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INTRODUCTION

Melanoma is the deadliest skin cancer: it is estimated that 91,270 cases will be diagnosed in 2018 and of these, 9,320 patients will die of melanoma.[1] The incidence of melanoma has been increasing relentlessly over the last few decades, and while melanoma only comprises approximately 3% of all skin cancers, it accounts for a large fraction of mortality due to skin cancer. The most effective treatment for melanoma is early detection and surgical removal of the primary lesion. In order to effectively diagnose melanoma, pathology plays a key role in differentiating melanoma from other melanocytic skin lesions. In the first article of this issue of *Seminars in Cutaneous Medicine and Surgery,* Drs Messina and Gibbs review the pathology of melanocytic lesions. They have provided an excellent review and commentary on our current understanding of the molecular and clinical features of different subtypes of melanoma and the prognostic implications of these molecular and pathologic features

Surgical therapy remains the most effective treatment for cure in early stage melanoma. In addition, surgical therapy is an essential component of multidisciplinary care in regional and advanced melanoma. The review by Burke and Sondak reprises surgical therapy for melanoma and discusses the complexities of surgical treatment. They discuss margins and reconstruction in primary excision and the issue of melanoma and spitzoid lesions in children, an issue often arising in multidisciplinary melanoma programs. The current state of knowledge in sentinel lymph node biopsy and completion lymphadenectomy is discussed as well as metastatectomy for late-stage melanoma patients. Burke and Sondak also discuss intratumoral therapy, which is increasingly used (especially with the approval of the oncolytic virus, talimogene laherpervec) for in-transit and satellite metastases.

Recently, the adjuvant (postoperative) therapy of melanoma has undergone drastic change. While the choices were restricted to a single agent 5 years ago, several more effective choices are available today. Moser and Grossmann review these options and provide data on PD-1 and CTLA-4 antibodies and on targeted therapies and put these in perspective in light of recent clinical trials. This remains an area that is currently in flux and the review provides a roadmap for where we are currently.

The therapy of advanced melanoma has probably changed most drastically of all. While chemotherapy was the mainstay of therapy 10 years ago, it is infrequently used today. In its place are two effective approaches, targeted therapy and immunotherapy. About 50% of all melanomas have mutations in the BRAF gene and another 15% have mutations in the NRAS gene. Dr Ryan Sullivan reviews the data for these genomic mutations and their biology in melanoma. He discusses targeted therapy in melanoma and provides an expert analysis and commentary for clinicians confronted with these issues as well as various combinations of BRAF and MEK inhibitors that are clinically useful, along with side effect profiles.

Another area of great advance in the management of melanoma is the area of immunotherapy. While the immune system has been used to treat cancers since ancient times, the discovery of the immune checkpoint inhibitors and their astounding efficacy in some patients with melanoma has led to transformational changes. However, it is clear that not all patients benefit, and making the right choice is of enormous importance although the data here are fluid and constantly evolving. Johnson et al bring to life the tumor microenvironment, review this enormous field, and discuss the various biomarkers and experimental data supporting their association with response. The last article, from our group at UCSF, discusses the use of immune checkpoint inhibitors and immunotherapy in melanoma.

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