Immunotherapy for Malignant Melanoma: Single Institution Experience

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Background

The advent of immunotherapy has revolutionised systemic anti-cancer treatment (SACT) for advanced melanoma.

Pembrolizumab was accepted by the Scottish Medicines Consortium in November 2015 for treatment of advanced (unresectable/metastatic) melanoma in adults based on extended median progression free survival and overall survival compared with ipilimumab.[1]

Immunotherapy shows great potential for long-term control of cancer in some patients but it has novel immune-related toxicities compared with cytotoxic chemotherapy which are still not well-recognised in non-specialist settings.

Objectives

An audit of pembrolizumab monotherapy in metastatic melanoma was carried out to compare outcomes of NHS Highland patients with pivotal trial results (Keynote-006[2]), including overall survival and toxicities.

This work aimed to identify factors to predict positive/negative outcomes and improve cost-effective use of immunotherapy in malignant melanoma.

Method

Patients diagnosed with metastatic malignant melanoma in the period February 2016 to June 2018 were identified. Data was retrieved from the records of patients treated with pembrolizumab.

Results

33 patients were identified. The audit population comprised 17 patients who started treatment with pembrolizumab before June 2018, of whom 16 have at least one year's follow-up.

Approximately 50% of all identified patients were male and 30% were BRAF mutant. Median age was 67 years (range 41 to 86).

Toxicity outcomes

Toxicities occurred in almost all patients who received more than 1 cycle.

System	One or few patients	Several patients
Endocrine	Hypophysitis, Hypogonadism	Hyperglycaemia, Thyroid dysfunction
Musculoskeletal	Arthritis	Arthralgia/myalgia
Respiratory	Pneumonitis	
Dermatology	Spongiotic dermatitis	Pruritis/rash, Loss of pigmentation
Gastrointestinal	Colitis	Nausea
Eyes/Ears/Nose	Uveitis, Hearing loss, Follicular Conjunctivitis, Rhinorrhea	
Other	Renal impairment	Fatigue, Dry mouth

Table 1: Toxicity outcomes

Toxicities were managed with symptomatic treatment, topical/systemic steroids and withholding immunotherapy.

Analysis

Crude 1 year survival was 56%. Median survival was not reached at data censoring, with a maximum of 26 months follow-up.

Outcomes:

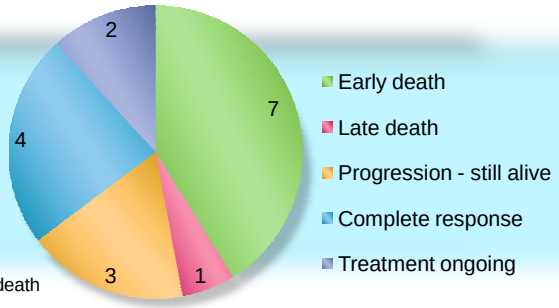

Chart 1: Outcomes composite
- "early death": within 4 months of starting treatment
-"late death": initial response, progressive disease, off-treatment death

Characteristic/Result	Highland patients (inc. Western Isles)	KEYNOTE-006 3-week arm
ECOG performance status – no (%)		
0	9 (53)	189 (68.2)
1	4 (24)	88 (31.8)
2	3 (18)	0 (0)
3	1 (5)	0 (0)
Elevated baseline LDH – no (%)	Yes: 8 (47); No: 5 (29); Not recorded: 4 (24)	98 (35.4)
Brain metastasis – no (%)	3 (18)	27 (9.7)
Median follow-up	26 months	7.9 months (33.9 months*)
Complete response	23.5%	13% *
Crude 12-month survival	56.3%	
Estimated 12-month survival (Kaplan-Meier)		68.4%

Table 2: Benchmarking against Keynote-006: Baseline demographics and outcomes
*combined long-term follow-up data for both pembrolizumab arms as presented at ASCO 2017

Discussion

Performance status >1 and/or presence of brain metastases correlated with poorer outcomes. Cost-effective use of immunotherapy for this indication has improved because of better selection of those patients who are likely to live long enough to benefit from treatment

Conclusions

Overall, results were comparable with the pivotal trial, taking into account limitations such as patient numbers and retrospective nature of the analysis. Four complete responses is a remarkable result in the setting of metastatic malignant melanoma.

Future work will address further analysis of factors relating to outcomes (e.g. baseline LDH, disease bulk/tempo, and considerations relating to stopping treatment in responders.

References

1. HIS and SMC. SMC ID 1086/15. Accessed via https://www.scottishmedicines.org.uk
2. Robert C, Schachter J, Long GV et al. Pembrolizumab versus ipilimumab in advanced melanoma. NEJM 2015; April 19, DOI: 10.1056/NEJMoa1503093