1237 LONG TERM OUTCOMES OF SEVERE ENDOCRINE IMMUNE-RELATED ADVERSE EVENTS (IRAES): ADRENAL INSUFFICIENCY (AI) AND INSULIN-DEPENDENT DIABETES (IDDM)

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Background Immune checkpoint inhibitor induced AI and DM are severe endocrine IrAEs and little is known about their long-term morbidity and associated oncology outcomes.

Methods From January 2010 to September 2022, patients that were diagnosed with ICI induced AI and/or IDDM by a board-certified endocrinologist were studied. Out of the 139 patients identified, 101 had secondary AI, 5 had primary AI, and 33 had IDDM. Patients that had high dose steroid use was defined as a daily dose of hydrocortisone 30mg (or equivalent) for more for 2 months. Secondary AI cohort was subclassified as CTLA-4 based (CTLA-4 C) and non CTLA-4 based cohorts (nCTLA-4 C).

Results Among the 101 patients in the secondary AI cohort, 55 (55%) patients received CTLA-4-based ICI, including 35 (64%) patients who received combination PD-1+CTLA-4 ICI. Melanoma (45%) and genitourinary malignancies (25%) were the most common tumor types. The majority of patients had stage IV disease (74%). 52% and 11% developed hypothyroidism and hypogonadism with secondary AI, respectively. 20% (n=20) of patients received initial treatment with high-dose steroids, including 33% (n=18) of the CTLA-4 cohort and 4% (n=2) of the nCTLA-4 cohort. At a median follow-up of 45.5 months, the majority of patients had undetectable ACTH and cortisol levels (table 1). All patients remained on replacement steroids except for two (2%) patients who had recovery in both ACTH and cortisol values (table 1). Among 33 IDDM patients, all patients received PD-(L)-1 based ICIs combinations. GU and melanoma were the most common tumor types. 94% of patients had stage IV disease. Most patients presented with diabetic ketoacidosis [(DKA, 58%)] and required inpatient support with insulin drip (58%). 70% of patients discontinued ICI after IDDM diagnosis, including 39% primarily due to IDDM. Among 45% patients with long-term data (median follow-up 27 months), all patients remained on insulin (table 1).

Conclusions Our study followed patients with ICI induced AI and/or IDDM with a median follow up time of over 45 months. We found that secondary AI due to CTLA-4-based ICIs tends to occur earlier and presents more with symptoms of headache and hyponatremia, while nausea/vomiting is more common with nCTLA-4 based ICI. Almost all patients required long-term replacement steroids, but most of them were rechallenged with ICI after secondary AI. IDDM occurred predominately after PD(L)-1 based ICIs. Most patients presented with DKA and required hospitalization. All patients remained on long-term insulin and only a small subset of patients continued ICI after IDDM.

Abstract 1237 Table 1 shows the long-term outcomes of patients diagnosed with immune checkpoint inhibitor induced adrenal insufficiency and/or insulin dependent diabetes

	Secondary AI CTLA-4 C (n=55)	Secondary A nCTLA-4 C (n=46)	IDDM (n=33)
Median Age (years)	65 (34 — 81)	65 (38 – 84)	63 (27-78)
Gender-Female (%)	25 (45)	17 (37)	15 (45)
Time to diagnosis (months)	3.6 (0.6-69.3)	7.7 (1.3-19.8)	3.4 (0.6 – 18.7)
Any other irAEs (%)	48 (87)	29 (63)	21 (64)
Initial Presenting symptoms (%)	Fatigue (78), Headache (38),	Fatigue (93), N/V (41)	Fatigue (58) Polydipsia/polyuria (58)
ICI continue after initial diagnosis (%)	34 (62)	26 (57)	10 (30)
Long Term ACTH before AM hydrocortisone (< 5 pg/ml; n=45/54)	29 (91)	16 (73)	N/A
Long Term Cortisol before AM hydrocortisone (<1 mcg/dl; n=35/58)	21 (58%)	14 (64%)	N/A

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