Acceptance Code PT34

Impact in health outcomes of PD-(L)1 inhibitors in early-stages cancers in Switzerland

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Background

- It is estimated that 45,000 new cases of all cancers and 17,300 deaths due to cancer occur in Switzerland every year.[1] Worldwide, there were approximately 19.3 million new cancers in 2020, projected to rise to 28.4 million in 2040[2]
- Anti-programmed cell death 1/anti-programmed death-ligand 1 (anti-PD-(L)1) agents are mainstay treatments for several advanced/metastatic cancers, and their expansion into the early-stage settings is further changing the treatment paradigm
- Treatment of early-stage tumors with PD-(L)1 inhibitors is linked to better outcomes and improved recurrence-free survival after surgery and is expanding rapidly

Objective

- A health outcomes projection model, originally developed for Belgium[3], was adapted to Switzerland to assess the health benefits of adopting PD-(L)1 inhibitors in multiple early-stage cancers. Two scenarios were developed to compare health outcomes (**Figure 1**):
  a. PD-(L)1 inhibitors can be used for patients with early-stage disease (world with PD-(L)1 inhibitors)
  b. PD-(L)1 inhibitors are reserved for patients who develop advanced/metastatic disease (world without PD-(L)1 inhibitors for early-stage disease)

Methods

- The health outcomes model focuses on 3 cancers: melanoma stage III, renal cell carcinoma (RCC), and triple-negative breast cancer (TNBC)
- The model predicts clinical outcomes throughout the patient pathway following a Markov model with 4 health states, in weekly cycles from when they initiate neoadjuvant and/or adjuvant treatment, over a time horizon of 10 years
- Clinical outcomes estimates include life-years (LY), without event or recurrence and in total, quality-adjusted life-years (QALY), events or recurrences, active treatments for metastatic disease, adverse events (AE), and deaths
- The model leverages cost-effectiveness and budget impact models developed for HTA purposes, data from pivotal trials, and Swiss-specific data on projected eligible patients and market shares[4-8]

