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Adoption of Extended-Interval Dosing of Single-Agent Pembrolizumab and Comparative Effectiveness vs Standard Dosing in Time-to-Treatment Discontinuation

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Why this question?

- Extended-interval dosing of pembrolizumab- 400 mg every 6 weeks was approved by US FDA in April 2020 as an alternative to 200 mg every 3 weeks.
- Extended-interval dosing may enhance access, alleviate patient and health system financial toxicity, and improve patient quality of life, particularly during the COVID-19 pandemic.
- Neither adoption nor effectiveness of extended interval in the US has been adequately described.

Objective

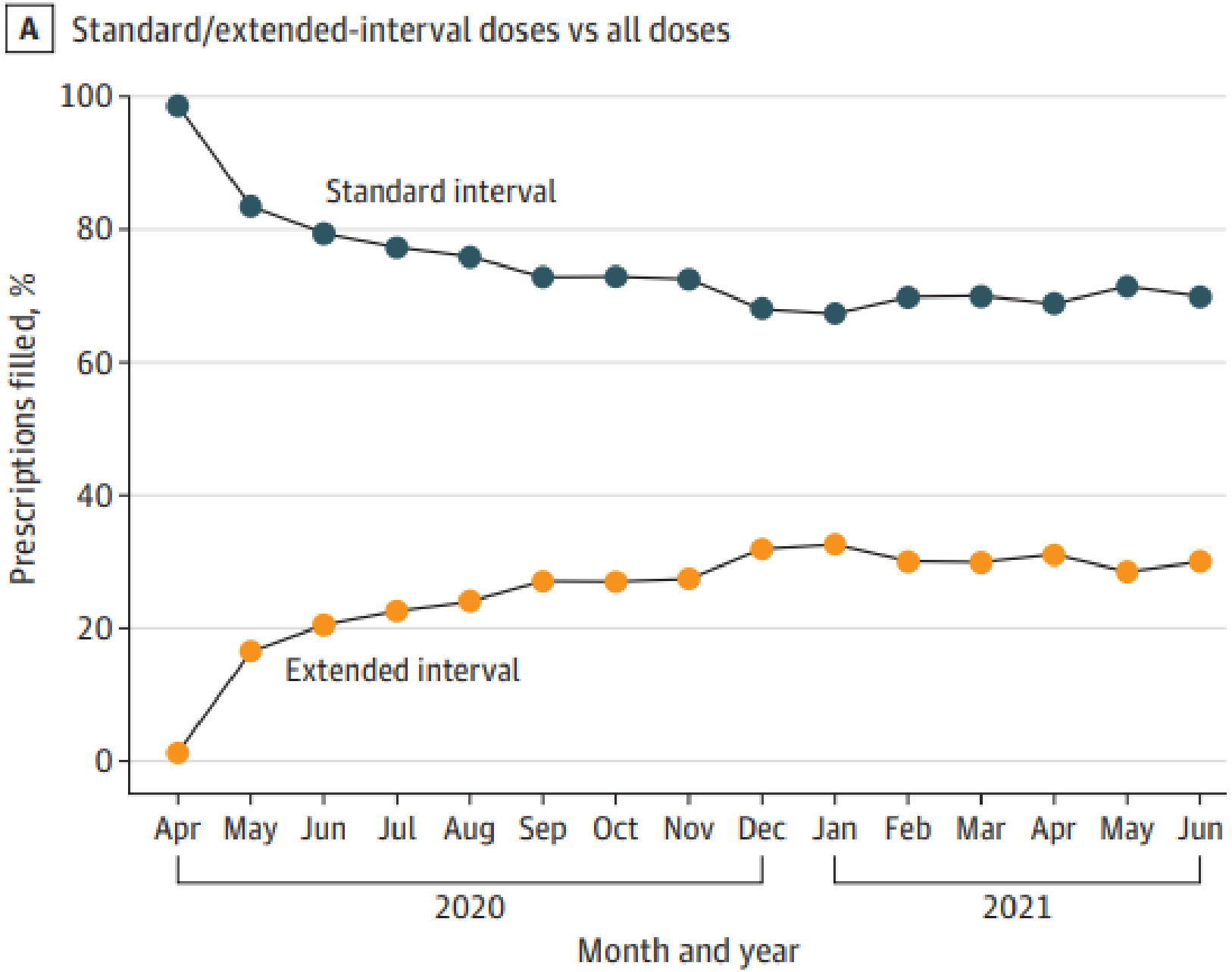
- To describe adoption of extended-interval dosing of pembrolizumab since its FDA approval and to measure its preliminary real-world effectiveness compared with standard-interval dosing.

