Impact of Adverse Event Definitions on Real-World Detection of Oncology Immune-Related Adverse Events

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Poster/Abstract
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OBJECTIVES

- Immune checkpoint blockade (ICB), now widespread, represent a major advance in cancer care , but have also introduced novel toxicities, denoted immune-related AEs (irAEs)
- Accurate irAEs identification in real-world data (RWD) is vital for assessing the long-term safety profile of ICB
- A barrier to this identification is a lack of consensus in the definitions of AEs
- Here, we apply three different peer-reviewed irAE definitions in a RWD cohort of non-small cell lung cancer (NSCLC) patients

SUMMARY

- Identification of oncology-associated irAEs in RWD varies significantly based on the classification approach
- Using three peer-reviewed definitions applied to the same cohort, we identified irAEs in 79.7%, 41.0%, and 5.5% of patients
- Researchers working with RWD should clearly communicate irAE definitions to support reproducible identification of these events in post-marketing surveillance

METHODS

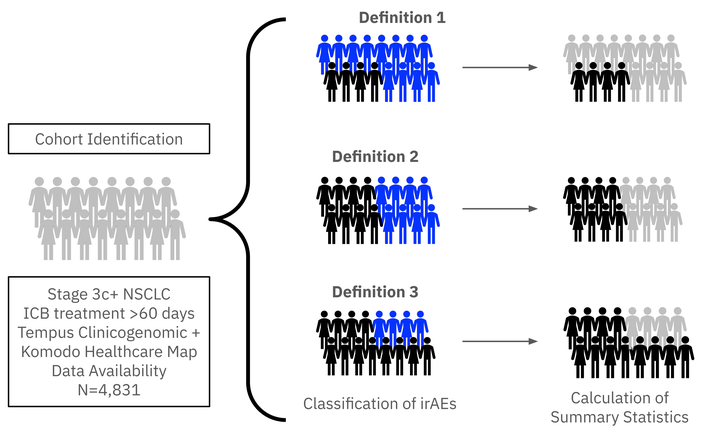
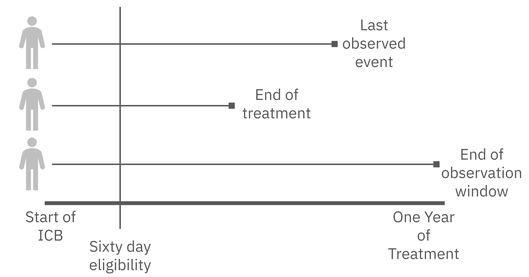


Table 1. ICD Counts per Organ System Associate with irAEs

Organ System	irAE Definition 1	2	3
Cardiac	27	4	
Dermatologic	33	25	
Endocrine	41	28	
GI	**32**	**14**	**2**
Heme	25		
Hepatic		15	2
Musculoskeletal	7		
Nervous	30	74	
Ocular	2		
Pulmonary	**32**	**9**	**2**
Renal	3	19	
Total	**232**	**188**	**6**

Schematic of observation window for representative patients



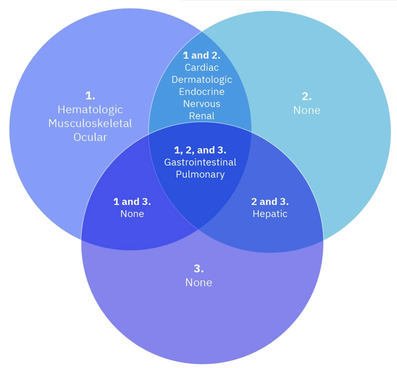


Figure 1. We evaluated RWD from Tempus clinicogenomic data linked to Komodo Health's claims. Patients were included if they had a diagnosis of stage 3C+ NSCLC, and were treated with ICB therapy for ≥ 60 days. We assessed irAEs for up to one-year of ICB treatment or the last clinical record or claim if one-year follow-up was not available. We applied three definitions of irAEs to this cohort which varied in the irAEs included, the ICD-10 codes used to define them, and the length of pre-treatment washout period to exclude prevalent diagnoses. **Table 1** shows the count of ICD-10 codes per organ system identified under each definition. GI and Pulmonary are highlighted as organ systems represented across all three definitions, and explored in downstream results

