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Impact of Individualized Neoantigen Therapies on Health, Productivity, and Health System Capacity Outcomes in Resectable Melanoma in England

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Background

- The National Health Service (NHS) Long Term Plan seeks to improve cancer survival, partly by increasing early diagnoses.[1] However, better outcomes from early diagnosis hinge on rapid, effective treatment
- Anti–programmed cell death 1 (anti-PD-1) agents have improved survival outcomes in early-stage tumors, prompting a shift in the treatment paradigm for these life-limiting diseases.[2,3] Despite this, there is scope to further improve outcomes with innovative treatments
- Individualized neoantigen therapies (INTs) are a type of cancer immunotherapy that focuses on targeting unique antigens derived from mutations in a patient's tumor[4]
- As INTs are being investigated for various cancers with promising early results, understanding their potential long-term impact is crucial[4]
- We estimated the potential impact on health, productivity, and health system capacity outcomes with the availability of INTs for patients with resectable melanoma in England

Methods

- A 4-state Markov model with a 1-week cycle length and weekly cohort entry was developed to assess the health, productivity, and health system capacity outcomes of introducing INTs in resectable stage IIIB-IV melanoma (**Figure 1**)
- Outcomes were compared over 10 years (2024-2033) for 2 scenarios (**Figure 2**):
  - Current environment: where only anti-PD-1 agents and traditional adjuvant treatment/management are available
  - Future environment: where INTs, anti-PD-1 agents and traditional adjuvant treatment/management are available
- The model leveraged cost-effectiveness models developed for health technology assessment (HTA) submissions to National Institute for Health and Care Excellence (NICE), data from clinical trials, and England-specific epidemiology data and market shares. The model assumptions are found in **Table 1**
- Uptake of INT was hypothetical and assumed to increase over time. Sensitivity analyses exploring lower (50%) and higher (100%) uptake from year 1 were conducted
- A sensitivity analysis exploring a projected future increase of 9% in the melanoma incidence rate was also conducted[13]
- Outcomes included: life-years (LYs), recurrence-free LYs, quality-adjusted LYs (QALYs), recurrences, active treatments for metastatic disease, deaths, productive hours lost, and number of intravenous (IV) metastatic treatment administrations

Figure 1. Model structure

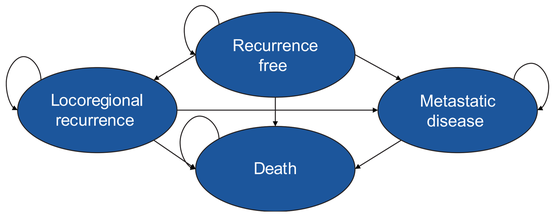
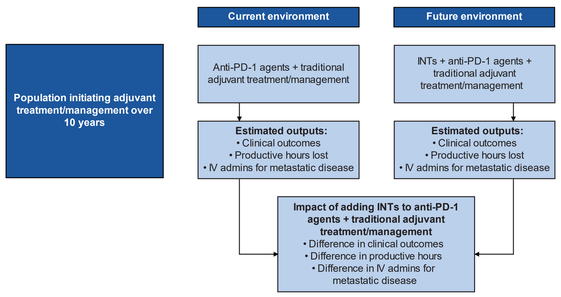


Figure 2. Model structure



Admins, administrations; INT, individualized neoantigen therapy; IV, intravenous; PD-1, programmed cell death 1.

