

601 – Survival and Treatment Patterns in Metastatic NSCLC on First-Line Immunotherapy: Large Contemporary Canadian Real-World Study



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Objectives

The aim of this study was to evaluate outcomes for patients with metastatic non-small cell lung cancer (NSCLC) receiving first-line immune checkpoint inhibitors using a contemporary population-based Canadian cohort from province of Ontario.

Conclusions

In this large Canadian real-world study, first line immune checkpoint inhibitors for metastatic NSCLC showed poor outcomes: short median overall survival (OS), limited durability, and high attrition after first-line.

There remains a critical need for more effective frontline strategies incorporating novel agents for metastatic NSCLC.

Plain Language Summary



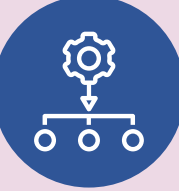
Why did we perform this research?

- Immune checkpoint inhibitors have improved outcomes for people with advanced lung cancer, but results in everyday practice may differ from those seen in clinical trials.



How did we perform this research?

- We reviewed healthcare claims records of 3,793 adults in Ontario with stage IV non-small cell lung cancer who received immune checkpoint inhibitors as their first treatment.
- We looked at two groups: those treated with immune checkpoint inhibitors alone (n=1,925) and those treated with immune checkpoint inhibitors in combination with another treatment (e.g., chemotherapy) (n=1,868).



What were the findings of this research?

- On average, patients lived for about 8 to 10 months after starting treatment, and most stayed on treatment for less than 6 months.
- About 3 in 4 patients never received a second treatment, and nearly half died while still on their first treatment.



What are the implications of this research?

- Outcomes with current first-line immune checkpoint inhibitors remain poor in routine practice, highlighting a strong unmet need for more effective frontline treatment options in advanced non-small cell lung cancer.

Introduction

- First-line immune checkpoint inhibitors** have improved outcomes in advanced NSCLC without actionable alterations (**trial median OS 17.2–26.3 months; 3-year OS 29.9–43.7%**).¹⁻³
- However, outcomes remain inferior to patients with actionable genomic alterations, and **real-world generalizability** of trial data is uncertain.
- We assessed first-line immune checkpoint inhibitors outcomes in a **contemporary population-based cohort** from Ontario, Canada.

Methods

- Design:** Retrospective population-based cohort study using deidentified linked datasets from ICES.
- Population:** Adults diagnosed with Stage IV NSCLC between Jan 2018-Dec 2023 in Ontario receiving first-line Health Canada-approved **PD-(L)1 as monotherapy (cohort 1) or in combination (cohort 2)** were followed through Aug 31, 2025.
- Public funding eligibility required physician declaration of PD-L1 ≥50% (cohort 1) and no EGFR/ALK alterations with ECOG 0–2 (both cohorts).
- The cohorts were defined by treatment received and different clinical eligibility criteria; cohort comparisons are descriptive and should not be interpreted as comparative treatment effectiveness.
- Outcomes:** Treatment patterns, OS, time to treatment discontinuation (TTD), and attrition rates.
- Subgroup analyses** were conducted by histology (squamous vs. non-squamous cell carcinoma).

Results

- Cohort derivation:** Of 14,969 patients with stage IV NSCLC, **1,925 (cohort 1, monotherapy)** and **1,868 (cohort 2, combination)** comprised the final analytic cohorts after excluding those receiving targeted therapy in any line.^a Baseline characteristics are shown in **Table 1**.

