IMMUNE-RELATED ADVERSE EVENTS ASSOCIATED WITH PD-1/PD-L1 INHIBITORS IN METASTATIC NSCLC PATIENTS: A SINGLE-CENTER STUDY FROM HONG KONG

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Background

- Real-world data on immune-related adverse events (irAEs) related to anti-programmed-death (PD1) or programmed-death ligand-1 (PD-L1) antibodies in metastatic non-small cell lung cancer (NSCLC) remains scarce.
- Asian populations are often under-represented in trials and the incidence of irAEs among Chinese patients with NSCLC remain unknown.

Objectives

- To examine (1) the incidence, (2) time to onset, (3) management, and (4) predictive risk factors of irAEs among Chinese patients with NSCLC in Hong Kong.

Methods

- This is a single center, retrospective review study.
- Clinical data of metastatic NSCLC patients at the Prince of Wales Hospital (PWH) were extracted from electronic health records.

Inclusion Criteria

- Chinese patients ≥18 years old and diagnosed with metastatic NSCLC
- Started on Atezolizumab, Nivolumab or Pembrolizumab between June 2016 and March 2020

Exclusion Criteria

- Concurrent chemotherapy/targeted therapy/CTLA-4 inhibitors
- Incomplete medical record

Primary Outcome

- Incidence of irAEs
- Defined as all adverse events reported after initiating immune checkpoint inhibitors, which were not present prior to the initiation of treatment.
- Classified by organ systems and graded according to clinician notes and grouped into (1) Unknown/Grade I/II and (2) Grade III/IV.

Secondary Outcomes

- Time to onset of irAEs
- Management of irAEs
- Predictive risk factors of irAEs

Predictive risk factors (identified a priori from the literature)

- Clinical factors: age, sex, Charlson comorbidity index (CCI), chronic infections, drug allergy, previous chemotherapy use, previous TKI use, EGFR mutation, PD-L1 status
- Lifestyle factors: drinker status, smoking status
- Baseline drug use (Anti-hypertensive, anti-psychotic, anti-arrhythmic, anti-convulsant, statin)

Statistical Analysis

- Descriptive statistics to describe incidence, onset and management of irAEs
- Poisson regression to identify predictive risk factors of irAEs.

Table 1. Patient Demographics

		Atezolizumab		Nivolumab		Pembrolizumab	
		N=	%	N=	%	N=	%
		27	22%	38	31%	56	47%
Age (Mean)		59.7		62.4		62.7	
Gender	M	20	74%	24	63%	36	64%
	F	7	26%	14	37%	20	36%
PD-L1	≥50%	2	7%	3	8%	32	57%
	<50%	15	56%	10	26%	12	21%
	N/A	10	37%	25	66%	12	21%
EGFR	Positive	8	30%	8	21%	14	25%
	Negative	18	67%	26	68%	40	71%
	N/A	1	4%	4	11%	2	4%
No. of cycles	1-5	22	81%	22	58%	31	55%
	6-10	1	4%	10	26%	13	23%
	>11	4	15%	6	16%	12	22%
Reason of Discontinuation*	irAEs	1	4%	2	5%	8	14%
	Progression	20	74%	21	55%	31	55%
	Death	5	19%	11	29%	9	16%
	Treatment Complication	1	4%	1	3%	3	5%
	Others	2	7%	1	3%	4	7%
	Ongoing	0	0%	2	5%	4	7%

*4 cases due to both irAEs & progression; 1 case due to progression & treatment break

Table 2. Summary of irAEs

	Atezolizumab	N=27	Nivolumab	N=38	Pembrolizumab	N=56	Total	N=121
	N=	N=	N=	N=	N=	N=	N=	N=
Patient Count	16		16		34		66	
Event Count	Grade I/II/ungraded	Grade III/IV	Grade I/II/ungraded	Grade III/IV	Grade I/II/ungraded	Grade III/IV	Grade I/II/ungraded	Grade III/IV
General	11		12		25		48	0
Skin	4	1	13		25	1	42	2
GI	7		8		14	1	29	1
Respiratory	3		2		11		16	0
Musculoskeletal	2		3		4		9	0
Hepatic	4		0	1	9		13	1
Endocrine	4		3		9	1	16	1
Renal	1		1		3		5	0
Neurological	0		0	1	2		2	1
Others	0		0		0	1	0	1
Total	36	1	42	2	102	4	180	7

Results

Primary Outcome

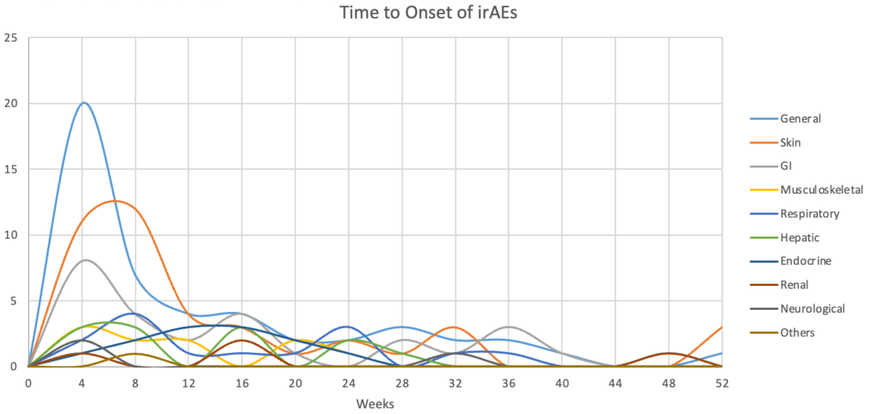
Incidence of irAEs

- 187 any-grade irAEs observed in 66 patients (54.5%)
- Grade III/IV events include thrombocytopenia, confusion, hyperglycemia, ALT elevation, diarrhea and 2 cases of rash

Secondary Outcomes:

Time to onset of irAEs

- Median time to onset of any-grade irAEs: 70.5 days (Range: 2 to 1005 days)
- Median time to onset of grade III/IV irAEs: 142 days (Range: 15 to 571 days)
- Peak onset observed within 6 weeks



Management of irAEs

- Most cases managed symptomatically
- 11 cases required systemic corticosteroids for pneumonitis (n=6), liver function test derangement (n=2), thrombocytopenia (n=1), colitis (n=1), or encephalopathy (n=1)
- 8 cases required hormone replacement therapy

Predictive Risk Factors of irAEs

- Absence of EGFR mutation (RR = 0.26, 95%CI = 0.11 - 0.66)
- Chronic HepB/HepC/HIV infections (RR = 1.49, 95% CI = 1.01 - 2.21)
- PD-L1 expression >50% (RR = 2.28, 95% CI = 1.59 - 3.29)

Conclusion

- Half of the Chinese patients treated with PD-1/PD-L1 inhibitors experienced irAEs.
- Future work includes developing institutional protocols for monitoring/managing immunotherapy-induced toxicities in at-risk patients.

References

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