Figure 1. Model structure – calculations

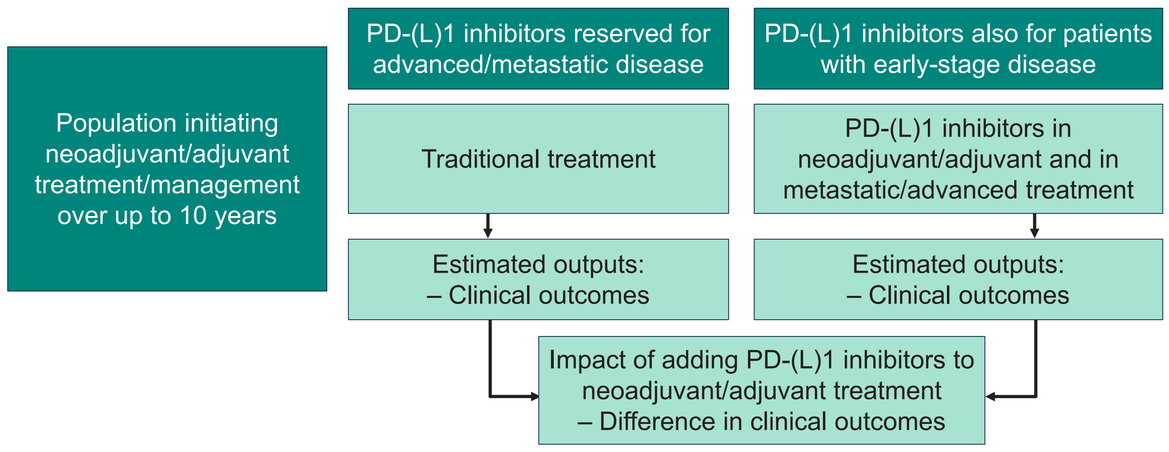


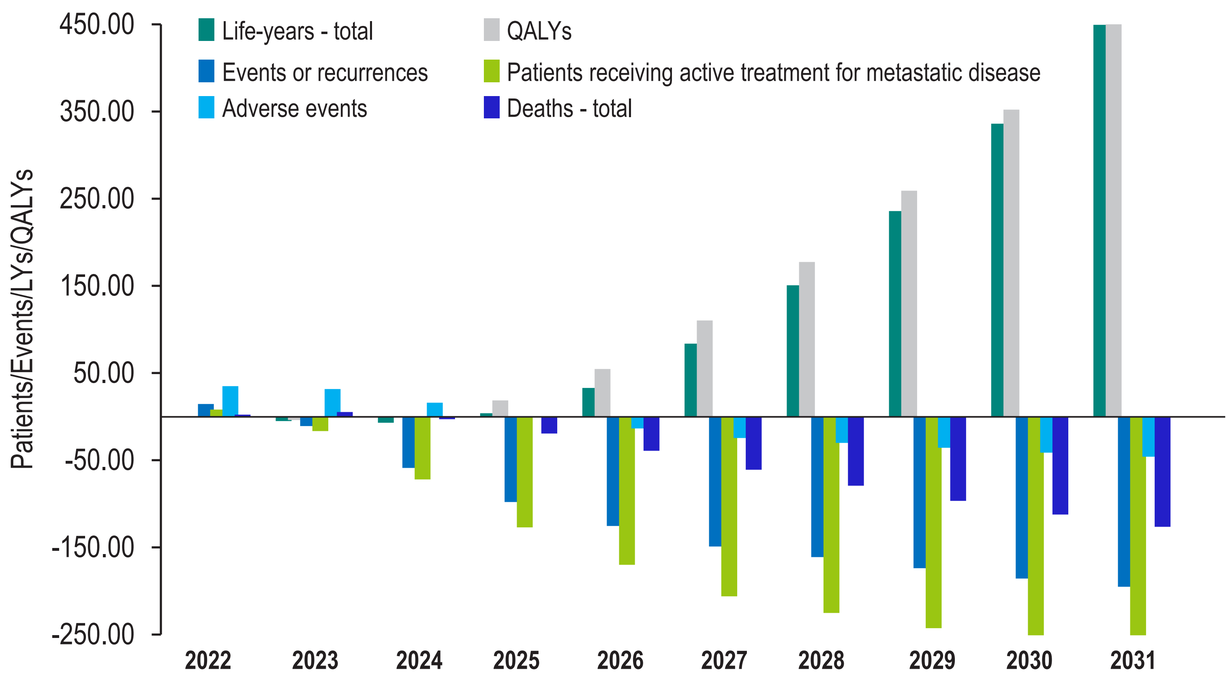
Table 1. General base-case setting and model assumptions

Category	Input
Perspective	Swiss healthcare system
Time horizon	10 years
Discounting for clinical outcomes	1.50%
Tumor sites	Stage III melanoma RCC at increased risk of recurrence following nephrectomy +/- resection of metastatic lesions Locally advanced or early-stage TNBC at high risk of recurrence
Population[9]	2022 population: 8,826,016 Growth rate (annual) of 4.4% applied to year 2023 onwards Females: 50.37%
Health state transitions [4-6]	Markov model. Transition probabilities informed from clinical trials and subsequent NMA or published research.
Treatment duration	Specific to the treatment options received in adjuvant/neoadjuvant setting or in 1L and 2L treatment.
Market shares	Are based on market research and expert opinion
Retreatment with PD-(L)1 inhibitors	Retreatment with any or the same PD-(L)1 inhibitor is possible 6 months after the neoadjuvant/adjuvant treatment completion
AEs[10-12]	AEs included are drug-related, and of Grade 3+ with ≥ 5% incidence in any treatment arm. AEs and corresponding disutilities are accounted for as one-off events at treatment initiation
Health state utilities[10-12]	Informed from relevant clinical trials and are mapped to local values using European algorithms. Age- and sex-related disutilities are also considered

Results

- Of the estimated 10,659 eligible patients over 10 years (2022-2031), 9,050 are estimated to initiate neoadjuvant and/or adjuvant treatment with PD-(L)1 inhibitors for early treatment of melanoma stage III, RCC, and TNBC
- Compared to PD-(L)1s being available only in the metastatic setting, introducing PD-(L)1 inhibitors in the neoadjuvant/adjuvant setting for melanoma stage III, RCC, and TNBC is anticipated to (over 10 years):
  – Avoid 1,144 recurrences (27% fewer recurrences)
  – Prevent 1,577 active treatments in the metastatic setting (35% fewer treatments)
  – Avoid 530 deaths (23% fewer deaths)
  – Increase life-years without recurrence by 3,416 (10% increase in life years)

Figure 2. Change in clinical outcomes when PD-(L)1 inhibitors are used in early-stage cancer



Conclusions

- Early-stage treatment with PD-(L)1 inhibitors is linked with better outcomes by reducing the number of recurrences and deaths, extending the time patients spend free of recurrences/events/disease, and reducing the number of treatments for metastatic disease
- This health outcomes projection tool can support discussions around investment in PD-(L)1 inhibitors in the neoadjuvant/adjuvant settings (in both upcoming and already approved uses) and generally inform planning around investment in innovative treatments for early-stage cancers
  – Importantly, a longer time horizon is needed to fully capture the range of health benefits experienced by patients using PD-(L)1 inhibitors. The results generated by the tool considering 5- and 10-year time horizons are anticipated to be an underestimate of these health benefits

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Presented at ISPOR Europe 2023; Copenhagen, Denmark; November 12-15, 2023.