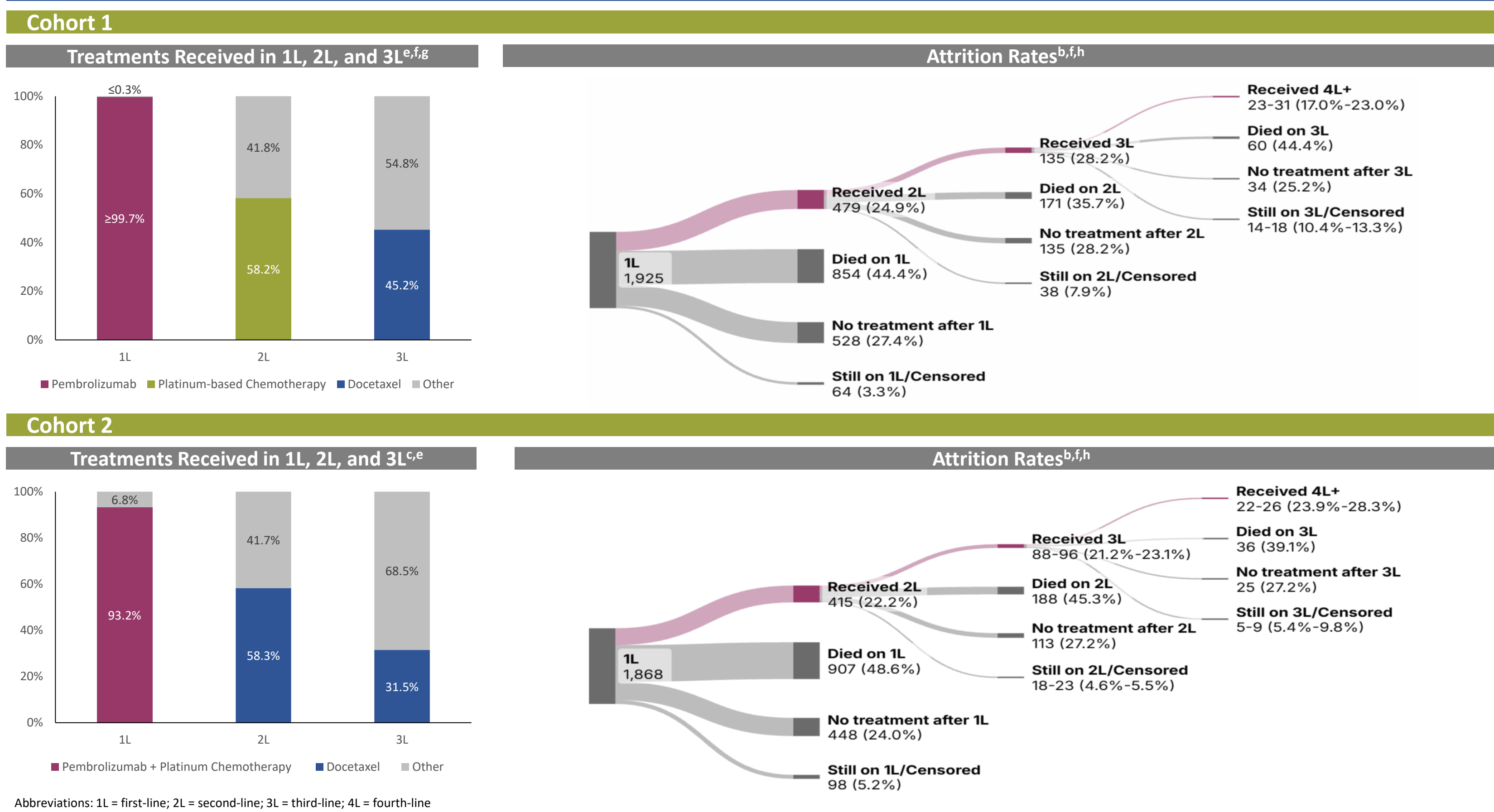
Table 1. Baseline characteristics

	Cohort 1, Immune checkpoint inhibitor monotherapy (n=1,925)	Cohort 2, Immune checkpoint inhibitor combination (n=1,868)
Year of diagnosis, n (%)		
2018	341 (17.7%)	11 (0.6%)
2019	394 (20.5%)	195 (10.4%)
2020	338 (17.6%)	372 (19.9%)
2021	324 (16.8%)	438 (23.4%)
2022	289 (15.0%)	521 (27.9%)
2023	239 (12.4%)	331 (17.7%)
Age		
Median (IQR)	70 (63-76)	67 (61-73)
≥65 years	1,366 (71.0%)	1130 (60.5%)
Female, n (%)	919 (47.7%)	874 (46.8%)
Academic hospital, n (%)	761 (39.5%)	821 (44.0%)
Non-squamous histology, n (%)	1,637 (85.0%)	1,581 (84.6%)
3+ Charlson's co-morbidity index, n (%)	825 (42.8%)	709 (38.0%)

Treatment Patterns & Attrition^b:

- The most common regimens were **pembrolizumab monotherapy (≥99.7%, cohort 1)** and **pembrolizumab + platinum-based chemotherapy^c (93.2%, cohort 2)**.
- Treatments by line are shown in **Figure 1**.
- Attrition from first- to second-line was high (74.3% cohort 1; 76.6% cohort 2). The attrition was driven by first-line discontinuation without further observed therapy (27.4% cohort 1; 24.0% cohort 2) and by deaths prior to second-line (44.4% and 48.6%, respectively; Figure 1).^d

