Impact of Individualized Neoantigen Therapies on Health, Productivity, and Health System Capacity Outcomes in Resected Melanoma in Belgium

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Background

- The upcoming Belgian Cancer Plan 2025-2030 seeks to improve cancer care, partly by increasing early diagnoses and access to innovation[1]
- Better outcomes from early diagnosis hinge on rapid, effective treatment
- Anti-PD-[L]1 inhibitors have improved survival outcomes in early-stage tumors, prompting a shift in the treatment paradigm for these life-limiting diseases.[2,3,4] 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[5]
- As INTs are being investigated for various cancers with promising early results, understanding their potential long-term impact is crucial[5]
- We estimated the potential impact on health, productivity, and health system capacity outcomes with the availability of INTs for patients with resectable melanoma in Belgium

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 two 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 a cost-effectiveness model used for HTA submission in Belgium, data from clinical trials, and Belgium-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
- Outcomes include: life years (LYs), recurrence-free LYs, quality-adjusted life years (QALYs), recurrences, active treatments for metastatic disease, deaths, productive years lost, and number of intravenous (IV) metastatic treatment administrations

Figure 1. Model structure

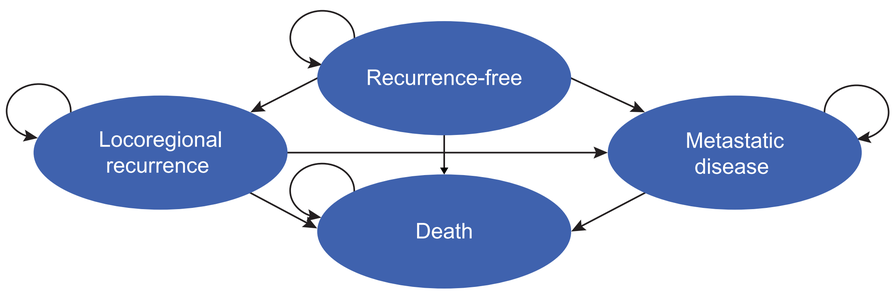
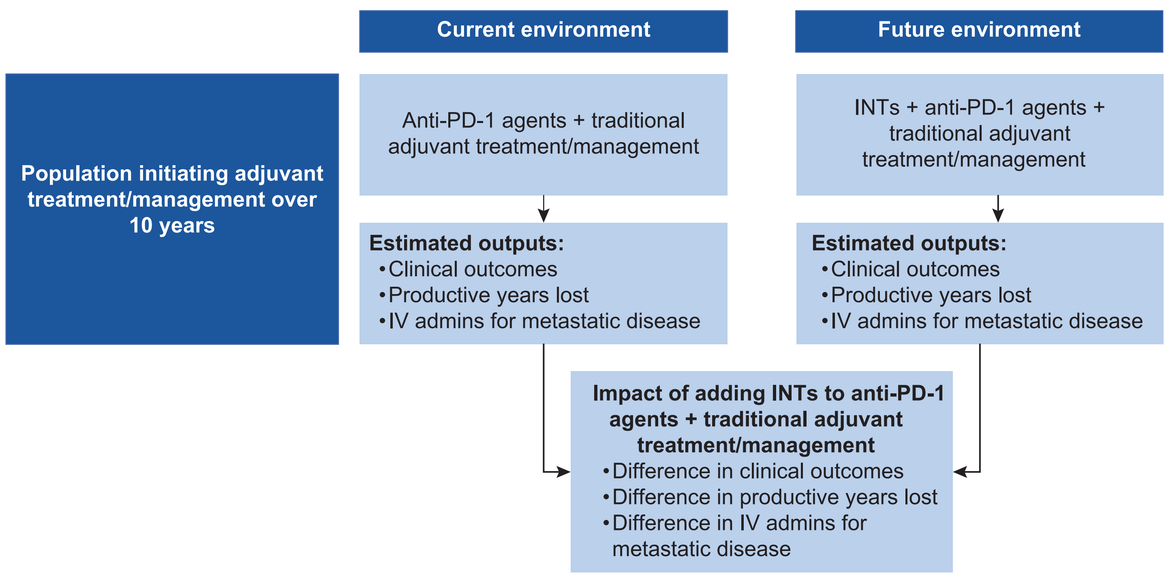


