AVELUMAB`S EFFECT ON REDUCING CANCER MORTALITY AMONG ADULT PATIENTS WITH LOCALLY ADVANCED OR METASTATIC UROTHELIAL CARCINOMA

Nikolay A Avxentyev[1], Yuliya V Makarova[1]

[1] Financial Research Institute, Moscow, Russia; Health and Market Access Consulting, Moscow, Russia; Pharmaceutical Analytics Middle East, Ras al Khaimah, United Arab Emirates

BACKGROUND

- Platinum-based chemotherapy (CT) and immune checkpoint inhibitors (ICIs) are treatment options for patients with locally advanced or metastatic urothelial carcinoma (mUC).
- While most ICIs are employed as first- or second-line treatments, avelumab is used for maintenance therapy following platinum-based CT.

OBJECTIVES

- The aim of this study is to evaluate the impact of ICIs on cancer mortality in adult patients with mUC in Russia

METHODS

- Platinum-eligible adult patients with mUC were identified as the target population. The number of these patients was estimated using statistical data on the diagnosis of stage III-IV bladder cancer and the proportion of cases eligible for platinum-based treatment[1].
- Considered treatment options were (Figure 1):
  o No use of ICIs (Scenario 1);
  o Use of pembrolizumab, nivolumab or atezolizumab for a subset of eligible patients (Scenario 2: current practice);
  o Maintenance therapy with avelumab after platinum-based CT in all eligible patients (Scenario 3);
  o Use of avelumab for a subset of eligible patients instead of other ICIs (budget-neutral Scenario 4).
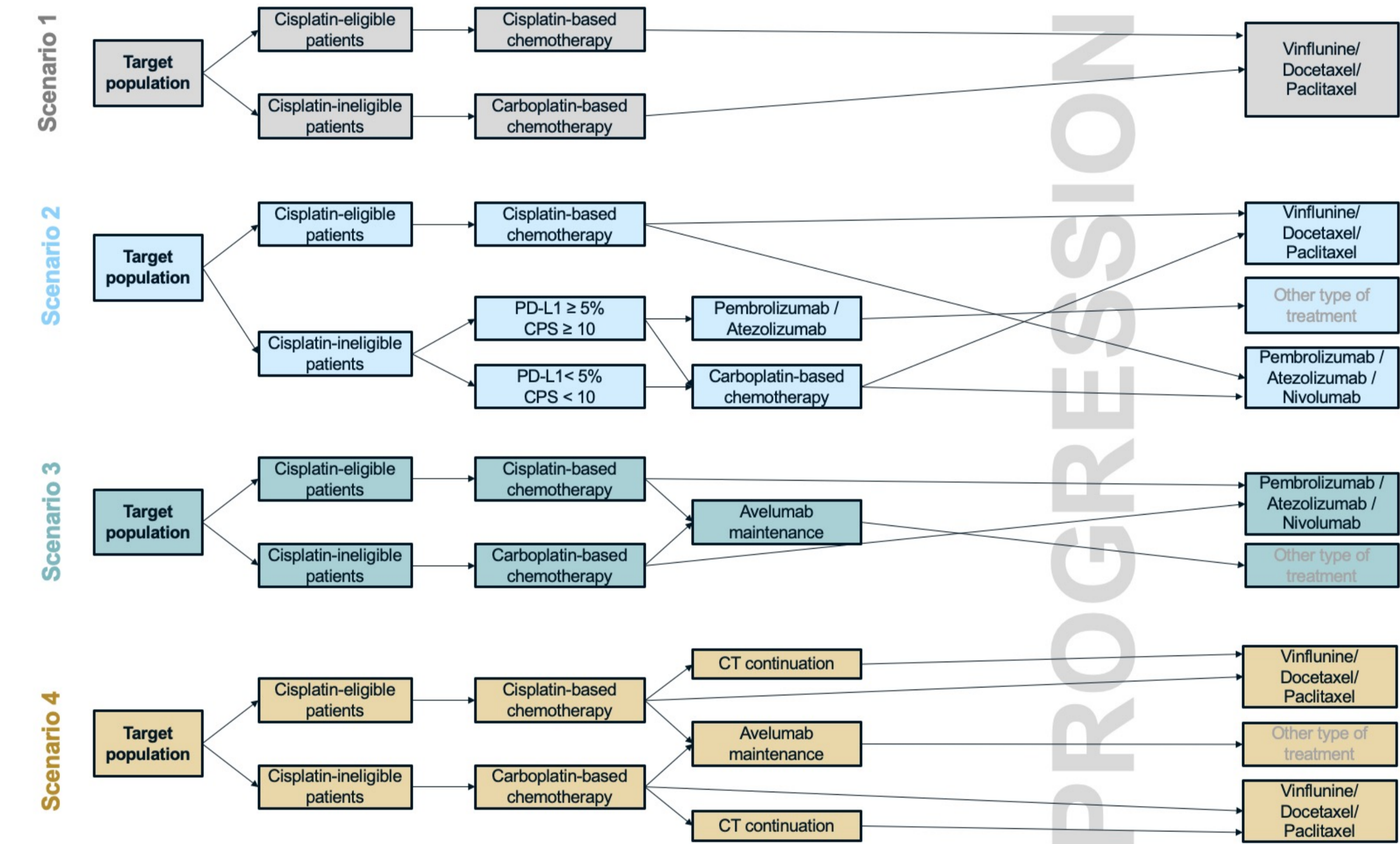

