

significantly higher baseline IL-17 ($p = 0.009$, figure 1B). There was a trend towards lower GCSF levels in patients developing colitis ($N = 8$, $p = 0.08$, figure 1C). We observed a harmonization of cytokine fold-change in patients who developed irAEs without receiving steroids: 269/276 (97.5%) of pairwise comparisons exhibited fold-change in the same upwards or downwards direction (figure 2). In contrast, corticosteroid treatment in patients with irAEs appeared to alter cytokine fold-change to a discordant pattern (214/276, 77.5%) mirroring patients who did not develop irAEs during the longitudinal profiling period (213/276, 77.2%). Example patient timelines are shown in figure 3.

Conclusions Baseline cytokine levels correlate with specific irAEs in melanoma patients receiving ICIs. irAEs appear to drive a concordant pattern of cytokine fold-change, which is disrupted by corticosteroid administration. These findings should be validated in larger cohorts.

Ethics Approval Patients were identified from DFCI's melanoma bio-specimen banking protocol (DFCI protocol 05-042)

REFERENCES

- Rahma OE, Ott PA. General Principles of Immune-Related Toxicities. In: Ennstoff M, Puzanov I, Robert C, Diab A, Hersey P, ed. *SITC's Guide to Managing Immunotherapy Toxicity*. Society for Immunotherapy of Cancer; 2018: Chapter 5.
- Hodi FS, O'Day SJ, McDermott DF, et al. Improved survival with ipilimumab in patients with metastatic melanoma. *N Engl J Med* 2010;**363**:711–723.
- Faje AT, Lawrence D, Flaherty K, et al. High-dose glucocorticoids for the treatment of ipilimumab-induced hypophysitis is associated with reduced survival in patients with melanoma. *Cancer* 2018;**124**(18):3706–3714.
- Arbour KC, Mezquita L, Long N, et al. Impact of baseline steroids on efficacy of programmed cell death-1 and programmed death-ligand 1 blockade in patients with non-small-cell lung cancer. *J Clin Oncol* 2018;**36**(28):2872–2878.
- Libert C, Dejager L. How Steroids Steer T Cells. *Cell Reports* 2014;**7**(4):938–939.

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INCIDENCE OF THROMBOEMBOLISM (TE) IN PATIENTS WITH MELANOMA RECEIVING IMMUNE CHECKPOINT INHIBITOR (ICI) THERAPY AND ITS ADVERSE IMPACT ON SURVIVAL

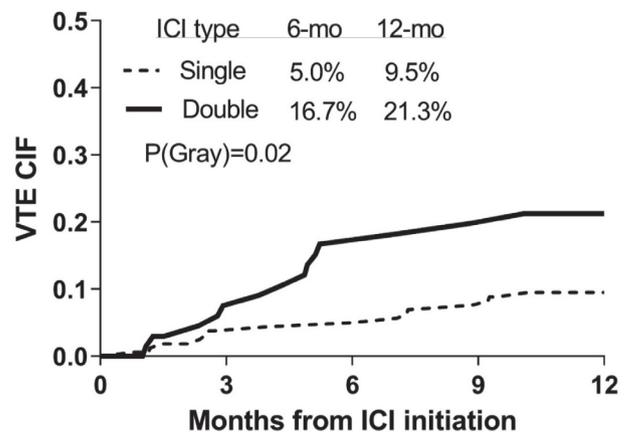
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Background Little is known about rates of arterial thromboembolism (ATE) and venous thromboembolism (VTE) in patients with melanoma on ICI. We assessed incidence and outcomes of ATE and VTE in patients with melanoma receiving ICI.

