Projected survival to population Average Life Expectancy (ALE) with pembrolizumab use in early-stage cancer setting in Greece: **A modelling study of 3 pembrolizumab indications**

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BACKGROUND

- Identifying interventions that improve cancer **survival** and **quality of life (QoL)** is a public health priority. This study complements our previous analysis[1] by adding **muscle-invasive bladder cancer (MIBC)**, **head and neck (H&N) cancer** and **stage III melanoma**.
- **The cancer burden is high and rising** Greece records an estimated **64,530** new cases and **33,166** deaths per year[2], projected to rise by **16.5%** and **23.7%** by 2045;[3] worldwide, **20.0 million** cases and **9.7 million** deaths were estimated according to GLOBOCAN 2022.[4]
- **MIBC is a leading cancer in Greece:** it is the **5th** most common cancer in Greece (**5,122** new cases and **1,554** deaths in 2022)[5]. Cisplatin-ineligible patients could not receive standard perioperative chemotherapy.
- **H&N cancer is the 8th most common cancer worldwide** (**771,694** cases, **385,004** deaths)[4]; in Greece **1,629** new cases and **667** deaths per year[5]. In locally advanced disease 5-year survival is only **~50%** and up to **55.7%** of patients recur, mostly within 1–2 years[6].
- **Melanoma is among the fastest-growing cancers** global incidence and mortality are projected to rise by **>50%** and **69%** by 2040[7]; in Greece it shows the highest rise in incidence in men and the second highest in women[8]. Moreover, resected stage III disease carries a high risk of recurrence.[9]
- **Pembrolizumab covers an unmet medical need.** Patients with cisplatin-ineligible MIBC and resectable locally advanced H&N cancer (no new treatment in 20 years) had no other perioperative systemic treatment alternative. Patients are expected to **live longer** and stay **free of recurrencies** for longer –while their QoL is preserved during treatment.[10]
- **Cost effectiveness assessment of these indications in Greece** Pembrolizumab is cost-effective in Greece under the assumption of the WHO recommendation of using the GDP per capita up to three times, with a threshold of €64,900/QALY.[15] Henceforth the three indications included in this analysis fall within the threshold of Greece. More specifically, in stage III melanoma (€15,186/QALY), H&N cancers (€35,875/QALY)[14] and bladder cancer (€22,362/QALY).

METHODS

- **Three early-stage Markov models** were used for this analysis, **MIBC** (KEYNOTE-905)[12] **H&N cancer** (KEYNOTE-689[10]) and **stage III melanoma** (KEYNOTE-054[9]). The **mean baseline age** of each pivotal trial was used as the cohort starting age. Models were run over a **lifetime horizon and the individual Markov traces of each indication were used to make projections about patients reaching average life expectancy,** using the **same methodology** as our previous analysis.[1]
- Analyses follow the **EMA-approved labels**[13]. **Efficacy** inputs were taken directly from the **pivotal trials**; **parametric extrapolations** were selected using goodness-of-fit metrics and clinical plausibility and validated by clinical experts. Inputs were updated from the indication-specific **Greek cost-effectiveness models** and **Greek DRG's.**[14]
- The outcome calculated was the **percentage of patients reaching aLE** of the Greek population (81.8 years of age)[11] with pembrolizumab compared to the the previous SoC.