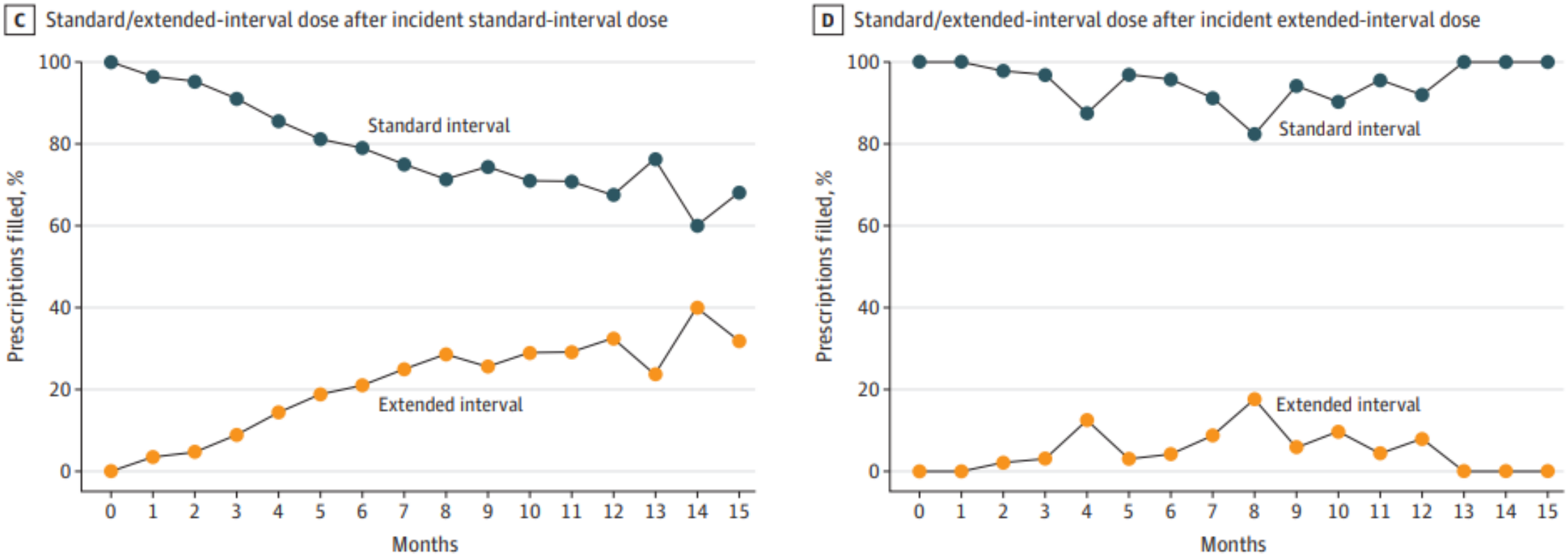
Design , Setting & participants

- Retrospective cohort study
- Veterans Health Administration
- Participants were veterans who were prescribed single-agent pembrolizumab within the VHA between April 1, 2020, and July 1, 2021.
- Patients receiving combinations of pembrolizumab and cytotoxic chemotherapy or tyrosine kinase inhibitors were excluded.
- A subcohort of veterans with non−small cell lung cancer (NSCLC) was also identified using claims-based codes.