Table 1. General base-case setting and model assumptions

Category	Input/assumptions
Perspective	Health & capacity outcomes: NHS and Personal Social Services in England Productivity outcomes: Societal
Time horizon	10 years (2024-2033)
Discounting	3.50% for all outcomes
Indication	Melanoma (resectable stage IIIB-IV)
Population[5-6,15-19]	• 2024 population: 58,059,854; subsequent annual growth of 0.64% • Target population estimated based on publicly available melanoma epidemiology data, applied to the annual estimated population of England • *Sensitivity analysis: 9% increase in melanoma incidence rate*[13]
Model structure & health state transitions[4,7-8,14]	4-state Markov model with weekly cycles • Transition probabilities for anti-PD-1 agents, BRAF inhibitors and watchful waiting informed by clinical trials, NMA or published research, based on cost-effectiveness models used in recent NICE appraisals[7-8] • Transition probabilities for INTs from the recurrence-free state estimated by applying the HR from KEYNOTE-942 to the anti-PD-1 agent patient trace (based on KEYNOTE-054)[4,14] • Annual incident population averaged to estimate incident patients per week, with a new weekly incident cohort entering the model each cycle
Treatment duration[4,9-10]	Specific to the treatment options received in the adjuvant setting, or in the 1L and 2L metastatic setting, based on observed time on treatment in relevant trials
Market shares	• Current treatments: based on resource impact templates from a recent NICE appraisal,[7] market research, and clinical expert opinion • INT uptake: hypothetical linear uptake over time, averaging 68% over 10 years • *Sensitivity analysis: 50% INT uptake from year 1; 100% INT uptake from year 1*
Retreatment with anti-PD-1 inhibitors	Retreatment with any or the same anti-PD-1 agent permitted 6 months after adjuvant anti-PD-1 agent treatment completion, in line with NICE appraisal[7]
Health state utilities[9-10]	• Informed by clinical trials and mapped to local values using UK-specific algorithms, adjusted for age and sex • Disutility of adverse events (grade 3+ adverse events with ≥ 5% incidence in any treatment arm) assumed to be experienced at treatment initiation
Productivity[11-12]	Inputs taken from a patient and carer survey assessing productivity impact of early-stage cancer, and UK labor statistics

1L, first-line; 2L, second-line; HR, hazard ratio; INT, individualized neoantigen therapy; NHS, National Health Service; NICE, National Institute for Health and Care Excellence; NMA, network meta-analysis; PD-1, programmed cell death 1; UK, United Kingdom.

Results

- Over 10 years, 9,163 (68%) of the 13,416 patients eligible for adjuvant therapy for stage IIIB-IV melanoma were estimated to initiate treatment with INT + anti-PD-1 agents (instead of anti-PD-1 agents or traditional adjuvant treatment/management)
- This is anticipated to result in overall health gains by increasing LYs and QALYs, whilst decreasing recurrences, the number of patients requiring metastatic treatment, and deaths
- It is also estimated to result in fewer IV metastatic treatment administrations due to fewer recurrences, therefore reducing the health system capacity burden for metastatic disease
- The anticipated increased survival for patients, and lower absenteeism and presenteeism for both patients and carers, also results in overall productivity gains
- The benefits accumulate steadily over the 10-year horizon and are anticipated to extend beyond this time frame (**Figure 3** and **Figure 4**)

Table 2. Total 10-year impact on health, productivity, and capacity outcomes of using INT in combination with anti-PD-1 agents as adjuvant treatment of early-stage melanoma

		Impact on outcomes, n (%)[a]							
	Patients initiating INT + anti-PD-1, n (%)	Recurrence-free LYs	Total LYs	QALYs	Recurrences	Patients receiving metastatic disease treatment	Deaths	IV metastatic treatment admins	Productive years gained[b]
Base case	9,163 (68%)	3,092	1,269	1,341	-1,207	-1,010	-457	-12,292	2,696
		8%	3%	3%	-19%	-17%	-15%	-18%	15%
Sensitivity analyses									
Increase melanoma incidence rate by 9%	9,987 (68%)	3,370	1,383	1,461	-1,315	-1,101	-498	-13,399	2,939
		8%	3%	3%	-19%	-17%	-15%	-18%	15%
Lower INT uptake (50%)	6,708 (50%)	2,679	1,197	1,236	-916	-780	-372	-9,928	2,364
		7%	2%	3%	-14%	-13%	-12%	-15%	13%
Higher INT uptake (100%)[c]	13,416 (100%)	6,365	2,815	2,905	-2,121	-1,833	-867	-21,490	5,601
		17%	6%	7%	-33%	-31%	-28%	-32%	30%