Figure 1: Key model Results

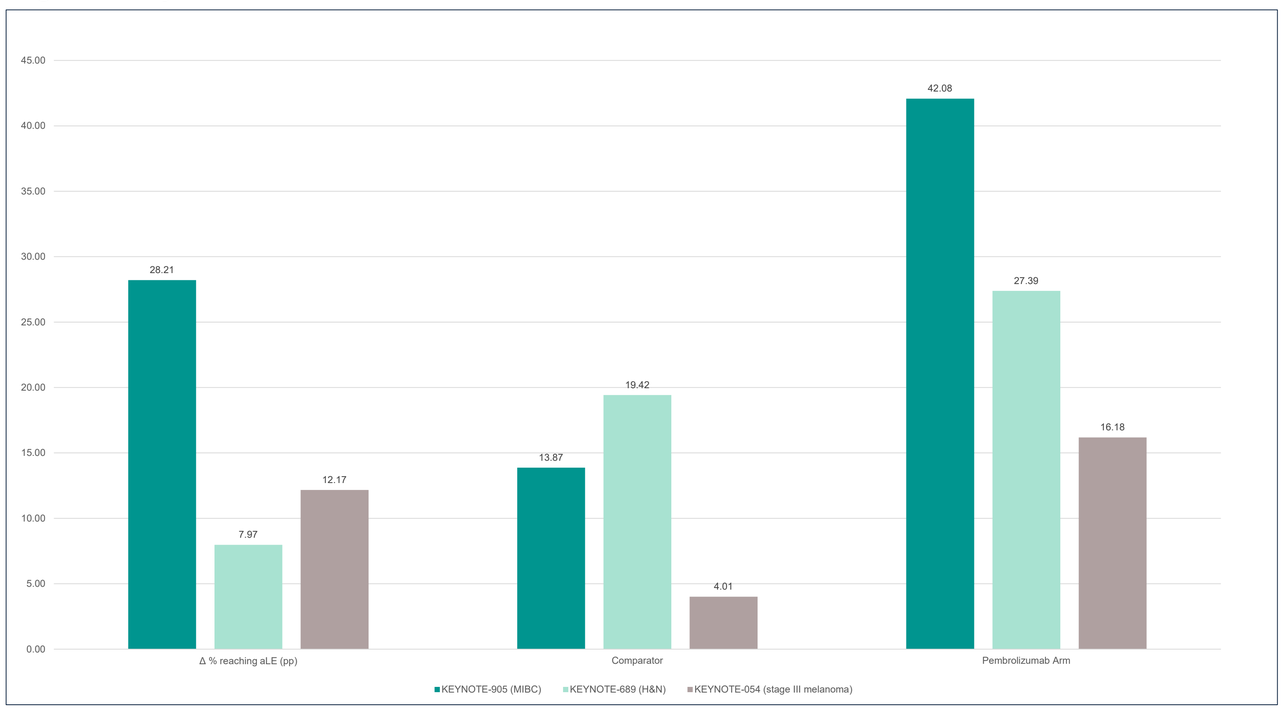
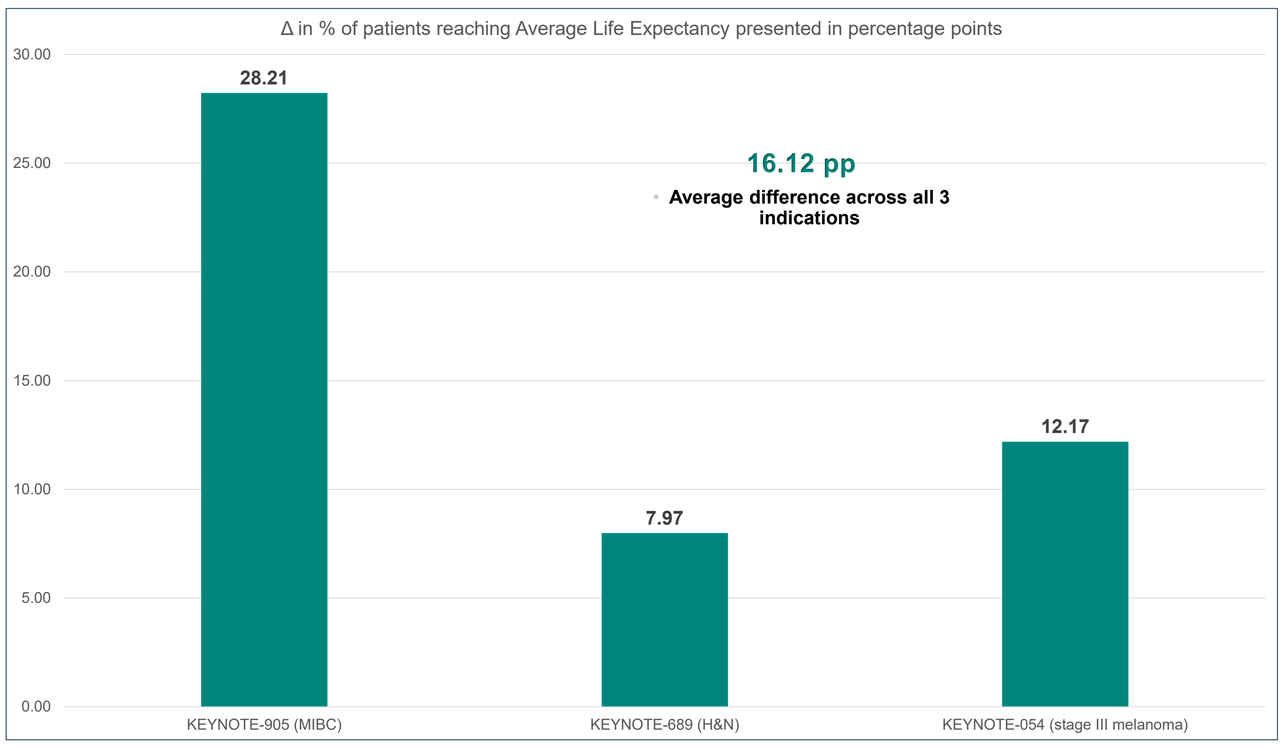