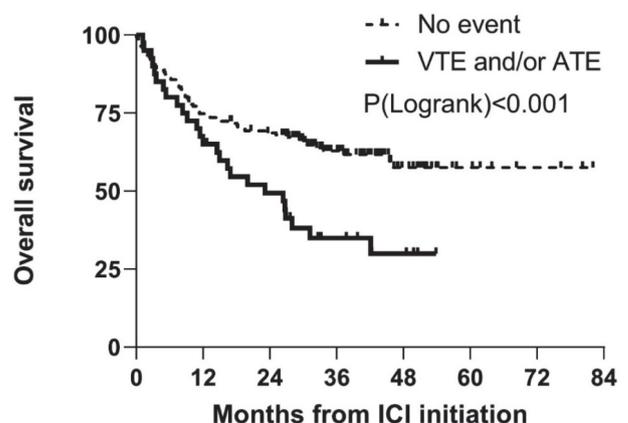
Methods We conducted a retrospective cohort study of patients with melanoma receiving ICI from July 2015 through December 2017 at Cleveland Clinic. TE including VTE events of deep venous thrombosis (DVT), pulmonary embolism (PE), visceral vein thrombosis (VVT), and ATE events of myocardial infarction (MI), stroke, or transient ischemic attack (TIA) after ICI initiation were identified. Overall survival (OS) from ICI initiation was estimated by Kaplan-Meier and Cox hazard models; associations between TE, ICI regimen, and clinical risk factors were evaluated using log-rank test.

Results The study population comprised 228 patients with median age 65 (23–91) years, 67% male, and median follow up 27.3 months. Pembrolizumab was most commonly used (38.7%), followed by combination ipilimumab plus nivolumab (29.4%), ipilimumab (20%), and nivolumab (12.3%). Most had stage IV disease (81.1%) and 11% had brain metastases (BM) at treatment initiation. Fifty-one TE events occurred in

47 patients (20.6%), including 37 (16.2%) VTE and 14 (6.1%) ATE. Of VTE, DVT comprised 46.0%, PE 24.3%, DVT+PE 21.6%, VVT 5.4%, and DVT+VVT 2.7%. Of ATE, stroke comprised 57.2%, MI 35.7%, and TIA 7.1%. Of all TE events, 72% resulted in hospitalization and 19% resulted in clot-related mortality. Cumulative incidence of TE after ICI initiation was 9.3% (95%CI,6.0–13.6%) at 6 months, and 16.0% (95%CI,11.6–21.2%) at 12 months. The 6- and 12-month VTE cumulative incidence rates were 8.0% (95%CI,4.9–12.0%), and 12.9% (95%CI,8.9–17.7%), respectively. The 6- and 12-month ATE cumulative incidence rates were 2.2% (95%CI,0.84–4.8%), and 4.5% (95%CI,2.3–7.8%), respectively. The 6- and 12-month VTE cumulative incidence rates were higher with combination ICI than single agent (16.7% vs. 5.0% and 21.3% vs. 9.5%, respectively; $p=0.02$) (figure 1). Risk factors associated with VTE in univariate analysis included BM, stage IV disease, combination ICI, and Khorana score ≥ 1 ($p<0.05$ for all). In multivariate analysis, combination ICI (HR 2.21; [95%CI,1.04–4.72]; $p=0.04$) and Khorana score ≥ 1 (HR 2.48; [95%CI,1.18–5.20]; $p=0.02$) remained significantly associated with VTE. Of patients without BM, OS was worse in patients with TE compared to those without (3-year OS 34.9% vs. 62.9%; HR 1.84; [95%CI,1.16–2.93]; $p<0.001$), when adjusted for age, stage, and Khorana score (figure 2).



Abstract 649 Figure 1 Cumulative incidence of VTE, stratified by ICI type
*Death before VTE was considered a competing risk in CIF estimation



Abstract 649 Figure 2 OS in patients without BM stratified by TE status

Conclusions ICI is associated with a high incidence of TE in patients with melanoma; TE is associated with substantial worsening of survival.

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651 NEUROLOGICAL ADVERSE EVENTS ASSOCIATED WITH IMMUNE CHECKPOINT INHIBITORS: OUR EXPERIENCE IN A TERTIARY CARE CENTER

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Background Immune checkpoint inhibitors (ICIs) have become a revolution in the treatment of many tumoral diseases, resulting in a significant increase in terms of life expectancy and quality of life. Despite these outstanding advances in long-life survival, a new spectrum of adverse events has been developed and is known to be one of the biggest challenges in clinical practice nowadays. Immune-mediated neurotoxicity stands out as a rather unusual complication, but its potentially lethal consequences make the characterization and right management of this adverse event a crucial issue in this field.

Methods This is a retrospective study including all the cancer patients that have developed any neurological adverse event related to ICIs treatment, in a period of 4 years (from 2017 to 2020).

