Real-world Dosing of Pembrolizumab in Advanced NSCLC: Inputs for Real-world Cost-effectiveness Analysis Using Two Hospital Settings

EE243

Z. Al-Khayat[1,2], N. Franzen[3], M. Rijnen[4], S. Badrising[1], A. Bressers[5], M. Voets[1], S. Siesling[2], W. Van Harten[1,2], V. Retèl[1,3]

Affiliation: 1; The Netherlands Cancer Institute - Antoni van Leeuwenhoek, Amsterdam, The Netherlands, 2; Twente university, Enschede, The Netherlands, 3; Erasmus university Rotterdam, Rotterdam, The Netherlands, 4; IQVIA, Amsterdam, The Netherlands, 5; Rijnstate hospital, Arnhem, The Netherlands

Introduction

- The high cost of pembrolizumab poses a challenge to healthcare system sustainability.
- **Dosing:** first approved at 2 mg/kg Q3W, KEYNOTE-024 used a fixed 200 mg Q3W, and the Dutch Society of Medical Oncology (NVMO) recommends 100/150/200 mg Q3W for <65, 65-90, >90 kg.
- **Gap:** it is unclear which dosing strategies are used in real-world practice, and which is most cost-effective.
- **Aim:** to describe real-world pembrolizumab dosing in advanced NSCLC and assess the cost-effectiveness of the strategies used.

Methods

- Retrospective study at two Dutch hospitals: including patients with stage III/IV NSCLC, PD-L1 TPS ≥50%, on first-line pembrolizumab monotherapy (May 2017–October 2024).
- The NVMO weight bands equal about 1.5–2.3 mg/kg, so exposure was classified as within-guideline (≤2.3 mg/kg) or above-guideline (>2.3 mg/kg).

Results

- 251 patients were included, 97 had within-guideline and 154 above-guideline exposure (Table 1).
- During treatment, doses varied widely (Fig. 1); 33 patients (13.7%) moved to the mixed group (Fig. 2).
- Within-guideline exposure was associated with longer OS and PFS, but the differences were not statistically significant (Table 2).

Table 1. Baseline characteristics

Characteristic	Within guideline ≤2.3 mg/kg (n = 97)	Above guideline >2.3 mg/kg (n = 154)	P-value
Age, years, median (IQR)	69 (63 - 74)	67 (60 - 75)	0.59
Sex, n (%)			**0.07**
Male	57 (58.8)	71 (46.1)	
Female	40 (41.2)	83 (53.9)	
Centre, n (%)			**0.001**
Centre A	58 (59.8)	59 (38.3)	
Centre B	39 (40.2)	95 (61.7)	
Weight, kg, median (IQR)	77 (68 - 94)	68.5 (62.6 - 76)	**<0.001**
Stage, n (%)			1.00
III	9 (9.3)	14 (9.1)	
IV	88 (90.7)	140 (90.9)	
ECOG performance status, n (%)			**<0.001**
0	31 (32)	19 (12.3)	
1	39 (40.2)	93 (60.4)	
≥2	23 (23.7)	38 (24.7)	
Missing	4 (4.1)	4 (2.6)	
Histology, n (%)			0.51
Non-squamous	81 (83.5)	125 (81.2)	
Squamous	14 (14.4)	29 (18.8)	
Missing	2 (2.1)	0 (0)	
Smoking status, n (%)			**0.07**
Current	39 (40.2)	64 (41.6)	
Former	48 (49.5)	84 (54.5)	
Never	10 (10.3)	5 (3.2)	
Missing	0 (0.0)	1 (0.6)	