Figure 2: Incremental Gains in Projected Survival with Pembrolizumab Treatment



OBJECTIVE

The aim of this study is to estimate the proportion of patients expected to reach the **average life expectancy (aLE)** of the general Greek population (**81.8 years**)[11] with early-stage pembrolizumab, compared with the previous **standard of care (SoC)**.

RESULTS

- Among patients with **MIBC**, **42.08%** of those receiving perioperative pembrolizumab combination (with enfortumab vedotin) were projected to reach aLE vs. **13.87%** of those treated with surgery alone (**×3.0**).
- In **H&N cancer**, **27.39%** of patients receiving perioperative and adjuvant pembrolizumab combination therapy were expected to reach aLE vs. **19.42%** of those treated with the previous SoC, adjuvant radiotherapy.
- In **stage III melanoma**, **16.18%** of patients receiving pembrolizumab were estimated to reach aLE vs. **4.01%** of patients under routine surveillance (**×4.0**).
- Across the three indications, pembrolizumab increased the proportion of patients reaching aLE by **16.1 percentage points** on average (Table 2, Figure).

Table 1: Base-case results

MIBC (KEYNOTE-905)		
Effectiveness	**Perioperative pembrolizumab + EV**	**Surgery alone**
Life years (LYs), total	**7.63**	**4.66**
Event-free LYs	7.01	3.26
LYs after recurrence / progression	0.62	1.40
% patients reaching aLE	**42.08%**	**13.87%**
Difference vs. comparator	**+28.21 percentage points (×3.0)**	
H&N cancer (KEYNOTE-689)		
Effectiveness	**Perioperative + adjuvant pembrolizumab**	**Adjuvant radiotherapy (SoC)**
Life years (LYs), total	8.83	7.07
Event-free LYs	8.42	6.50
LYs at locoregional recurrence	0.14	0.22
LYs after recurrence / progression	0.26	0.35
% patients reaching aLE	**27.39%**	**19.42%**
Difference vs. comparator	**+7.97 percentage points (×1.4)**	
Stage III melanoma (KEYNOTE-054)		
Effectiveness	**Pembrolizumab**	**Routine surveillance**
Life years (LYs), total	10.01	6.50
Event-free LYs	8.28	4.04
Locoregional Recurrence	0.26	0.39
Distant Metastasis	1.46	2.07
% patients reaching aLE	**16.18%**	**4.01%**
Difference vs. comparator	**+12.17 percentage points (×4.0)**	

CONCLUSION

- Early-stage pembrolizumab has the potential to **extend long-term survival** and **increase the number of patients reaching the average life expectancy** in Greece. Thus, patients have the opportunity to life longer through **reduced premature mortality**.
- **1. MIBC:** demonstrates the largest incremental gain – **42.08% vs. 13.87%** reach aLE (**+28.2 pp**) among patients who previously had no perioperative systemic alternative.
- **2. H&N cancer: 27.39% vs. 19.42%** (**+8.0 pp**) in a disease with ~50% 5-year survival and no new treatment in 20 years.
- **3. Stage III melanoma:** 4-fold more patients reach aLE (**16.18% vs. 4.01%**), offering long-term survival to patients at high risk of recurrence.
- **QoL in the event free survival health state:** Patients are expected to live longer and spend more time event-free with Pembrolizumab use, the state with the highest Quality of life among all three types of cancer (H&N utilities: 0.783 event-free vs. 0.662 after progression)[14].

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