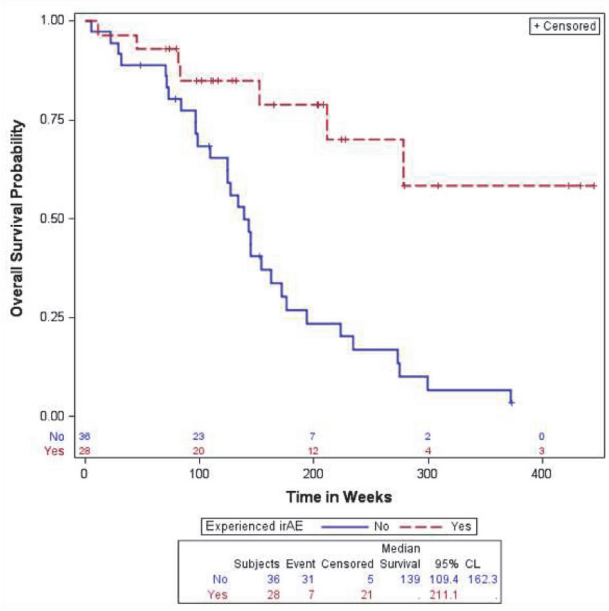
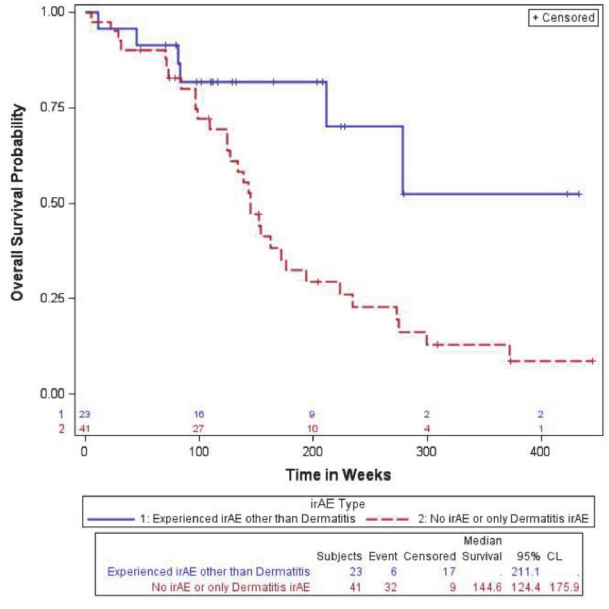


Abstract 191 Figure 1 Kaplan-Meier survival plot of OS between patients with any irAE and those without any irAE

Cox proportional hazards and logistic regression models, and Kaplan-Meier curves were plotted for subgroups.

Results A total of 64 unique charts were reviewed. 18 patients (28%) of patients were treated with ICI as first-line therapy. 28 patients (44%) experienced immune-related adverse events with a total of 40 irAE's identified. Most irAE were grade I-II (78%), with 7 (17%) grade III and 1 (2.4%) grade IV irAE's. Most common sites were skin (29%), thyroid (20%) and gastrointestinal (15%). Patients with irAE had increased survival compared to those who did not have irAE (median survival not reached, vs 139 weeks, p=0.0004) (figure 1). This finding remained after excluding patients who had only experienced dermatologic irAE (median survival not reached in non-derm



Abstract 191 Figure 2 Kaplan-Meier survival plot of OS between patients with non-dermatologic irAE and those without any irAE or only dermatologic irAE

irAE subgroup, vs 144 weeks for dermatologic or no irAE, p=0.01) (figure 2). Patients treated with ICI as first line therapy had greater rates of developing irAE (72%) than those who had prior therapies (32%) (OR 5.4; p = 0.006). There was no association between histology type and rate of irAE.

Conclusions The development of irAE's in patients with mRCC treated with ICI is associated with longer survival. This study joins the growing body of evidence showing that presence of irAE's is associated with increased treatment efficacy. Use of ICI as first-line therapy is associated with higher risk of irAE. Given growing use of ICI as first-line therapy, further study to predict onset and severity of irAE's is required.

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Ethics Approval This study was approved by the University of Pittsburgh Institutional Review Board. Approval number STUDY19100386.

