BACKGROUND

- Anti-PD-1 antibodies (PD1) have activity in many cancers
- All trials have excluded pts with significant preexisting autoimmune disorders (ADs)
- Only one trial has included pts with major irAEs with ipilimumab:
  - Grade 1 in 3 pts (52%)
  - Grade 1-2 in 5 pts
- We sought to explore the safety and efficacy of PD1 in such patients

METHODS

- Advanced melanoma treated with PD1
- Preexisting autoimmune disease (AD)
- Active or reactive autoimmunity
- Immunosuppressants (IS)
- Severity of prior irAE
- Highest level of IS needed
- Resolution of irAE at PD1 start

AD - Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, median (range)</td>
<td>61.0 (19-85)</td>
</tr>
</tbody>
</table>
| Sex | Male: 18/32 (56%)
| Race | White: 20/32 (63%)
| Sites | Skin: 27/32 (84%)
| Efficacy | ORR 17/52 (33%)
| Level of immunosuppression | NO IS
| Grade 1 - 2 irAEs | 6/32 (19%)
| Grade 3 - 4 irAEs | 15/32 (47%)

AD - Flares

- 38% flared, after median 38 days
- Most flares grade 1-2
- Rheumatologic conditions flared often
- Flares occurred more often in those with active symptoms (p=0.01)
- Trend to more flares in those on IS at start of PD1 (p=0.05)

AD - Conventional irAEs

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
</table>
| AE | 34/31 (108%)
| TEAE | 34/31 (108%)
| AE | Blood/lymphatic: 8/32 (25%
| G1 | 10/32 (31%)
| G2 | 11/32 (34%)
| G3 | 1/32 (3%)
| G4 | 0/32 (0%)

AD - Efficacy

- ORR 17/52 (33%)
- Median PFS 6.2 months (95% CI 4.2-8.2)
- Median DoR, OS not reached

IPI TOX - Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
</table>
| AE | 31/32 (97%)
| TEAE | 31/32 (97%)
| AE | Blood/lymphatic: 7/32 (22%)
| G1 | 3/32 (9%)
| G2 | 11/32 (34%)
| G3 | 1/32 (3%)
| G4 | 0/32 (0%)

IPI TOX - irAEs

- Recurrence of ipi irAEs in 3% (arthritis, colitis)
- 34% developed new irAEs, 21% grade 3
- No need for high level immunosuppression (i.e. > IV steroids)
- 12% discontinued PD1
- No treatment related deaths.

IPI TOX - Efficacy

- ORR 27/67 (40%)
- Median PFS 7.2 months (95% CI 3.1-11.3)
- Median DoR, OS not reached

RESULTS

- 119 pts, 95 with prior PPI
- 109 received pembrolizumab, 10 nivolumab.
- 86 (72%) had ≥3 mo follow-up, median 4.6 mo
- 52 with autoimmune disorders (ADs)
- 67 with ipilimumab toxicity (PI TOX)

DISCUSSION

- Selection bias
  - Majority of ADs were clinically inactive and not requiring IS
  - Only those with ADs deemed suitable for treatment included

- Short follow-up
  - Precluded meaningful survival analyses
  - Further toxicities may have emerged over time.

- PD1 antibodies have efficacy in metastatic melanoma patients with preexisting autoimmune disorders and/or major irAEs with ipilimumab:
  - ORR 33% with ADs, 40% with ipilimumab irAEs
  - Most pts had received ipilimumab, had poor prognostic variables

- In patients with ADs:
  - Flares were common, more in those with active symptoms at PD1 start
  - Often occurred in patients with rheumatologic conditions
  - Rate of IRs appeared similar to clinical trial populations.
  - IRs similar in those who flared vs not, but may be lower in those on IS

- In patients with prior major irAEs with ipilimumab:
  - recurrence of the same irAE was rare
  - new irAEs occurred at higher rates than expected.

CONCLUSIONS

- Anti-PD-1 antibodies induce relatively frequent immune toxicities in patients with baseline autoimmunity or prior irAEs with ipilimumab, but these immune toxicities are often mild and easily managed, and the patients achieve high rates of clinical response.
- Anti-PD-1 antibodies may flare preexisting autoimmune disorders, particularly in patients with rheumatologic disorders or requiring active immunosuppression.
- In patients with prior major irAEs with ipilimumab, recurrence of the same irAE is rare, but new irAEs can occur at high rates.
- Thus, clinicians may consider anti-PD-1 antibodies for appropriately selected patients with pre-existing autoimmune disease or prior severe irAE with ipilimumab, provided there is close monitoring and adherence to standard irAE treatment algorithms.

REFERENCES


AFFILIATIONS

1. Princess Alexandra Hospital, Greenslopes Hospital and University of Queensland, Brisbane, Australia
2. Princess Alexandra Hospital, Greenslopes Hospital and University of Queensland, Brisbane, Australia
3. Princess Alexandra Hospital, Greenslopes Hospital and University of Queensland, Brisbane, Australia
4. Princess Alexandra Hospital, Greenslopes Hospital and University of Queensland, Brisbane, Australia
5. Princess Alexandra Hospital, Greenslopes Hospital and University of Queensland, Brisbane, Australia
6. Princess Alexandra Hospital, Greenslopes Hospital and University of Queensland, Brisbane, Australia
7. Princess Alexandra Hospital, Greenslopes Hospital and University of Queensland, Brisbane, Australia
8. Princess Alexandra Hospital, Greenslopes Hospital and University of Queensland, Brisbane, Australia
9. Princess Alexandra Hospital, Greenslopes Hospital and University of Queensland, Brisbane, Australia
10. Princess Alexandra Hospital, Greenslopes Hospital and University of Queensland, Brisbane, Australia
11. Princess Alexandra Hospital, Greenslopes Hospital and University of Queensland, Brisbane, Australia
12. Princess Alexandra Hospital, Greenslopes Hospital and University of Queensland, Brisbane, Australia
13. Princess Alexandra Hospital, Greenslopes Hospital and University of Queensland, Brisbane, Australia
14. Princess Alexandra Hospital, Greenslopes Hospital and University of Queensland, Brisbane, Australia
15. Princess Alexandra Hospital, Greenslopes Hospital and University of Queensland, Brisbane, Australia
16. Princess Alexandra Hospital, Greenslopes Hospital and University of Queensland, Brisbane, Australia
17. Princess Alexandra Hospital, Greenslopes Hospital and University of Queensland, Brisbane, Australia
18. Princess Alexandra Hospital, Greenslopes Hospital and University of Queensland, Brisbane, Australia