Figure 1. Treatment path for each considered Scenario.

- A mathematical model was developed to estimate overall survival (OS) and medication costs across the evaluated scenarios. It was assumed that all eligible patients began 1st-line treatment and remained on therapy for the median progression-free survival duration[2,3,4,6,7,8,9]. Following disease progression, all surviving patients transitioned to 2nd-line treatment. The composite OS was constructed by integrating OS[2,3,5,6,7,8,10] for each respective treatment option and model state.
- This model was used to estimate the number of lives saved, healthcare system costs and impact on one-year mortality when transitioning between different scenarios (from Scenario 1 to Scenario 2, from Scenario 2 to Scenario 3, and from Scenario 1 to the budget-neutral Scenario 4) over a three-year horizon, considering the number of mUC patients, who may start platinum-based therapy annually in Russia.

RESULTS

- Annually, up to 4,182 patients with locally advanced or metastatic UC in Russia can initiate platinum-based CT.
- The estimation of avoided deaths resulting from the transition between different scenarios is shown in Figure 2:
  o If 4,182 eligible patients were to receive therapy according to the Scenario 3, 777 deaths could be prevented in the first year compared to the Scenario 2;
  o By the end of the second year 1,870 patients would still be alive in the Scenario 3 group, resulting in 1,030 deaths during that year. In the Scenario 2 group, there would be 924 surviving patients, with 1,199 deaths in the second year. Consequently, the Scenario 3 cohort would experience 169 fewer deaths. However, a new cohort would start`treatment in the second year, and an additional 777 deaths would be prevented if they were treated according to the Scenario 3. Thus, the cumulative impact in the second year would be 946 prevented deaths;
  o Similar estimations were performed for the third year, indicating that transitioning to avelumab therapy in Scenario 3 could potentially save an additional **2,506 lives** over a three-year period.
- By applying the same methodology, it was concluded that:
  o Compared to Scenario 1, the current use of ICIs in a subset of eligible patients (Scenario 2) saves **553 lives** over three years;
  o Replacing other ICIs with avelumab within the same budget (Scenario 4) could save **1,602 lives** without incurring additional costs (see Figure 3).
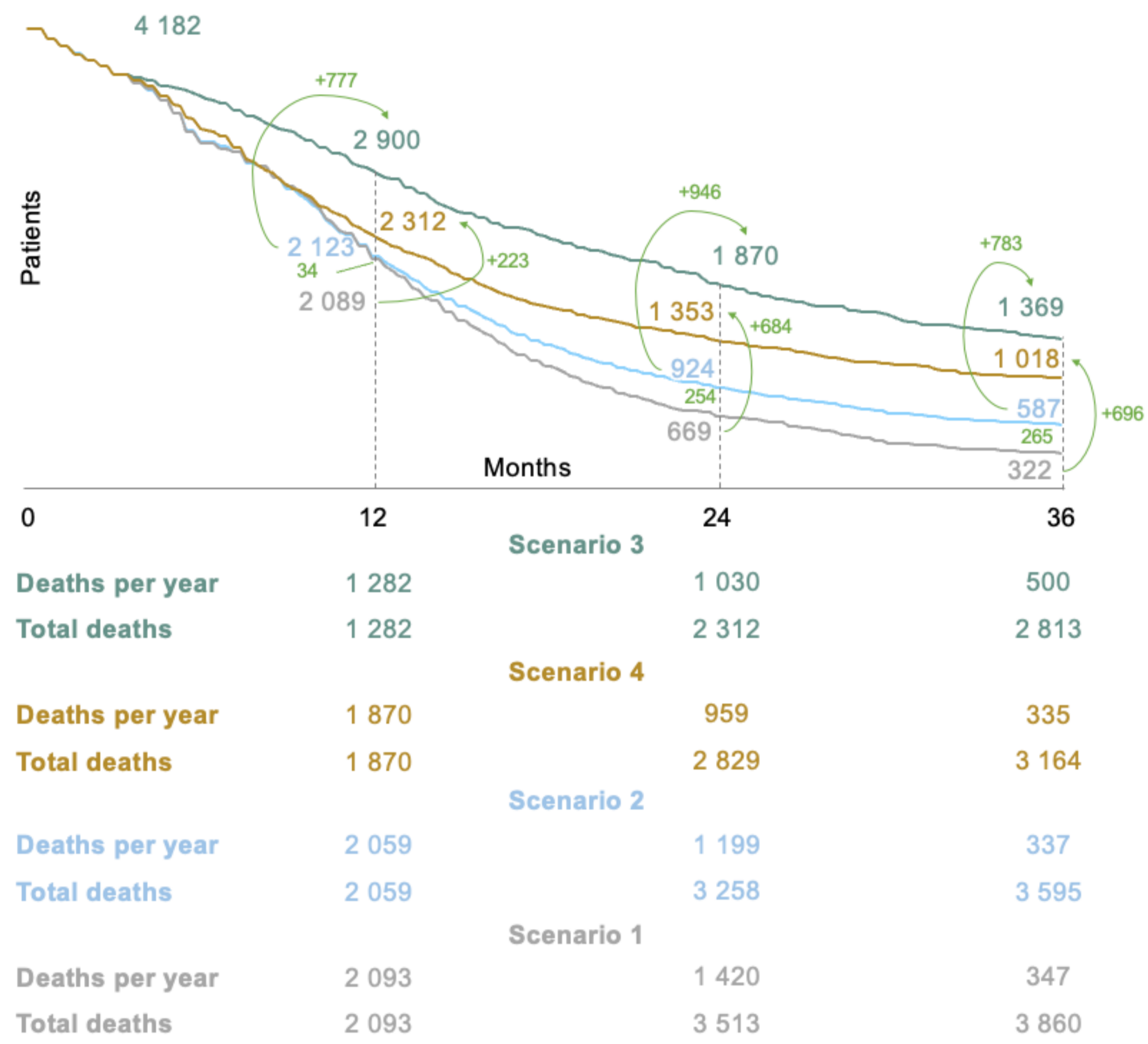