Figure 2. Model overview



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	Belgian health care system
	Time horizon	10 years
	Discounting[6]	Clinical outcomes: 1.50% in line with Belgium HTA modelling guidelines
	Indication	Melanoma (Stage IIIB-IV)
	Population[7-10]	• 2024 population: 11,763,650 • Growth rate of 0.57% applied to Year 2025 and onwards • Females: 50.72% • Target population estimated based on publicly available melanoma epidemiology data, applied to the annual estimated population of Belgium
	Model structure and health state transitions[11]	4-state Markov model with weekly cycles • Transition probabilities for anti-PD-1, BRAF inhibitors, and watchful waiting informed by clinical trials, NMA or published research, based on a cost-effectiveness model used in Belgium[7] • Transition probabilities for INTs from the recurrence-free state estimated by applying HR from KEYNOTE-942 to the anti-PD-1 patient trace (based on KEYNOTE-054) • Annual incident population averaged to estimate newly eligible patients per week, with a new weekly eligible cohort entering the model each cycle
	Treatment duration[5,11]	Specific to the treatment options received in adjuvant setting, or in 1L and 2L metastatic setting, based on observed time on treatment in relevant trials
	Market shares	• Current treatments: Based on market research and clinical expert opinion • INT uptake: Hypothetical progressive increase in uptake from 2024 to 2030 resulting in a 10-year average uptake of 60%
	Retreatment with anti-PD-1 inhibitors	Market shares in the metastatic treatment setting are conditional on the adjuvant treatment received. Anti-PD-(L)1 agents may be used in the metastatic setting by patients who received them in the adjuvant setting after 53 weeks
★★☆	Health state utilities[12-15]	• Informed by clinical trials and mapped to local values using European 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[16]	Inputs taken from a patient and caregiver survey assessing the productivity impact of early-stage cancer, and Belgian labour statistics

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

Results

- Over 10 years, 1,781 of the 2,985 (59%) patients eligible for adjuvant therapy for Stage III-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 increase eligible population LYs without recurrence by 681 (7%) and QALYs by 304 (3%), while avoiding 225 (15%) recurrences, 173 (11%) metastatic treatments, and 102 (14%) deaths
- It is also anticipated to result in 2,014 (11%) fewer IV metastatic treatment administrations needed, and a gain of 600 (14%) productive years for both patients and caregivers
- The benefits accumulate steadily over the 10-year horizon and are anticipated to extend beyond this time frame (**Figure 3-4**)

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 (%)									
	Patients initiating INT + anti-PD-1, n (%)	Recurrence-free LYs	Total LYs	QALYs	Recurrences	Metastatic disease treatments	Deaths	IV metastatic treatment admins	Productive years gained-patients[a]	Productive years gained-carers[a]
Base Case	1,781 (59%)	680.52	319.75	303.95	-224.80	-172.63	-101.71	-2,014	548.32	51.56
		7%	3%	3%	-15%	-11%	-14%	-11%	14%	14%

INT, individualized neoantigen therapy; LY, life years; PD-1, programmed cell death 1; QALY, quality-adjusted life years. For each scenario and each outcome, results are presented as the absolute (n) and relative (%) change for the future environment vs current environment.

[a]Resulting from lower absenteeism and presenteeism for both patients and carers, and improved survival for patients.