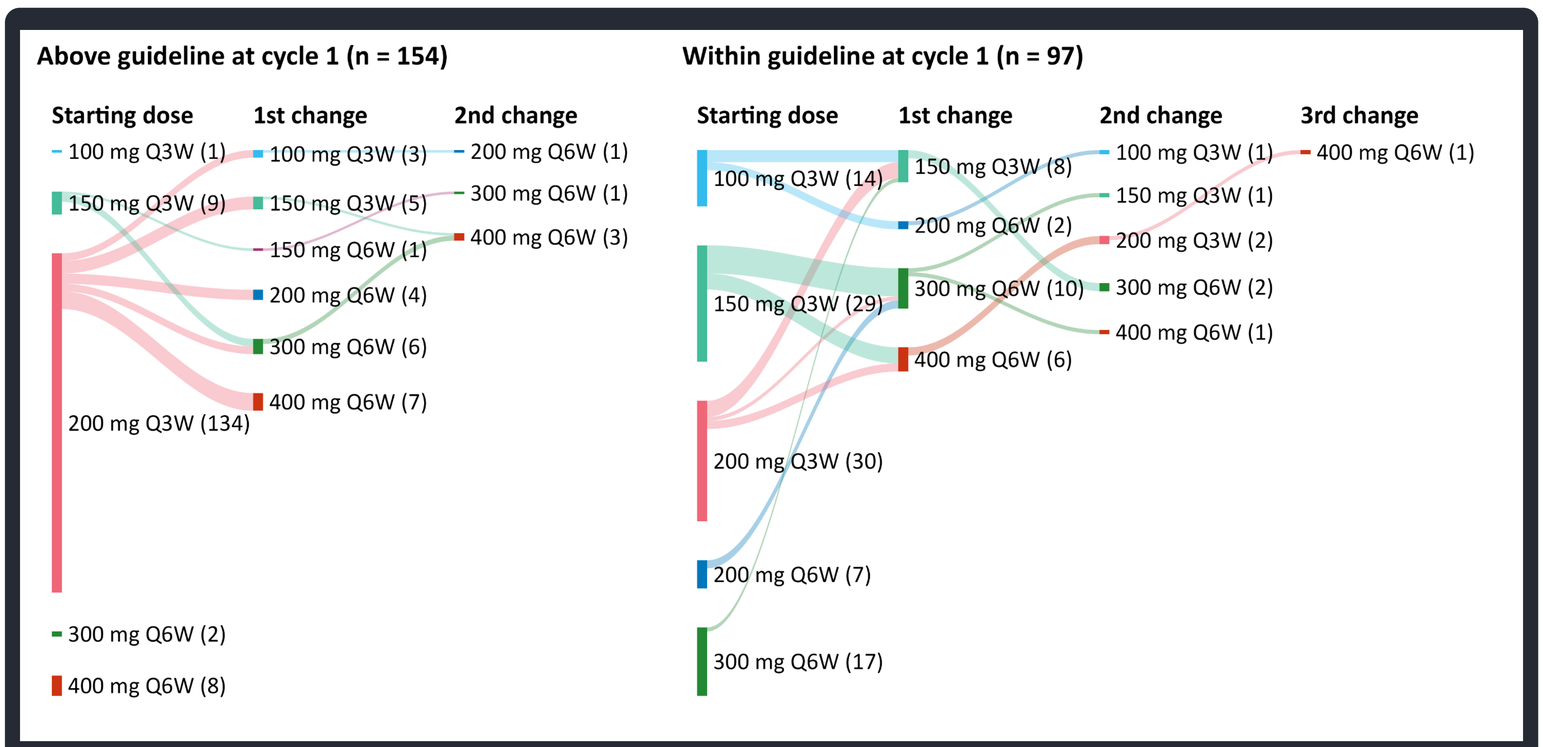


Figure 1. Sankey diagram showing pembrolizumab regimen sequence.

