

Could this be the tip of the iceberg? Endocrine dysfunction of immune checkpoint inhibitors at Kent Oncology Centre

T. Wang, S. Anandappa, S. Sivappriyan, J. Kumar
Endocrinology Department, Maidstone Hospital

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INTRODUCTION

- Immune checkpoint inhibitors generate immune responses to tumours, causing them to be rejected, and break tumour-induced immune tolerance. Used for advanced neoplasias (incl. metastatic melanoma, non-small-cell lung cancer, and advanced renal-cell carcinoma), their mechanism of action can lead to a variety of inflammatory toxicities.
- Baseline clinical and biochemical endocrine assessment at the start of immune checkpoint treatment and each treatment cycle¹ is important given the treatable nature of it.
- The improvements in survival of these patients necessitate further long-term screening.
- Our study was to look at various aspects of this screening with a view to improve our knowledge and also patient care.

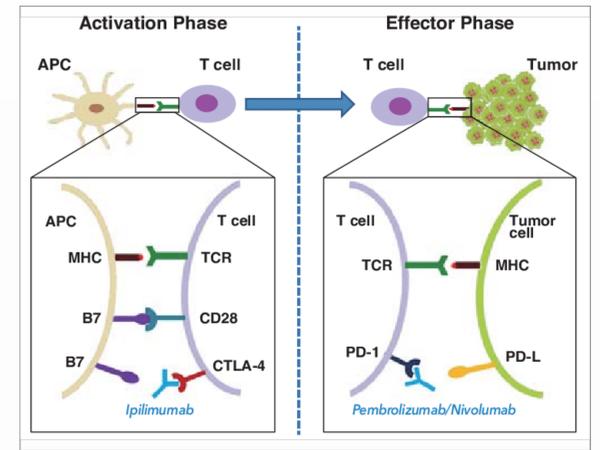


Fig 1²: Mechanisms of action of Ipilimumab & Pembrolizumab

METHODS

- Patients receiving Ipilimumab &/or Pembrolizumab between 01/01/2016 and 30/09/2016 at Kent Oncology Centre were identified using ARIA prescribing system.
- Data for 31 patients were collected using Telepath, PACS, KOMS & Allscript letter records and analysed using Microsoft Excel.
 - 1 patient excluded due to lack of access to their blood results.
- Reviewed to see if baseline endocrine tests (TSH, FT4, 9 am cortisol, pituitary functions +/- imaging) then subsequently 3 weekly thyroid function tests were carried out as per local guidelines; and the outcomes of these results for 39 weeks following administration of the immune checkpoint inhibitor.

Fig 2: Indication for Immunotherapy

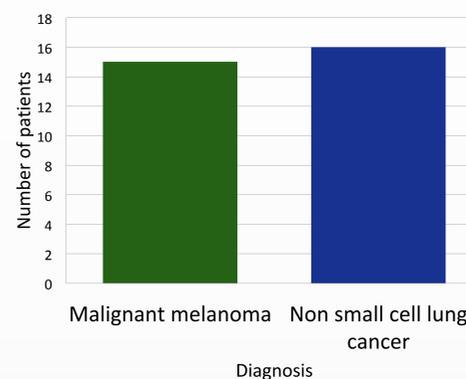
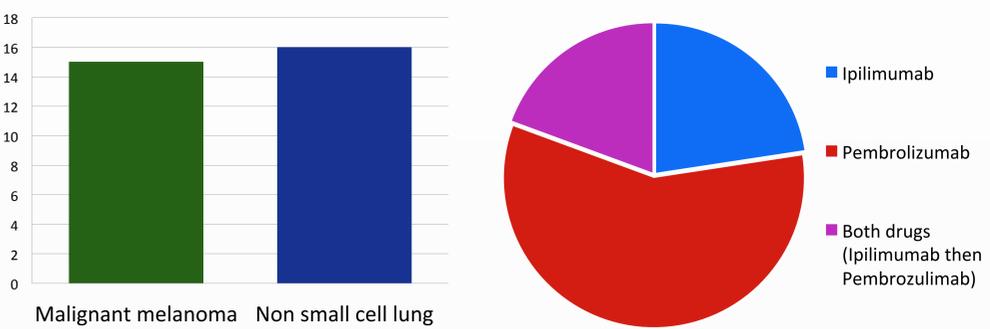


Fig 3: Type of Immunotherapy used



- Malignant melanoma patients were treated with Ipilimumab or Pembrolizumab or both.
- Non small cell lung cancer patients were treated with Pembrolizumab only.