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

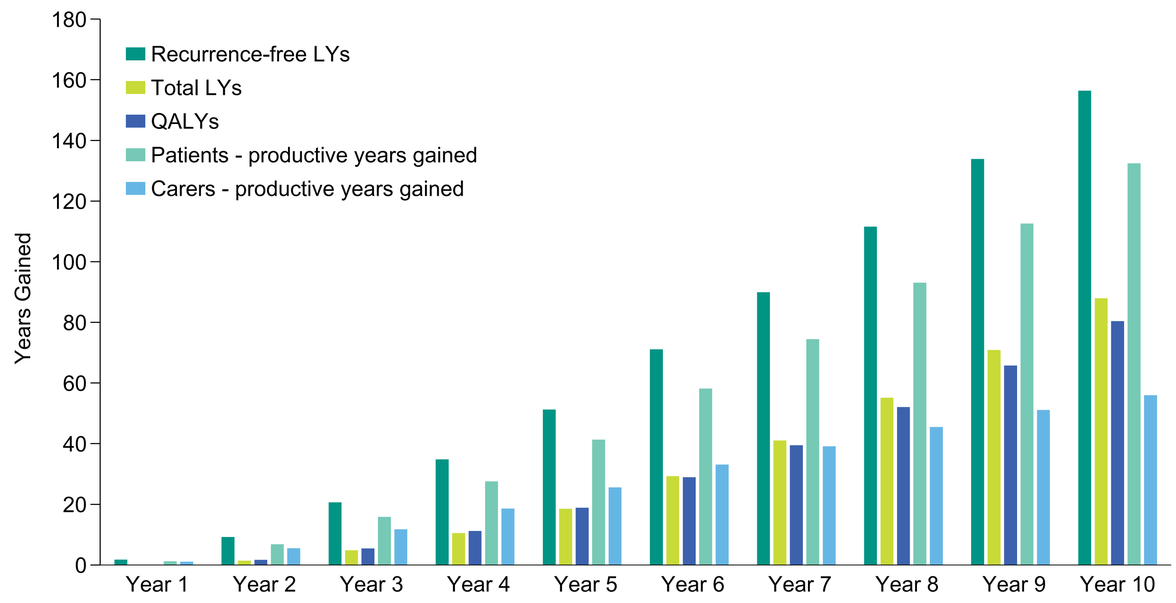
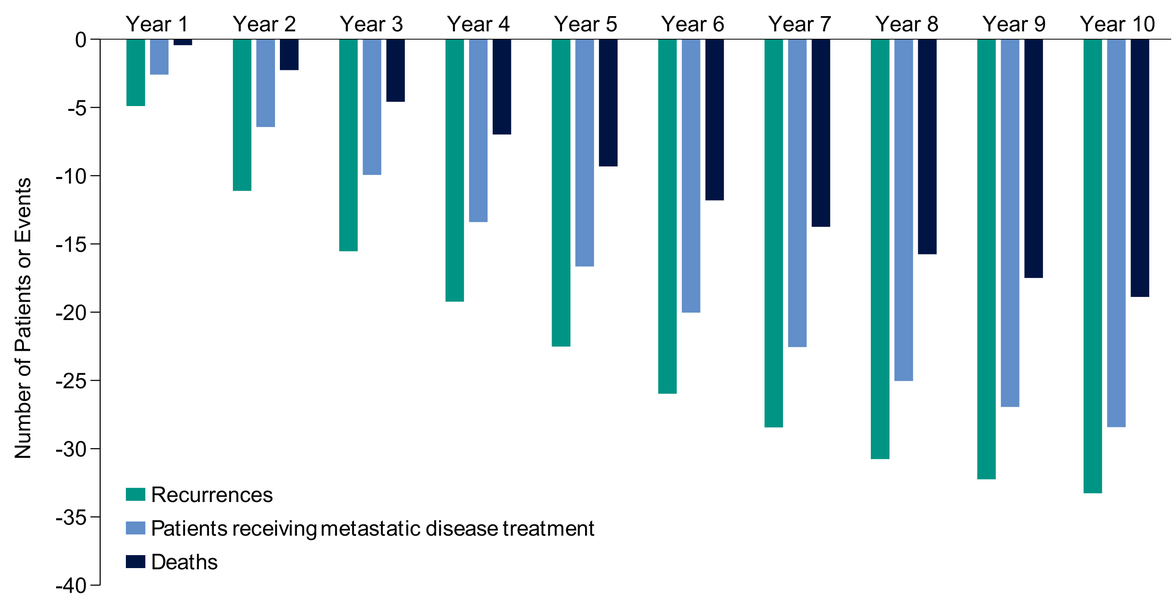


Figure 4. Annual impact on event-based outcomes



Conclusions

- INTs currently in development have the potential to bring substantial health outcome benefits
- Additionally, by increasing recurrence-free and overall survival, INTs can help lower absenteeism and presenteeism, resulting in work productivity gains
- Introducing INTs as an adjuvant treatment option has the potential to reduce the number of metastatic treatment administrations required, alleviating the associated cost for INAMI/RIZIV
- 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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