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192 'IMMUNE-BRAIN': A CASE SERIES OF COGNITIVE DYSFUNCTION/DECLINE IN CANCER PATIENTS ON IMMUNOTHERAPY

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Background Immunotherapy agents are now the standard of care for many types of malignancies and use of checkpoint inhibitor immunotherapy (IO) is widespread across oncology. Cognitive dysfunction/decline (CD) is a well-known side effect of conventional chemotherapy (i.e. 'chemo-brain'), but the neuro-cognitive impact of checkpoint inhibitor immunotherapy (IO) is not well described, despite the known potential for inflammatory neurotoxicities and encephalitis. Though high grade neurologic events are reported in <1% of patients receiving IO, less severe or possibly transient neurocognitive effects that do not lead to formal neuropsychological evaluation are probably under-reported. Combination of IO with other anti-cancer modalities like cytotoxic chemotherapy and radiation could theoretically compound neurotoxicity through neuroinflammation.

Methods From January 2015-Decmber 2018 at University of Vermont Medical Center, we retrospectively identified cancer patients who received at least one infusion of IO and had a concurrent diagnosis of CD on the problem list, medical history, or billing codes. We used the search terms: cognitive impairment, mild cognitive impairment, neurodegenerative cognitive impairment, memory change/memory deficit/memory difficulty/memory impairment, altered mental status, or encephalopathy to define cognitive impairment. We manually reviewed the charts of all patients meeting this criteria and excluded patients with an alternative diagnosis that was causal for CD (stroke, sepsis, seizure, brain tumor).

Results We identified 55 patients and excluded 16 for CD before IO started, 23 with toxic/metabolic causes (including

stroke, sepsis, medications, seizures), 4 for primary central nervous system malignancy, and 6 for CD related to new or worsening brain metastases. Six had CD possibly related to IO (table 1). Most had also received chemotherapy either concurrently or prior to starting IO, but two patients had only ever received IO cancer therapy. Four of the six had documented MMSE or neuropsychological testing. On careful chart review, no alternative diagnosis was identified as clearly causal for the change in cognition.

Abstract 192 Table 1 Patient Characteristics

PATIENT AGE/SEX	CANCER TYPE	IO/ #INFUSIONS	PRIOR CHEMO	CLINICAL COURSE
54 M	Nasopharyngeal	Pembrolizumab, 47	5-FU, cisplatin	After 43 cycles of IO, patient reported progressive short-term memory loss, inattention, slowed information processing, speech, language, and executive function changes worsening over 6 months. Confirmed by formal neuropsychological testing
69 F	Non-small cell lung	Nivolumab, 15 Pembrolizumab, 18	carboplatin/pemetrexed EC1456 gemcitabine/vinorelbine	After 14 cycles pembrolizumab (and 1 year after 15 cycles nivolumab) patient reported memory loss and word finding difficulties worsening over 6 months. Confirmed with formal neuropsychological testing
77 M	Non-small cell lung	Pembrolizumab, 11	Carboplatin/paclitaxel	Patient with dementia had worsening dementia after 6 cycles IO, confirmed on MMSE (15 to 10 to 8)
85 M	Melanoma	Nivolumab, 9	-	Patient with dementia had worsening dementia after 9 cycles IO, confirmed on MMSE (13 to 11)
67 F	Non-small cell lung	Pembrolizumab, 2	-	Patient had an episode of encephalopathy without identified cause and skin rash following second dose of IO, which was then discontinued
75 M	Non-small cell lung	Nivolumab, 9	Carboplatin/gemcitabine Docetaxel	After 9 cycles of IO (with docetaxel 1st 6 cycles), patient reported memory loss first attributed to metabolic causes. This was again noticed in throughout 2017 with unclear cause, patient refused formal testing

Conclusions Patients receiving IO cancer therapy do report CD, which has not been broadly described. Though our data is corollary, it opens the question as to whether prospective pre- and post-treatment cognitive monitoring may identify more patients with neurocognitive symptoms related to immunotherapy. Future research is needed to report incidence of potential IO-related CD and to develop preventative or therapeutic strategies.

