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Controlling the balance between cancer and autoimmunity

OP0003 RHEUMATIC IMMUNE RELATED ADVERSE EVENTS OF CHECKPOINT THERAPY FOR CANCER: CASE SERIES OF AN EMERGING NOSOLOGIC ENTITY

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Background: Immune checkpoint therapy is a major advance in the field of oncology. Agents targeting CTLA-4, programmed cell death protein 1 (PD-1) and PD-ligand 1 have produced significant survival benefits in patients with malignancies. With these therapies have come a unique spectrum of adverse events related to over-activation of the immune system with resultant autoimmune disease. To date reports of rheumatic immune related AEs (irAEs) have not been adequately characterized, as they are infrequently reported in clinical trials. We describe the largest series of rheumatic irAEs secondary to checkpoint inhibitors to date.

Objectives: To report our 22 month experience with 19 patients evaluated in the Cleveland Clinic Rheumatology department.

Methods: A retrospective chart review was performed on 19 patients, 16 without pre-existing autoimmune disease (AID) and 3 with pre-existing AID, seen in our rheumatology department February 2015-December 2016. 2 designated rheumatologists evaluated all patients. Recorded information included gender, age, age at malignancy diagnosis, malignancy details, checkpoint inhibitor, nature of rheumatic irAE, time of onset, diagnostic data, treatment of irAE and response to treatment.

Results: In the group without pre-existing AID 56% developed a rheumatic irAE within 16 weeks of starting immunotherapy, with median time to onset of 14.5 weeks (table 1). Of the 3 patients with pre-existing AID, 1 experienced a disease flare after starting immunotherapy.

Conclusions: Rheumatic irAEs is a new field that will continue to grow. At

this stage we have more questions than answers regarding their epidemiology, natural history and pathophysiology. Our findings reinforce that rheumatic irAEs are complex, at times require aggressive immunosuppression and can impact checkpoint inhibitor therapy for the underlying malignancy.

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OP0004 RHEUMATOID ARTHRITIS OCCURRING AFTER IMMUNE CHECKPOINT INHIBITORS

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Background: Immune checkpoints inhibitors (ICIs) targeting cytotoxic T lymphocyte-associated protein 4 (CTLA-4) and Programmed cell death protein 1 (PD-1) have demonstrated survival improvement in multiple cancers. Immune Related Adverse Events (irAE) have been described with ipilimumab and anti PD1. Relapse or flare of preexisting auto-immune diseases has been reported but occurrence of new auto-immune diseases seems to be less frequent. A series of 13 patients with non-classified rheumatic irAE has been published: 9 patients developed non-specific inflammatory arthritis but no seropositive rheumatoid arthritis (RA) and 4 presented with sicca symptoms but did not fulfill criteria for Sjögren syndrome [1].

Objectives: We did a retrospective study for collecting patients who developed seropositive rheumatoid arthritis (RA) after exposition to ICIs.

Methods: We used the "Club Rhumatismes et Inflammation (CRI)" network, a section of the French Society of Rheumatology and the Gustave Roussy Cancer

Abstract OP0003 – Table 1. Demographic features, cancer types, immunotherapy and rheumatic irAEs

Patient	Age	Sex	Malignancy	Immunotherapy	irAE	Serology	Time to onset (weeks)	Treatment	Improvement	Immunotherapy held for irAE
1	74	F	NSCL	Nivo	Arthritis	ANA 1:160 Anti-dsDNA 77	7.3	Prednisone 40 mg	Significant	Y
2	49	F	Melanoma	Ipi	Arthritis		52.7	Prednisone 20 mg HCQ	Moderate	Y
3	42	F	RCC	Pembrolizumab Ipi/Nivo	Arthritis		3	Prednisone Infliximab, MTX Etanercept	Moderate	N
4	57	M	RCC	Ipi/Nivo	Arthritis	RF 214	48.4	Prednisone, MTX Etanercept Adalimumab	Significant	N
5	59	F	Melanoma	Ipi/Nivo	Arthritis		21.7	Prednisone 60 mg	Minimal	N
6	81	M	Melanoma	Ipi/Nivo	Arthritis	ANA 1.5	13.1	Prednisone 15 mg	Moderate	Y
7	59	M	RCC	Ipi/Nivo	Arthritis	ANA 1.8	56	Prednisone 10 mg	Minimal	N
8	53	M	Melanoma	Ipi/Nivo	Arthritis		16	Methylprednisolone 80 mg IM	Minimal	Y
9	63	59	NSCL	Nivo	Arthritis	ANA 1:160	38	Prednisone 30 mg Methorexate	Minimal	Y
10	57	F	Melanoma	Ipi/Nivo	Arthritis	ANA 1:320 6.7	6.7	Prednisone 30 mg	Significant	Y
11	61	M	Melanoma	Ipi/Nivo	Sicca		5.3	Prednisone 60 mg*	Significant	Y^
12	63	M	RCC	Atezolizumab	Sicca		21.9	Prednisone 60 mg*	Significant	Y^
13	68	M	Melanoma	Ipi/Nivo	Sicca	ANA 1:1280 SSA	8.1	Prednisone 30 mg	Significant	Y
14	79	M	Melanoma	Nivo	PMR Sicca		2	Prednisone 20 mg	Moderate	Y
15	63	M	RCC	Nivo	PMR		213	Prednisone 40 mg Infliximab Tocilizumab	Moderate	Y
16	68	M	NSCL	Tremelimumab Durvalumab	Myositis		4.6	IV methylpred 60 mg Prednisone 60 mg	Moderate	Y

NSCL non-small cell lung cancer, RCC renal cell carcinoma, Ipi ipilimumab, Nivo nivolumab, RF rheumatoid factor HCQ hydroxychloroquine, MTX methotrexate, *Prednisone given for hypophysitis.

^Immunotherapy held for hypophysitis.

Abstract OP0004 – Table 1

Patients	Sex/age	Type of cancer	ICI	Date of first ICI exposure	Date of irAE	Type of rheumatic irAE	irAE response to treatment	Autoantibody results
1	F 55 y	Squamous cell carcinoma of the vagina	nivolumab	October 2015	October 2015	RA	resolution with NSAIDs	anti-CCP: 671 U/ml RF: 18 U/ml
2	F 66 y	Endometrial adenocarcinoma	pembrolizumab	March 2016	April 2016	RA	resolution with corticosteroids prednisone 10 mg/day	anti-CCP: 233 U/ml RF: 180 U/ml
3	M 59 y	Lung adenocarcinoma	nivolumab	May 2016	July 2016	RA	resolution with prednisone 10 mg/d tapered to 5 mg/d 1 months later	anti-CCP: 61 U/ml RF: 47 U/ml
4	F 56 y	Metastatic melanoma	pembrolizumab	August 2015	September 2015	RA	resolution with hydroxychloroquine 400mg/day and NSAIDs	anti-CCP: 22U/ml
5	M 80 y	Metastatic melanoma	nivolumab	April 2016	April 2016	RA	Resolution with prednisone 15mg/day (tapered) and hydroxychloroquine 200mg/day	anti-CCP: 42 U/ml
6	M 68 y	Lung adenocarcinoma	nivolumab	June 2015	July 2015	RA	Resolution after stopping nivolumab and after 1 month of methotrexate 10 mg/w (maintained 3 months)	anti-CCP >300U/ml RF: 246 U/ml