RESULTS

- 31 patients: 17 Males and 14 Females.
- No full set of baseline endocrine tests done.
- 7 out of 31 patients had appropriate TSH monitoring throughout their treatment.
- 25.81% developed endocrine complications following immunotherapy.**
- Onset varied between 3 weeks and 36 weeks after commencing treatment.**
- 2 out of 8 patients who developed an endocrine abnormality were referred to an endocrine team.
- 1 out of 8 patients had a full endocrine profile done after an abnormality was detected.
- None of the patients with an endocrine abnormality underwent pituitary imaging.

Fig 4: Types of endocrine complications

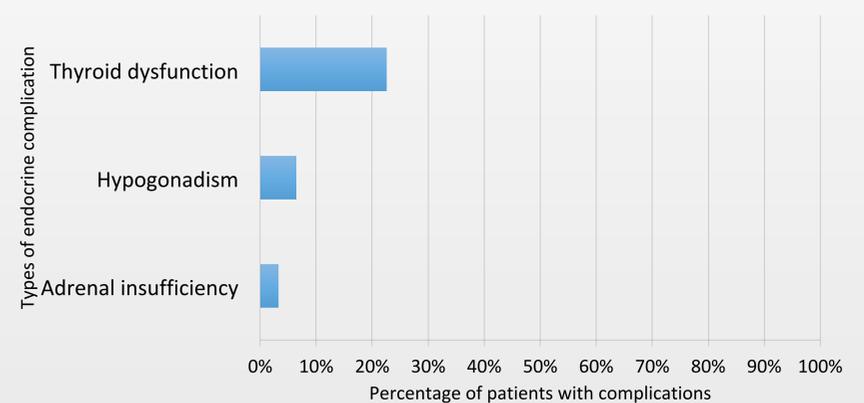
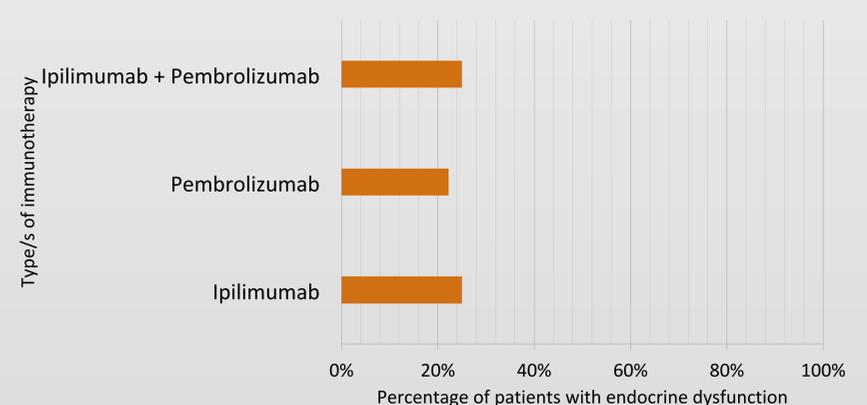


Fig 5: Percentage of patients experienced endocrine dysfunction in following immune checkpoint inhibitor/s



CONCLUSION

- A high prevalence of endocrine dysfunction indicates the need for collaboration between oncologists and endocrinologists
- Robust guidelines to be adhered to when prescribing an immune checkpoint inhibitor. If abnormalities are detected, a full pituitary screening (biochemistry and imaging) should be undertaken.
- The follow up period for endocrine function after administration of immune checkpoint inhibitors needs to be extended globally to at least 36 weeks.

REFERENCES

- Joshi et al, 13/04/2016; Immune checkpoint inhibitor-related hypophysitis and endocrine dysfunction: clinical review; <http://onlinelibrary.wiley.com/doi/10.1111/cen.13063/full>
- Review of Newly Registered Oncology Drugs in Hong Kong - Scientific Figure on ResearchGate. Available from: https://www.researchgate.net/Mechanism-of-Pembrolizumab-Nivolumab-Reprinted-from-permission-of-reference-29_fig3_311715429 [accessed 4 Nov, 2018]