RESULTS

Table 2. Study Cohort

Clinical Characteristic	Value	Number of patients	IO Only (N,%)	IO Combination (N, %)
IO Therapy	Atezolizumab	194	52, 26.8%	142, 73.2%
	Avelumab	5	3, 60%	2, 40%
	Cemiplimab	74	23, 31.1%	51, 68.9%
	Durvalumab	622	590, 94.9%	32, 5.1%
	Ipilimumab	217	147, 67.7%	70, 32.3%
	Nivolumab	555	451, 81.3%	104, 18.7%
	Pembrolizumab	3387	1027, 30.3%	2360, 69.7%
	Tremelimumab	6	2, 33.3%	4, 66.7%
CTLA-4 Treatment	No	4615	1994, 43.2%	2621, 56.8%
	Yes	216	147, 68.1%	69, 31.9%
Year of Primary Diagnosis	≤2016	797	540, 67.8%	257, 32.2%
	2018	561	276, 49.2%	285, 50.8%
	2019	804	326, 40.5%	478, 59.5%
	2020	892	360, 40.4%	532, 59.6%
	2021	861	329, 38.2%	532, 61.8%
	2022	604	223, 36.9%	381, 63.1%
	2023	312	87, 27.9%	225, 72.1%
Year of Stage 3B+ Diagnosis	≤2016	518	401, 77.4%	117, 22.6%
	2018	540	286, 53%	254, 47%
	2019	801	319, 39.8%	482, 60.2%
	2020	954	393, 41.2%	561, 58.8%
	2021	914	358, 39.2%	556, 60.8%
	2022	721	263, 36.5%	458, 63.5%
	2023	382	120, 31.4%	262, 68.6%
	2024	1	1, 100%	0, 0%
Year of ICB Start	≤2016	269	207, 77%	62, 23%
	2018	426	253, 59.4%	173, 40.6%
	2019	741	302, 40.8%	439, 59.2%
	2020	935	396, 42.4%	539, 57.6%
	2021	971	385, 39.6%	586, 60.4%
	2022	854	339, 39.7%	515, 60.3%
	2023	612	244, 39.9%	368, 60.1%
	2024	23	15, 65.2%	8, 34.8%

Table 3. Adverse Event Detection varies by Definition and Treatment Type

a.

Treatment	Any irAE	Definition 1	Definition 2	Definition 3
Any, N = 4831	Yes	79.7 %	41 %	5.5 %
Any, N = 4831	No	20.3 %	59 %	94.5 %
IO Combination, N = 2690	Yes	81.6 %	43.8 %	6 %
IO Combination, N = 2690	No	18.4 %	56.2 %	94 %
IO Only, N = 2141	Yes	77.2 %	37.5 %	4.8 %
IO Only, N = 2141	No	22.8 %	62.5 %	95.2 %

b.

Treatment	Any irAE	Definition 1	Definition 2	Definition 3
Any, N = 4831	Yes	29.3 %	5.2 %	3.7 %
Any, N = 4831	No	70.7 %	94.8 %	96.3 %
IO Combination, N = 2690	Yes	32.4 %	5.9 %	4.2 %
IO Combination, N = 2690	No	67.6 %	94.1 %	95.8 %
IO Only, N = 2141	Yes	25.4 %	4.3 %	3.1 %
IO Only, N = 2141	No	74.6 %	95.7 %	96.9 %

c.

Treatment	Any irAE	Definition 1	Definition 2	Definition 3
Any, N = 4831	Yes	31.3 %	3.1 %	1.4 %
Any, N = 4831	No	68.7 %	96.9 %	98.6 %
IO Combination, N = 2690	Yes	29.7 %	2.9 %	1.4 %
IO Combination, N = 2690	No	70.3 %	97.1 %	98.6 %
IO Only, N = 2141	Yes	33.4 %	3.4 %	1.5 %
IO Only, N = 2141	No	66.6 %	96.6 %	98.5 %

Table 3. Adverse event counts and rates by treatment type and definition. Subtable A includes all adverse events, while Subtable B includes gastrointestinal irAEs, and Subtable C includes Pulmonary irAEs, the two adverse events that were common across all three definitions.

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