Main Outcome & Measure

- The number and proportion of single-agent pembrolizumab prescriptions that were extended compared with standard interval.
- Effectiveness was described in terms of time-to-treatment discontinuation (TTD) and extended- to standard-interval pembrolizumab prescriptions were compared using Cox proportional hazards regression


A
Standard/extended-interval doses vs all doses
100
80
60
40
20
0
Prescriptions filled, %
Standard interval
Extended interval
Apr
May
Jun
Jul
Aug
Sep
Oct
Nov
Dec
Jan
Feb
Mar
Apr
May
Jun
2020
2021
Month and year



A and B, the x-axis corresponds to the month and year of the study. C and D, the x-axis corresponds to time since incident pembrolizumab. FDA refers to the US Food and Drug Administration.

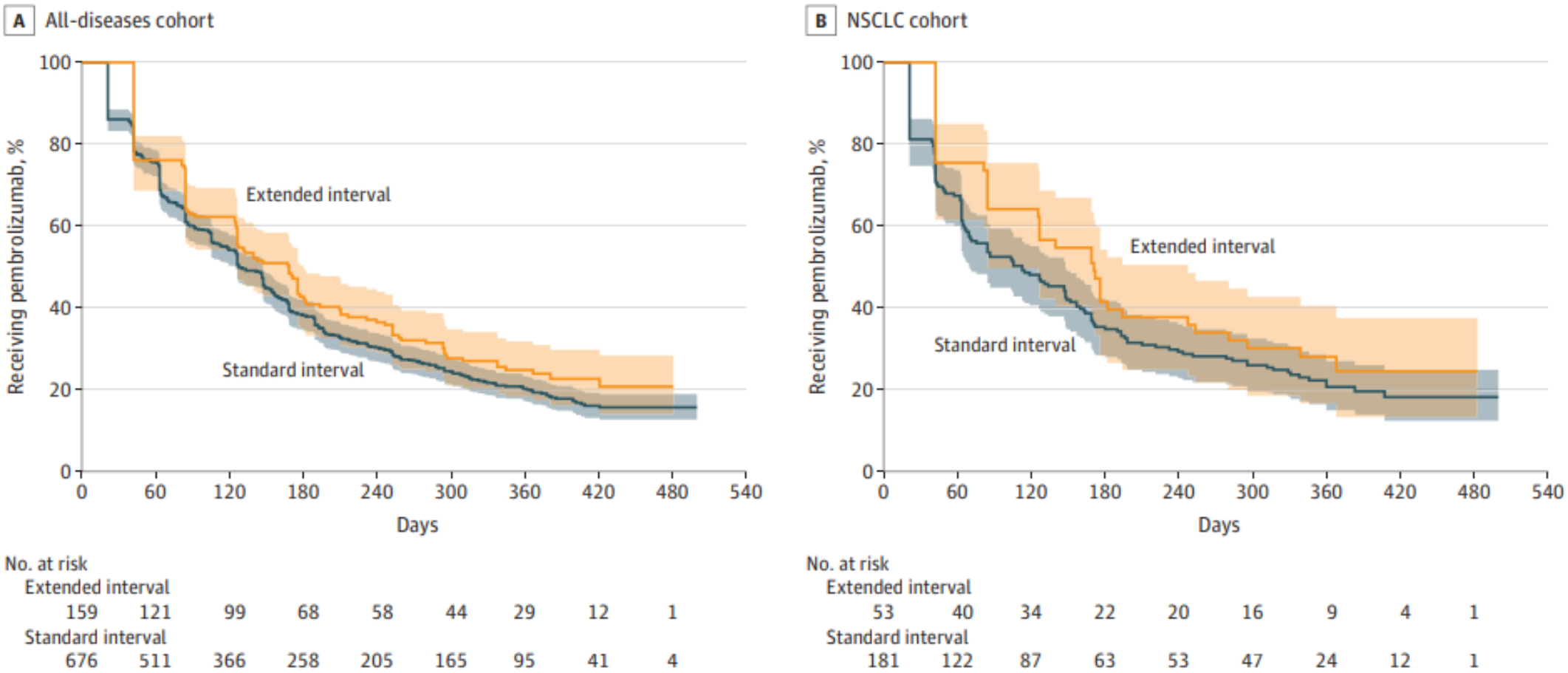
Of patients who began treatment with the standard-intervaldose,65%continuedwith it for the entire treatment duration (Figure 1C).