Results 13 patients were included in the study (8 were treated with antiPD-1/PD-L1 immunotherapy, 1 with antiCTLA-4 and 4 with the combination of both strategies). 4 patients developed generalized myasthenia gravis (GMG), 4 immune-mediated encephalitis (IME), 3 immune-related encephalopathy without radiological/analytical evidence of encephalitis, 1 mixed-polyneuropathy, and 1 polymyositis. 3 patients with GMG were seropositive, 3 developed the clinical feature within the first 21 days of immunotherapy treatment and all of them received antiPD-1/PD-L1 treatment. All patients with IME showed pleocytosis in cerebrospinal fluid, without any data in brain MRI. 12 patients suspended ICIs treatment after the event and were treated with high doses of intravenous corticosteroids. Half of them required treatment with intravenous immunoglobulins. 10 showed total or partial resolution as clinical outcome. However, 4 patients passed away due to toxicity (2 with GMG). In severe cases that precise ICU admission, 4 out of 6 patients (66%) showed a spectacular clinical improvement with complete recovery after early treatment with high doses of methylprednisolone and intravenous immunoglobulins. ICIs withdrawal was sustained indefinitely in all patients, showing a progression-free survival at six-months of 50%. In patients with tumoral diseases that have an indication of treatment with ICIs, the PFS at 6 and 12 months stands at 66%.

Conclusions In this series, the majority of neurotoxicity was related to anti-PD1/PD-L1 treatment, appearing in the first 21 days within the treatment. Most of the patients showed a favourable clinical outcome. In severe cases, an improvement in clinical features was objective after an early onset of treatment with high doses of intravenous corticosteroids and immunoglobulins. ICIs withdrawal did not suppose harm in terms of PFS in patients with tumoral types where ICIs are already indicated.

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652 EARLY OUTCOMES OF AN APP ACUTE CHECKPOINT INHIBITOR (CPI) CARE CLINIC

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Background Checkpoint inhibitors continue to be used for a wide variety of oncologic and hematologic indications. Early recognition and intervention is crucial to prevent significant morbidity and/or mortality from immune related adverse events (irAE's). Physicians and APPs outside of hematology/oncology practices are generally not familiar with these types of side effects which may lead to treatment delays, and inappropriate management. We recently identified this as a gap in continuity of care amongst patients undergoing CPI therapy for their malignancy, and therefore developed a CPI acute care outpatient clinic, designed to meet this need.

Methods Starting April 2020, we developed an CPI focused clinic led by 3 APPs to provide outpatient irAE management 5 days a week. Three types of needs were identified: acute (within 24 hours), post hospitalization (within 48 hours of discharge), and long term follow-up (high grade irAE).

Results From April 24-August 24, 2020 our CPI clinic had a total of 50 visits (30 unique patients). Given that many patients to our practice are from > 2 hours away, as well as the constraints of the current pandemic, visits were conducted as in person, video consult (telemedicine), or phone. The most common regimens for patients were PD-1 alone (10), PD-1 + targeted (7), dual CPI (6), PD-1 + chemotherapy, and clinical trial, PD-L1 alone, PD-L1 + chemotherapy (1 each). The top three types of malignancies seen were melanoma (7), lung (6) and gynecological (4). The most common irAE referral reason was hepatitis (8), diarrhea/colitis (6) and thyroiditis (4). Only three patients (10%) required higher level care (i.e ED or admission) than was able to be provided in the clinic. Twenty-two patients (73%) required steroids as their initial treatment for irAE, with 4 patients (13%) requiring referral to other specialties. Twelve patients (40%) presented with ≥ 2 irAE's at the time of being seen in clinic.

Conclusions Herein we present early data from an acute care APP led CPI outpatient clinic. Most patients required initiation of steroids for their irAE, however only a small majority required higher level of care and were able to be managed as an outpatient. We acknowledge that while our cohort of patients is small, it does provide early evidence of the utility of a CPI acute care clinic and additional hypothesis generating clinical questions.

Ethics Approval This study was approved by the institutional review board at Mayo Clinic

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653 DASATINIB AS A RAPID PHARMACOLOGICAL ON/OFF SWITCH FOR T CELL BISPECIFIC ANTIBODY-INDUCED T CELL ACTIVATION AND CYTOKINE RELEASE

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Background T cell bispecific antibodies (TCBs) are extremely potent T cell engagers, harboring a 2+1 format with one binder to the CD3 ϵ chain and two binders to specific tumor antigens. Crosslinking of CD3 with tumor antigens triggers T cell activation, proliferation and cytokine release, leading to