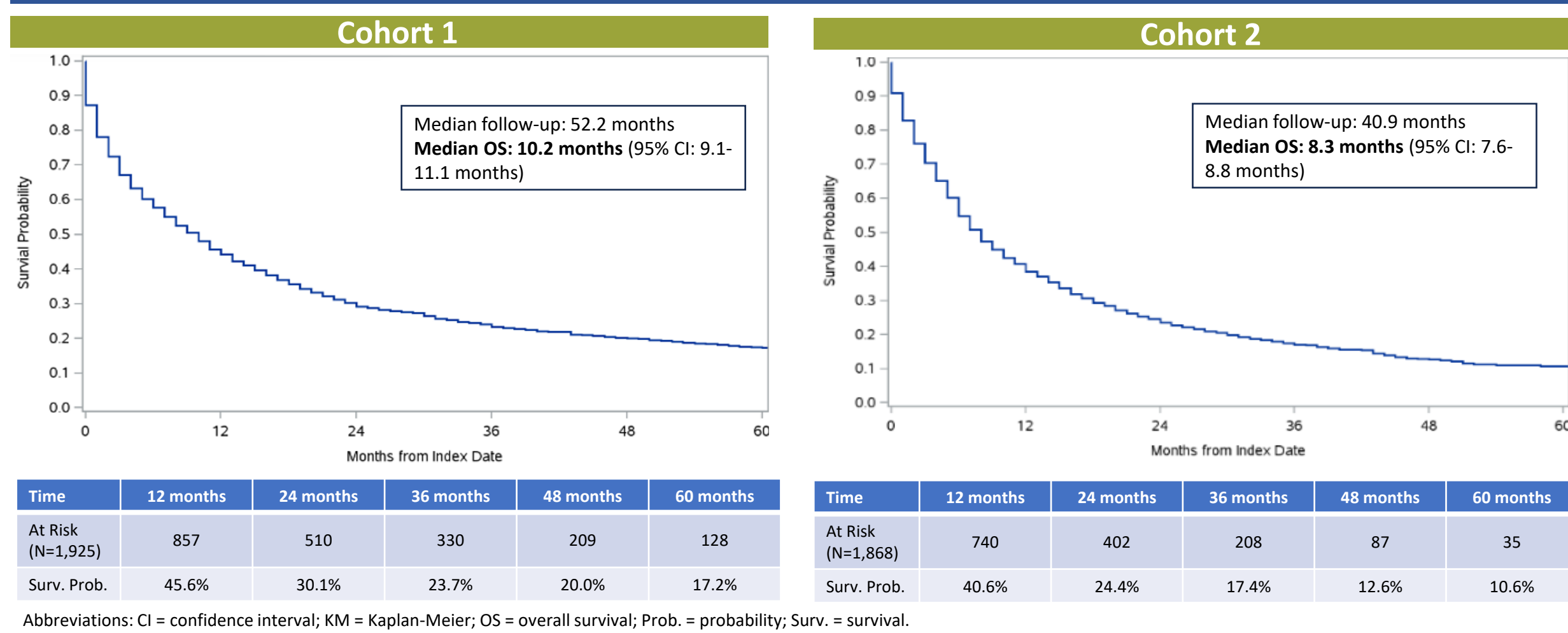
Figure 1. Attrition rates and treatments received



Effectiveness (OS):

- With median follow-up of 52.2 (cohort 1) and 40.9 months (cohort 2), median OS was **10.2 months** (95% CI, 9.1–11.1) and **8.3 months** (95% CI: 7.6–8.8), respectively, with low 3-year OS in both cohorts (**Figure 2**).
- Results were similar based on histology.^h