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193 DIFFERENCES IN THYROID IMMUNE-RELATED ADVERSE EVENTS BETWEEN LUNG CANCER TYPES, A RETROSPECTIVE ANALYSIS

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Background Immune modulation of the PD-1/PD-L1 pathway is a promising treatment of various malignancies however, alteration of the pathway is known to cause many immune related adverse events (irAEs) including thyroid dysfunction. Whether the frequency of thyroid irAEs differ between lung cancer types has not yet been studied.

Methods A total of three hundred twenty-nine lung cancer patients treated with immunotherapy at East Carolina University between April 2014 and July 2019 were included in a retrospective cohort analysis. Baseline TSH and TSH at each treatment cycle were recorded along with the type of lung cancer, specific agent used, timing of thyroid dysfunction and need for levothyroxine replacement. The frequency of thyroid irAEs as defined by TSH < 0.4 or > 4.0 and its relationship with lung cancer types were analyzed using chi square tests and logistic regression.

Results Of the three hundred twenty-nine patients; 54.4% had adenocarcinoma, 31.6% had squamous cell carcinoma, 11.3% had small cell carcinoma and 2.7% had poorly differentiated lung cancer. Overall, 135 patients (41.0%) developed thyroid irAEs (table 1). Pearson's chi square test was used to compare the frequencies of thyroid irAEs for each type of lung cancer against all other lung cancer types. Patients with squamous cell carcinoma developed significantly less thyroid irAEs (32.7%), compared to all other lung cancers (44.9%), X2 (1, N = 329) = 4.4, p = 0.037. Conversely, patients with lung cancer types other than squamous cell carcinoma were more likely to develop thyroid irAEs, OR = 1.68 (95% CI: 1.03 – 2.73).

Abstract 193 Table 1 Frequency of lung cancer type and thyroid dysfunction within each group

Type of Cancer (N=329)	Patients With Each Cancer Type	Patients With Thyroid Dysfunction Within Each Cancer Type (N=135)
Adenocarcinoma	179(54.4%)	81(42.3%)
Squamous Cell Carcinoma	104(31.6%)	34(32.7%)
Small Cell Carcinoma	37(11.3%)	17(46.0%)
Poorly Differentiated	9(2.7%)	3(33.3%)

Conclusions Thyroid irAEs occurred significantly less frequently in patients with squamous cell carcinoma than those with other lung cancer types. This analysis may allow clinicians to better identify patients more likely to develop irAE thyroid dysfunction based on lung cancer type.

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194 A MULTICENTER CHARACTERIZATION OF CHRONIC TOXICITIES FOLLOWING ADJUVANT ANTI-PD-1 THERAPY FOR HIGH RISK RESECTED MELANOMA

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Background Anti-programmed death-1 (anti-PD-1) therapies have improved long-term survival across many advanced cancers. However, chronic immune-related adverse events (irAEs) are not well-defined. We sought to determine the incidence, time-course, spectrum, and predictors of chronic irAEs arising from adjuvant anti-PD-1.

Methods In this retrospective cohort, we analyzed patients from 8 academic medical centers with stage III-IV melanoma treated with anti-PD-1 in the adjuvant setting. Acute and chronic (persisting at least 3 months after therapy cessation) irAEs were characterized by type, time-course, management, and incidence.

Results Among 387 patients, most were male (60.7%) with a median age of 63 years, had cutaneous primaries (85.8%), BRAF/NRAS WT (51.2%), and resected stage IIIb (33.1%) or IIIc (39.5%) melanomas. Median overall survival and relapse-free survival (RFS) were not reached. 359 patients (93.0%) were alive at median follow-up of 529 days. Patients with acute ($p<0.009$) or chronic ($p<0.001$) irAEs had superior RFS compared with patients lacking irAEs. Treatment was discontinued for therapy completion (50.0%), irAEs (25.3%), and disease progression (20.9%). 267 patients (69.0%) had any acute irAE, including 19.5% (n=52) with grade 3–5 events. Acute irAEs were most commonly dermatitis/pruritis (25.8%), thyroiditis/hypothyroid (16.3%), arthralgias (10.6%), colitis/diarrhea (9.8%) and required glucocorticoids in 109 patients