Of those who began the extendedinterval dosing, 95% to 100% continued with it (Figure 1D).

Table. Characteristics of the Comparative Effectiveness Analysis Cohorts of Standard-Interval vs Extended-Interval Dosing of Pembrolizumab

Characteristic	No. (%)					*P* value for differences[a]
	Standard interval	Standard interval to extended interval	Pooled standard interval	Extended interval	Cohort	
All-diseases cohort						
No.	534	142	676	159	835	
Age, mean (SD)	70.8 (8.5)	71.1 (10.0)	70.9 (8.8)	70.9 (8.5)	70.9 (8.7)	.99
Male sex	514 (96.3)	139 (97.9)	653 (96.7)	156 (98.1)	809 (96.9)	.32
Noncancer CCI	2.3 (2.0)	2.2 (1.9)	2.3 (2.0)	2.1 (1.8)	2.3 (2.0)	.25
Primary site						
Lung	238 (44.6)	59 (41.5)	297 (43.9)	76 (47.8)	373 (44.7)	.38
Bladder	82 (15.4)	27 (19.0)	109 (16.1)	28 (17.6)	137 (16.4)	.65
Kidney	64 (12.0)	19 (13.4)	83 (12.3)	11 (6.9)	94 (11.3)	.05
Head and neck	58 (10.9)	16 (11.3)	74 (10.9)	20 (12.6)	94 (11.3)	.56
Melanoma	44 (8.2)	19 (13.4)	63 (9.3)	13 (8.2)	76 (9.1)	.65
Gastroesophageal	54 (10.1)	8 (5.6)	62 (9.2)	8 (5.0)	70 (8.4)	.09
Colorectal	25 (4.7)	10 (7.0)	35 (5.2)	10 (6.3)	45 (5.4)	.58
Hepatocellular	26 (4.9)	4 (2.8)	30 (4.4)	9 (5.7)	39 (4.7)	.51
NSCLC cohort						
Age, mean (SD)	71.8 (7.2)	71.5 (9.2)	71.8 (7.5)	71.2 (6.6)	71.6 (7.3)	.59
Male sex	144 (95.4)	30 (100)	174 (96.1)	51 (96.2)	225 (96.2)	.98
Noncancer CCI	2.5 (1.9)	2.3 (1.7)	2.4 (1.9)	2.0 (1.7)	2.3 (1.9)	.12

Figure 2. Survival Curves of Extended- and Standard-Interval Pembrolizumab Time-to-Treatment Discontinuation (TTD)



A, median TTD was 127.5 days for standard interval and 168 days for extended interval (HR, 1.00; 95% CI, 1.00-1.00; P = .08). B, Median TTD was 112 days for standard interval and 170 days for extended interval (HR, 1.00; 95% CI, 1.00-1.00; P = .15). In both, the y-axis is the proportion of patients still receiving pembrolizumab and the x-axis is number of days since incident pembrolizumab. In both panels, standard interval is blue and extended interval is orange. Shaded portions indicate 95% CIs.

My Take

Conclusion

- Extended-interval dosing comprised a minority of single-agent pembrolizumab prescriptions despite the FDA approval and its potential health system and public health benefits.
- The findings support the TTD equivalence of standard- and extended-interval pembrolizumab across indications, complementing clinical pharmacology and single-arm clinical trial data in melanoma.
- This study provides further support for extended-interval pembrolizumab dosing.