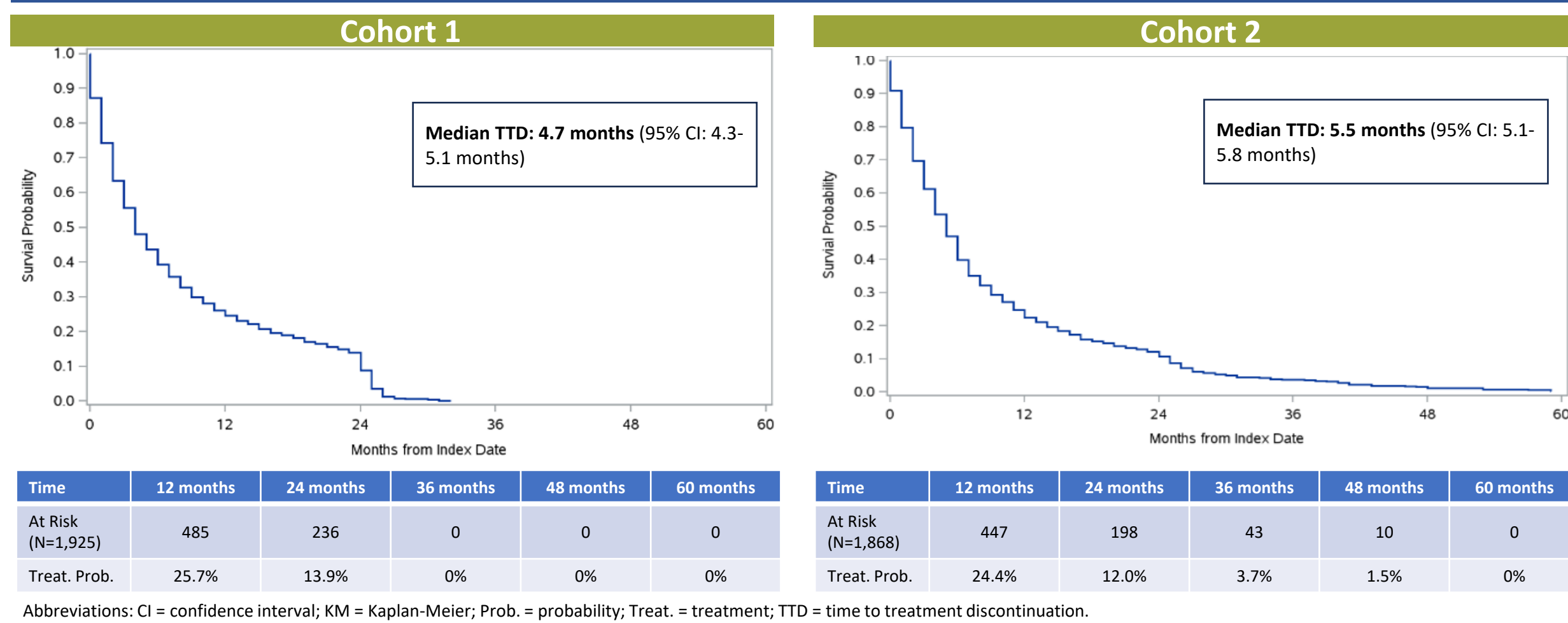
Figure 2. KM curves for OS (index: treatment initiation)



Effectiveness (TTD):

- Median TTD was **4.7 months** (95% CI, 4.3–5.1) and **5.5 months** (95% CI: 5.1–5.8) in Cohort 1 and Cohort 2, respectively (**Figure 3**).
- Results were similar based on histology.^h

Figure 3. KM curves for TTD (index: treatment initiation)



Strengths & Limitations

- Strengths:** Population-based analysis using linked Ontario administrative databases, capturing >95% of provincial cancer diagnoses — minimizing selection bias and providing a comprehensive view of real-world outcomes.
- Limitations:** Claims-based data lack certain clinical variables (e.g., ECOG, biomarkers); however, Canada's centralized reimbursement criteria (restricting funding by ECOG, molecular status, and PD-L1) mitigate this uncertainty and reinforce relevance to routine practice.

Acknowledgments

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Disclosures

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Footnotes

- ^a KRAS inhibitors-treated patients were retained, as KRAS-mutant NSCLC remains responsive to PD-(L)1 inhibition and is represented in ongoing first-line immune checkpoint inhibitor trials.
- ^b Attrition was calculated among patients who discontinued first-line therapy by data cutoff; those still on treatment or censored were excluded, as subsequent-line status was undetermined.
- ^c Pembrolizumab + platinum-based chemotherapy aggregates carboplatin + pembrolizumab + pemetrexed, cisplatin + pembrolizumab + pemetrexed, and carboplatin + paclitaxel + pembrolizumab.
- ^d Death occurring before second line initiation, with the death date within the first-line days-of-supply plus a 60-day gap period. Timing-based definition; no causal relationship with treatment is implied.
- ^e Other includes all regimens not individually specified, comprising chemotherapy, immune checkpoint inhibitors, or combinations thereof.
- ^f Some values based on small sample sizes are reported as ranges to comply with small-cell suppression rules protecting patient privacy.
- ^g Non-pembrolizumab monotherapy was received by fewer than 5 patients.
- ^h Attrition rates (1L→2L): Similar between non-squamous and squamous histology in both cohorts — cohort 1: 74.3% vs. 73.8%; cohort 2: 76.7% vs. 76.0%. Median overall survival (OS) by histology (non-squamous vs. squamous): cohort 1: 10.6 months (95% confidence interval [CI]: 9.4–11.7) vs. 8.3 months (95% CI: 7.2–10.2); cohort 2: 8.6 months (95% CI: 7.9–9.4) vs. 6.6 months (95% CI: 5.2–8.0). Median time to treatment discontinuation (TTD) by histology (non-squamous vs. squamous): cohort 1: 4.6 months (95% CI: 4.2–5.0) vs. 5.0 months (95% CI: 4.2–5.8); cohort 2: 5.7 months (95% CI: 5.3–6.1) vs. 4.4 months (95% CI: 3.8–5.1).