Figure 2. Estimation of avoided deaths due to transition between different scenarios.

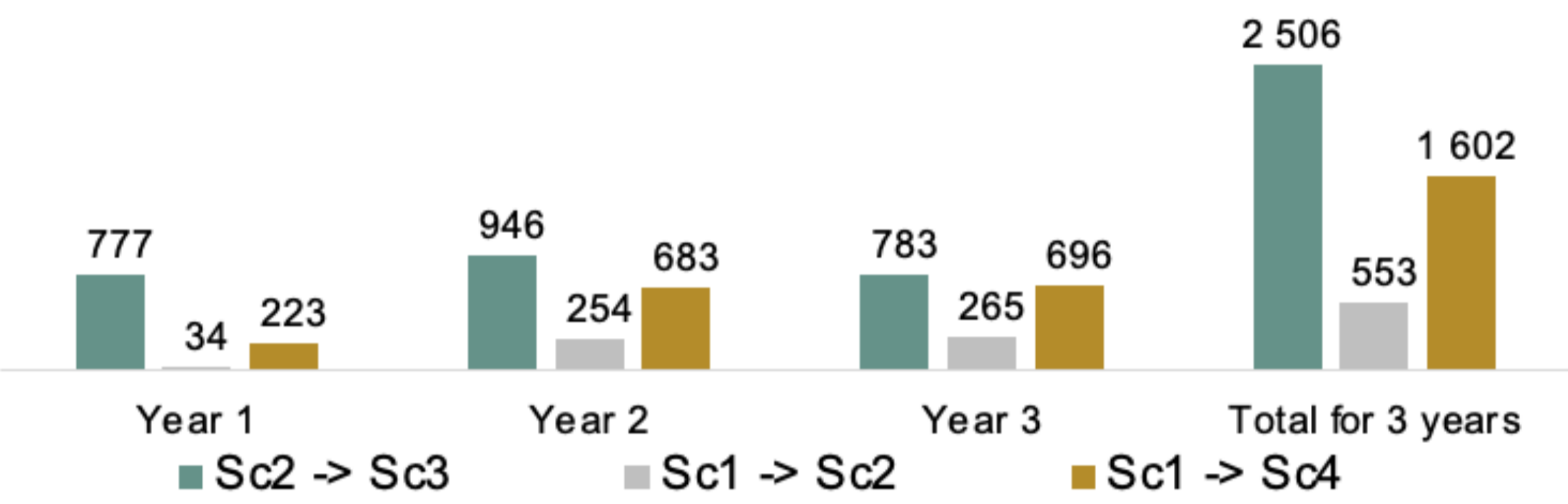|	Scenario 3		
Deaths per year	1 282	1 030	500
Total deaths	1 282	2 312	2 813
	Scenario 4		
Deaths per year	1 870	959	335
Total deaths	1 870	2 829	3 164
	Scenario 2		
Deaths per year	2 059	1 199	337
Total deaths	2 059	3 258	3 595
	Scenario 1		
Deaths per year	2 093	1 420	347
Total deaths	2 093	3 513	3 860

Figure 3. Number of lives saved.

