literature demonstrates that there is no definitive benefit derived from increased screening or more aggressive use of interval imaging for patients with treated melanoma.² Patient outcomes do not seem to be impacted by lower-intensity surveillance strategies compared with higher-intensity strategies.

Just as recommended tests target the most likely sites of recurrence and are best selected by measures of sensitivity and specificity, the suggested interval between follow-up visits should be informed by disease stage and its associated natural history. Albeit with varying parameters, most guidelines match the intensity of follow-up with relative risk of recurrence, and tend to promote decreased frequency of visits over time.

Shorter intervals between surveillance visits are resource intensive but could theoretically allow for earlier detection and treatment of disease. However, few data are available to suggest that surveillance improves survival for the majority of patients with stage I or II disease. In fact, to the contrary, data are available to suggest that most recurrences are detected by the patient or their partners

between surveillance visits, which highlights the importance of education even though the role of patient education and its effectiveness in advancing patient-based detection of new or recurrent disease remains generally unknown, although relatively well-accepted.

Surveillance should be goal-directed Melanoma is a heterogeneous disease. Prognosis varies greatly by stage at presentation, and outcomes are not uniformly excellent, even with early-stage disease. Recent data show that patients with stage I and II disease have 5-year melanoma-specific survival rates of 82–99%. With longer follow-up, these patients continue to experience appreciable rates of local, regional, and distant recurrences, and 10-year melanoma-specific survival rates are reported as 75–98%.³

The optimal intervals for surveillance are undoubtedly influenced by the relative lag in time to recurrence as patients and providers weigh the benefits of ongoing reassurance with the risks of anxiety associated with resource-intensive clinic visits over a long period of time. Also reporting from the Australian experience, a retrospective study of early-stage melanoma patients followed at 3- to 6-month intervals showed that for every 1000 patients, more than 8000 clinic visits were conducted. Only a very small difference in modeled delays in diagnosis was noted with a far less intensive follow-up plan—an estimated 3000 fewer visits per 1000 patients.⁴

Individualized or tailored surveillance regimens Minor variation in patterns of recommended follow-up were demonstrated in the study by Read et al.¹ Studying variation can certainly help detect best practices, but this descriptive study did not report associated outcomes. Undoubtedly, the need for relatively long surveillance in this patient population, along with many other patient and provider factors, influence compliance with any follow-up recommendations. In the current era of precision/personalized medicine, we are still woefully under-informed and unable to provide customized prognostication.

While there appears to be a high level of consensus around the importance of surveillance following melanoma

diagnosis and treatment, there is little evidence to guide what constitutes an optimal regimen. In the setting of modern melanoma treatment for advanced disease, goal-directed surveillance would ideally be tailored to a patient's individual risk of recurrence.

In the current era of immune checkpoint inhibition and targeted therapy, improvements in survival rates are already being seen for those with advanced disease.⁵ Furthermore, for patients with known nodal involvement, emerging data and treatment strategies are already challenging the paradigms of surveillance since completion lymph node dissection or careful observation are options for patients with low-risk micrometastatic disease detected with sentinel lymph node biopsy.⁶ However, it appears that 'one size fits none' and there are sizable knowledge gaps in the area of surveillance, including the need for better understanding of patient preferences and the related impact of surveillance on a patient's psychosocial fitness.

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