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Part II: Checkpoint inhibitors in cancer therapy

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The second part of this special focus issue on checkpoint inhibition in cancer therapy covers some exciting new directions. Stahl *et al.* report on research targeting the KIT receptor and pathway in innate immune cells [1]. The report focuses on myeloid-derived suppressor cells (MDSCs), which are known to play an important role in creating tumor tolerance. They summarize data using a novel monoclonal antibody to target KIT and show that it can add to checkpoint inhibition. The next report, from Loo *et al.* (our group at UCSF) reviews emerging biomarkers such as flow cytometry-derived assays and compares these to existing PD-L1 and tumor-infiltrating lymphocyte (TIL) assays [2]. While melanoma is the focus of much attention in immunotherapy, the checkpoint inhibitors are active in renal cell cancer (RCC) as well. Zibelman *et al.*, trace the evolution of immune therapy for RCC and describe the emerging data for these agents [3]. The authors show that there are some important differences with regards to biomarkers in RCC versus melanoma and lung cancer.

While checkpoint inhibitors are known to lack the side effects typical of chemotherapy or targeted therapy, the reality is that they

have their own unique and distinctive spectrum of side effects. These vary by organ site and by the specific pathway inhibited and the specific agent used as described in an extensive review by Kourie and Klaster-sky [4]. Immune checkpoint inhibitors show (unexpected) activity in lung cancer and in hematological malignancies. The spectrum of activity in lung cancer extends to both squamous and adenocarcinoma subtypes and has its distinctive organ-specific characteristics and an emerging pattern with regard to PD-L1 as described by Janakiram *et al.* in the next article [5]. These authors also describe the interesting observation that Hodgkin's disease appears to be very sensitive to PD-1 and the exploratory work in other hematologic malignancies. Last, but certainly not the least is a thought-provoking overview of immune checkpoint inhibitors by Kyi and Postow [6]. Given the activity seen in numerous locations and the emerging combinations being tested, these authors place these developments in context and provide an extensive bibliography for readers to explore. These reviews emphasize both the enormous distance traveled in the last few years and the gaps in our knowledge of immune checkpoint inhibition.

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References

- 1 Eder J, Stahl M, Gedrich R, LaVallee T, Peck R. Targeting KIT on innate immune cells to enhance the antitumor activity of checkpoint inhibitors. *Immunotherapy* 8(7), 764–774 (2016).
- 2 Loo K, Daud A. Emerging biomarkers as predictors to anti-PD1/PD-L1 therapies in advanced melanoma. *Immunotherapy* 8(7), 775–784 (2016).
- 3 Zibelman M, Ghatalia P, Geynisman D, Plimack E. Checkpoint inhibitors for renal cell carcinoma: current landscape and future directions. *Immunotherapy* 8(7), 785–798 (2016).
- 4 Kourie HR, Klásterský JA. Immune checkpoint inhibitors: side effect and management. *Immunotherapy* 8(7), 799–807 (2016).
- 5 Janakiram M, Pareek V, Cheng H, Narasimhulu DM, Zang X. Immune checkpoint blockade in human cancer therapy: lung cancer and hematologic malignancies. *Immunotherapy* 8(7), 809–819 (2016).
- 6 Kyi C, Postow MA. Immune checkpoint inhibitor combinations in solid tumors: opportunities and challenges. *Immunotherapy* 8(7), 821–837 (2016).