Risk of immune related adverse events (irAE) with immune checkpoint inhibitors (ICIs) in patients (pts) with family history of autoimmune disease.

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Background

- Genetic predisposition may have a role in the development of irAEs from ICIs.[1-4]
- Clinical trials of ICIs excluded pts with personal history of autoimmune disease due to potential increased risk of irAEs and flare of pre-existing autoimmune disease.[5,6]
- Pts with family history of autoimmune disease may have a predisposition to off-target effects of ICIs. The impact of family history of autoimmune disease on ICI related irAEs in cancer pts is unclear.

Objectives

- Determine the incidence of family history of autoimmune diseases in cancer pts.

In pts with family history of autoimmune diseases treated with ICIs,

- Establish the incidence, type and morbidity of irAEs.
- Examine the association of family relatedness (first, second or third degree relative) on frequency, type and severity of iRAEs. (Figure 1).

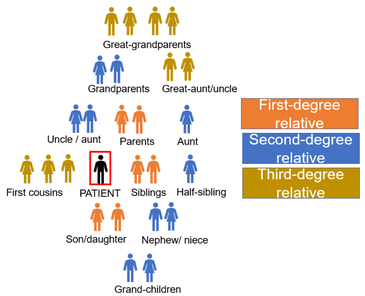

Figure 1. Family chart depicting degree of relatedness by first (orange), second (blue) or third (gold) degree relative to the patient (black).

Methods

- *Population of interest*- pts with family history of autoimmune disease treated with anti-PD-1 based ICI. Pts with personal history of autoimmune disease were excluded.
- Retrospective review of consecutive records from two Australian melanoma centers.
- Toxicity data was obtained using Common Terminology Criteria for Adverse Events v5.0. Descriptive statistics and Fisher's Exact test were used for analysis.

Results

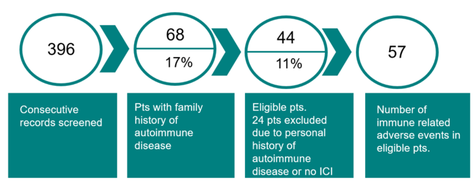

Figure 2. Flowchart of patient selection and number of immune related adverse events.

Table 1. A. Baseline characteristics of patients who received anti-PD1 based therapy (n=44) and **B.** nature of family history of autoimmune diseases in eligible patients.

Table 1A	
Variable	**N=44**
Age, median (years) (IQR)	61 (46-69)
Sex, n (%)	
Male	18 (41)
Melanoma sub-type, n (%)	
Cutaneous	35 (80)
Treatment setting, n (%)	
Adjuvant	24 (55)
Advanced	20 (45)
ECOG performance status, n (%)	
0-1	44 (100)
LDH pre-ICI, n (%)	
Normal	32 (73)
Mutation, n (%)	
Triple wildtype	21 (48)
BRAF V600	12 (27)
ICI, n (%)	
Anti-PD1 monotherapy	12 (27)
Anti- PD1 + ipilimumab	12 (27)
Anti-PD1 + other ICI*	20 (46)

Table 1B	
Variable	
Family history of autoimmune disease, n (%)	**N=44**
First degree only	27 (62)
Second degree only	8 (18)
Third degree only	1 (2)
First + second degree	5 (11)
Second + third degree	2 (5)
First, second and third degree	1 (2)
Type of autoimmune disease, n (%)	**N=56****
Rheumatoid arthritis	16 (29)
Other multi system rheumatological	5 (9)
Psoriasis	3 (5)
Inflammatory bowel disease	8 (14)
Coeliac disease	8 (14)
Type 1 diabetes mellitus	6 (11)
Grave's disease	8 (14)
Other	2 (4)

Anti-PD-1, anti-programmed death 1; ECOG, Eastern Cooperative Oncology Group; ICI, immune checkpoint inhibitor. * other ICIs included anti-LAG-3 or anti-TIGIT antibodies. ** family history of 56 autoimmune diseases in 44 patients.

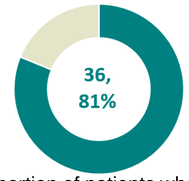

Figure 3. Proportion of patients who developed immune related adverse event (n=44).

Incidence of irAE in pts with family history of autoimmune disease was not statistically higher to that reported in registration trials of similar regimens (p=0.40).[7,8]

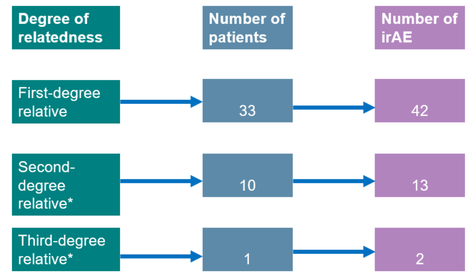

Figure 4. Immune related adverse events (irAE) by degree of relatedness. * Patients' higher degree of relatedness was prioritised for assessment of irAE.

There was no association in development of irAE between pts with family history of autoimmune disease in a first-degree relative and those with family history of autoimmune disease in second or third degree relative (p=0.17).

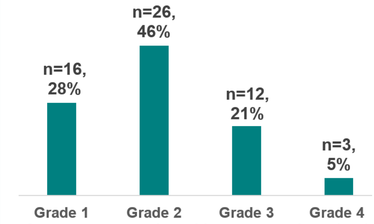

Figure 5. Severity of immune related adverse events (n=57).

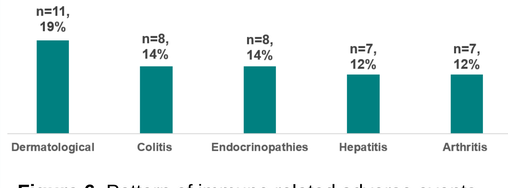

Figure 6. Pattern of immune related adverse events occurring at frequency of >10% (n=57).

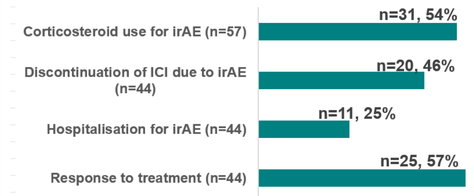

Figure 7. Outcomes in 44 patients with 57 immune related adverse events.

6 (13.6%) pts experienced irAE similar to the family history of that autoimmune disease.

Of these,

- 4 pts had a first-degree relative with an autoimmune disease.
- 3 pts discontinued ICI due to toxicity (peak toxicity Grade 3).
- 2 pts each developed arthritis and psoriasis like irAE. 1 patient each developed Crohn's disease and Grave's disease like irAE.
- 4 pts had response to treatment.

Conclusions

- Family history of autoimmune disease(s) is common in melanoma pts.
- The incidence of irAE, pattern of toxicity by organ system, corticosteroid use and hospitalisation rate in our series was similar to other ICI clinical trials suggesting a family history of autoimmune disease does not increase the risk of irAE.[7-11]
- The degree of relatedness of family history did not increase the likelihood or severity of irAE.

References

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