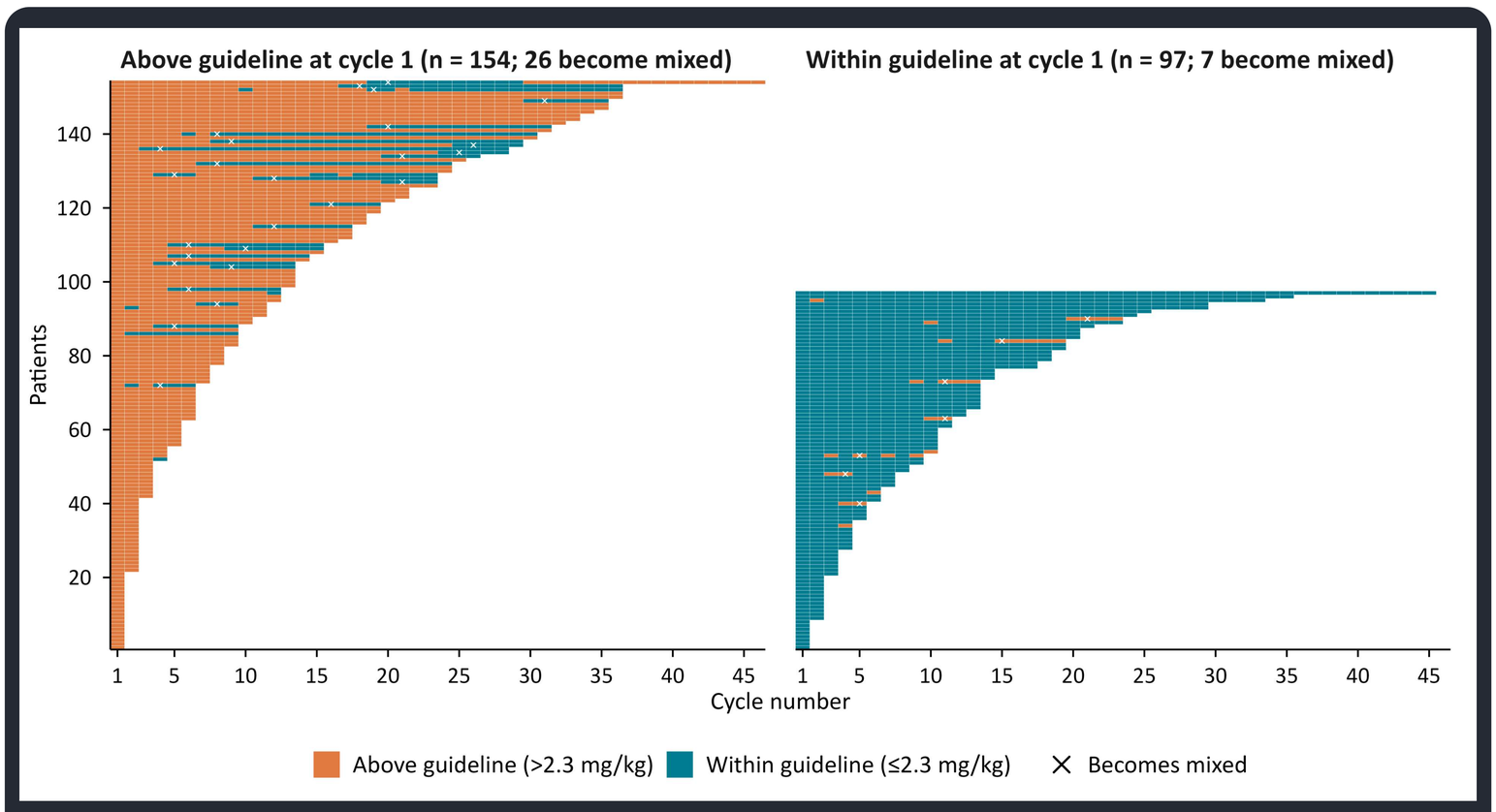


Figure 2. Dose exposure per cycle.
Rows are patients and tiles are cycles, coloured by mg/kg dose (Q6W doses converted to their Q3W equivalent). Patients are grouped by their cycle-1 dose. Mixed: more than one cycle on the other side of the 2.3 mg/kg threshold. Dose, dosing interval and body weight were recorded per cycle.

Table 2. Overall and progression-free survival by dose exposure

	Within guideline ≤2.3 mg/kg (n = 97)	Above guideline >2.3 mg/kg (n = 154)	P-value
Overall survival			
Events/patients, n (%)	50/97 (51.5)	107/154 (69.5)	
Median, months (95% CI)	28.4 (20.6 - 50.5)	18.2 (13.6 - 26.7)	0.188
HR, unadjusted (95% CI)	1 (reference)	1.25 (0.89 - 1.76)	0.189
HR, adjusted[a] (95% CI)	1 (reference)	1.67 (0.99 - 2.85)	0.057
Progression-free survival			
Events/patients, n (%)	62/97 (63.9)	116/154 (75.3)	
Median, months (95% CI)	13.6 (9.9 - 18.6)	10.7 (8.5 - 14.8)	0.576
HR, unadjusted (95% CI)	1 (reference)	1.09 (0.80 - 1.49)	0.577
HR, adjusted[a] (95% CI)	1 (reference)	1.55 (0.97 - 2.48)	0.069

Median and rates from Kaplan–Meier estimates; P-value for medians from the log-rank test.
[a] Time-dependent Cox model adjusted for weight at cycle 1, centre, age, sex, ECOG PS, stage, histology, smoking status and brain and liver metastases (primary analysis; complete cases).

Discussion and Next steps

- Most patients (61%) received above-guideline doses (>2.3 mg/kg), mainly because of the fixed 200 mg dose.
- Within-guideline exposure (≤2.3 mg/kg) was associated with numerically longer survival, though not significantly, suggesting that lower doses do not compromise effectiveness.
- Exposure was largely stable during treatment: only 33 patients (13.7%) changed group.
- Weight-based dosing could substantially reduce drug costs, especially for patients with lower body weight.
- These real-world findings support the NVMO recommendation and may inform dosing policy beyond the Netherlands.
- **Next steps:** Based on this hospital RWD, a DES will be constructed to calculate the cost-effectiveness of within- vs. above-guideline pembrolizumab dosing in advanced NSCLC with PD-L1 TPS ≥50%.

Contact: z.alkhayat@nki.nl

Funding: ONCOVALUE, EU Horizon Europe (grant agreement No 101095245).