- Shifting to avelumab maintenance therapy in Scenario 3 may also lead to decrease in one-year cancer mortality from 20.3% to 20.25% and one-year bladder cancer mortality from 13.8% to **12.12%** (see Table 2).
  o Using avelumab in budget neutral scenario (Scenario 4) leads to decrease in one-year cancer mortality to 20.29% and one-year bladder cancer mortality to 13.33%.

Type of neoplasm	One-year cancer mortality*	Scenario 2 -> Scenario 3		Scenario 1 -> Scenario 2		Scenario 1 -> Scenario 4	
		One-year mortality	Δ, p.p.	One-year mortality	Δ, p.p.	One-year mortality	Δ, p.p.
All neoplasms	20.3%	20.25%	-0.05	20.30%	<0.01	20.29%	-0.01
Bladder cancer	13.8%	12.12%	-1.68	13.73%	-0.07	13.33%	-0.47

*Note: * - 2021 actual; p.p. – percentage point.*

Table 1. Changes in one-year cancer mortality.

- The cost of saving one life with avelumab amounts **to 70.5 thousand US$,** which is 9% lower compared to the cost of saving one life with other ICIs (**77.5 thousand US$**, see Figure 3). Cost per life saved is at its lowest in the budget neutral Scenario 4 - **26.7 thousand US$** compared to Scenario 1 and **0 US$** compared to Scenario 2.
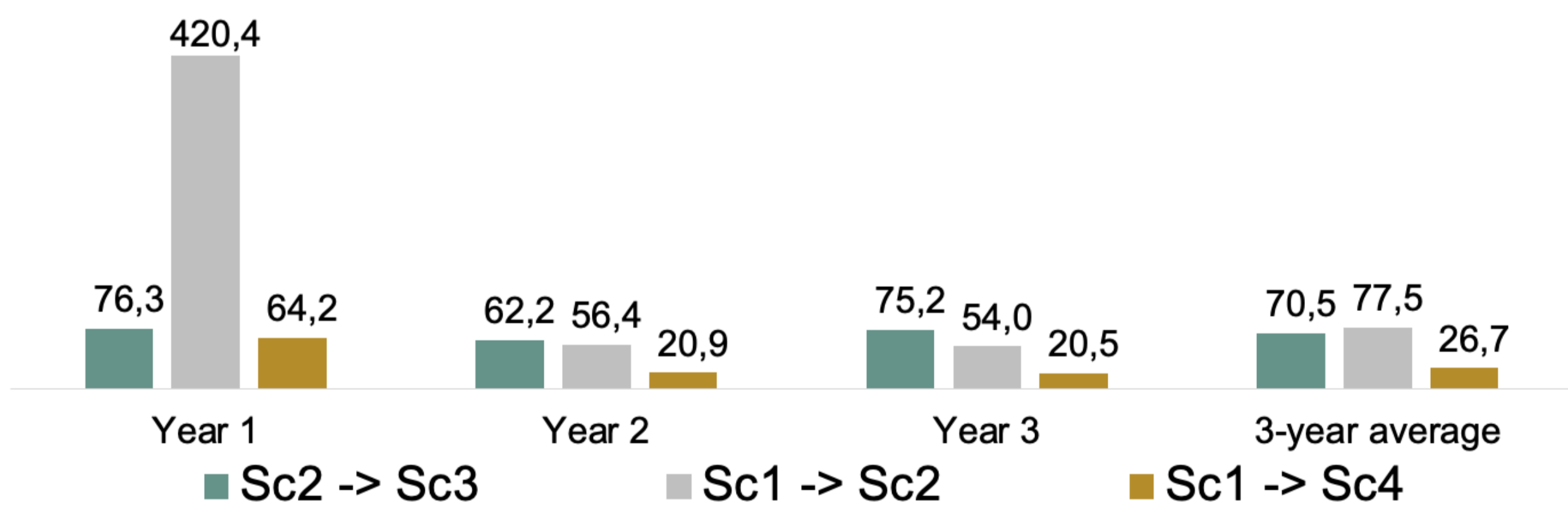

Figure 4. Cost of saving one life, thousand US$.

CONCLUSIONS

- Maintenance therapy with avelumab for patients with mUC may significantly reduce cancer-related mortality in Russia, even without incurring additional costs.

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