Admins, administrations; INT, individualized neoantigen therapy; IV, intravenous; LY, life year; QALY, quality-adjusted life year; PD-1, programmed cell death 1.
[a]For each scenario and each outcome, results are presented as the absolute (n) and relative (%) change for the future environment vs current environment.
[b]Resulting from lower absenteeism and presenteeism for both patients and carers, and improved survival for patients.
[c]While a small proportion of patients may be contraindicated to INT + anti-PD-1 therapy, this scenario estimates the most optimistic impact should there be full uptake of INTs.

Figure 3. Annual impact on LYs, QALYs, and patient and carer productivity

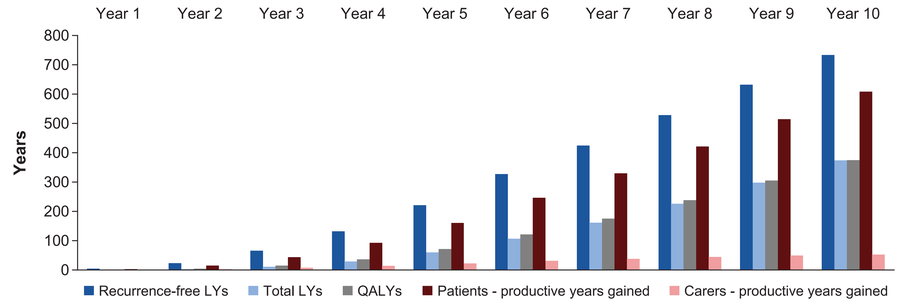
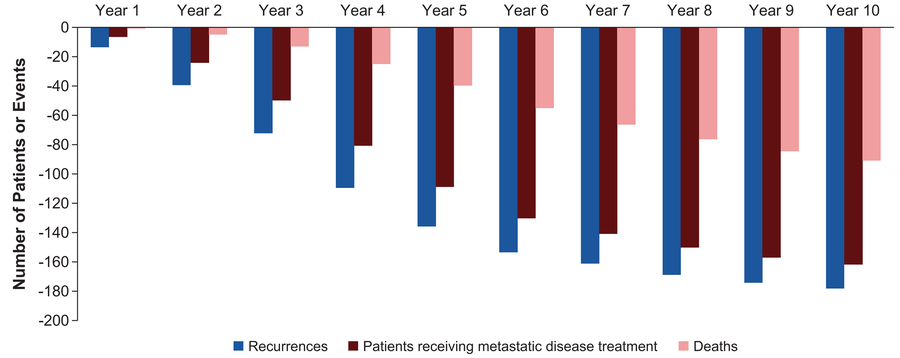


Figure 4. Annual impact on event-based outcomes



LY, life year; QALY, quality-adjusted life year. Results are presented as the absolute change for the future environment vs current environment.

Conclusions

- INTs currently in development have the potential to bring substantial health and productivity benefits
- By increasing recurrence-free and overall survival, INTs can help lower absenteeism and presenteeism for patients and carers, resulting in work productivity gains
- Introducing INTs as a potential adjuvant treatment also has the potential to reduce the number of IV metastatic treatment administrations required, alleviating the associated NHS burden
- The model used to project the estimated benefits of INT + anti-PD-1 agents builds on analyses for anti-PD-1 agents submitted to and assessed by international HTA agencies, such as NICE[7-8]
- One limitation of the model is its 10-year time horizon, which may not fully capture the value of treatments for early-stage melanoma. This is due to the possibility that events or recurrences for patients entering the model's cohort in the later years (years 8-10) of the analysis may occur after the 10-year period. As a result, the predicted benefits might be underestimated
- Investment and early planning in health systems in advance of launch to enable earlier, broad uptake once INTs are available will help maximize potential benefits of treatment

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