

P3.268: Cardiovascular Risk in Patients with Advanced ALK-Rearranged NSCLC Treated with ALK Tyrosine Kinase Inhibitors: A Nationwide Claims-Based Cohort Study

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INTRODUCTION

- **ALK tyrosine kinase inhibitors (TKIs)** have markedly improved systemic and intracranial disease control in ALK rearranged NSCLC, with median overall survival now exceeding 80 months in the first-line setting.
- As treatment duration has increased, long-term cardiovascular (CV) and metabolic toxicities have become increasingly relevant.
- We aimed to evaluate the risk of incident CV disease associated with ALK TKI and differences by treatment generation

METHODS

- Using the Korean Health Insurance Review and Assessment Service claims database, we identified patients with **lung cancer who received ALK TKIs between 2010 and 2023** and surgery-only controls who received no systemic chemotherapy.
- ALK-TKIs were categorized as 1st generation (Crizotinib), 2nd generation (Alectinib/Brigatinib), 3rd generation (Lorlatinib).
- **The primary outcome was incident CV disease:** ischemic heart disease, heart failure, atrial fibrillation/flutter, or stroke.
- A prespecified 3-month landmark analysis and 1:1 propensity-score matching were performed.

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DISCUSSION AND CONCLUSION

- Cumulative CVD incidence at 1, 2, and 3 years was 5.4%, 9.3%, and 12.6% with ALK-TKIs and 3.2%, 5.7%, and 8.0% with controls.
- ALK TKI was associated with higher CVD risk (HR, 1.57; 95% CI 1.38–1.77; $p < 0.001$).
- Generation-specific HRs were 2.50 (95% CI, 2.09–2.99), 1.28 (95% CI, 1.13–1.45), and 2.39 (95% CI, 1.96–2.91), respectively.
- The excess risk emerged early after treatment initiation and persisted during follow-up after propensity-score matching.
- ALK TKI therapy was associated with increased incident CVD risk, particularly with first- and third-generation agents.

PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE:

- First- and third-generation ALK TKIs, which have recognized cardiovascular and metabolic toxicity profiles, were associated with the highest risks of incident CVD in this nationwide cohort.
- These findings underscore the importance of generation-informed cardiovascular risk assessment and surveillance during long-term ALK TKI therapy.

TRANSLATIONAL OUTLOOK

- Prospective studies are needed to develop and validate risk-adapted cardiovascular surveillance strategies that integrate ALK TKI-specific toxicity profiles with baseline cardiovascular risk factors

RESULTS

Table 1 Patient Characteristics at Baseline

	Overall cohort (N=76,516)	ALK tyrosine kinase inhibitor (TKI)			Control (n=70,925)	p-value
		1 st G ALK TKI (n=1,717)	2 nd G ALK TKI (n=3,355)	3 rd G ALK TKI (n=519)		
Age group						<0.001
<65 y	35,037 (45.8)	933 (54.3)	2,010 (59.9)	386 (74.4)	31,708 (44.7)	
≥65 y	41,479 (54.2)	784 (45.7)	1,345 (40.1)	133 (25.6)	39,217 (55.3)	
Sex						<0.001
Male	41,536 (54.3)	799 (46.5)	1,573 (46.9)	243 (46.8)	38,921 (54.9)	
Female	34,980 (45.7)	918 (53.5)	1,782 (53.1)	276 (53.2)	32,004 (45.1)	
Comorbidities						
Diabetes	11,159 (14.6)	303 (17.7)	474 (14.1)	63 (12.1)	10,319 (14.6)	0.001
Hypertension	30,521 (39.9)	919 (53.5)	1,456 (43.4)	194 (37.4)	27,952 (39.4)	<0.001
Dyslipidemia	20,444 (26.7)	392 (22.8)	747 (22.3)	93 (17.9)	19,212 (27.1)	<0.001
Coronary artery disease	1,269 (1.7)	18 (1.1)	41 (1.2)	6 (1.2)	1,204 (1.7)	0.026
Heart failure	4,437 (5.8)	103 (6.0)	196 (5.8)	23 (4.4)	4,115 (5.8)	0.590
Chronic kidney disease	2,339 (3.1)	58 (3.4)	66 (2.0)	4 (0.8)	2,211 (3.1)	<0.001
Chronic liver disease	208 (0.3)	3 (0.2)	7 (0.2)	1 (0.2)	197 (0.3)	0.728

Values are n (%). A 2-sided p -value of <0.05 was considered to indicate statistical significance.

ALK TKI = anaplastic lymphoma kinase tyrosine kinase inhibitors

Figure 1. Generation-specific incidence of CVDs at 3-month landmark

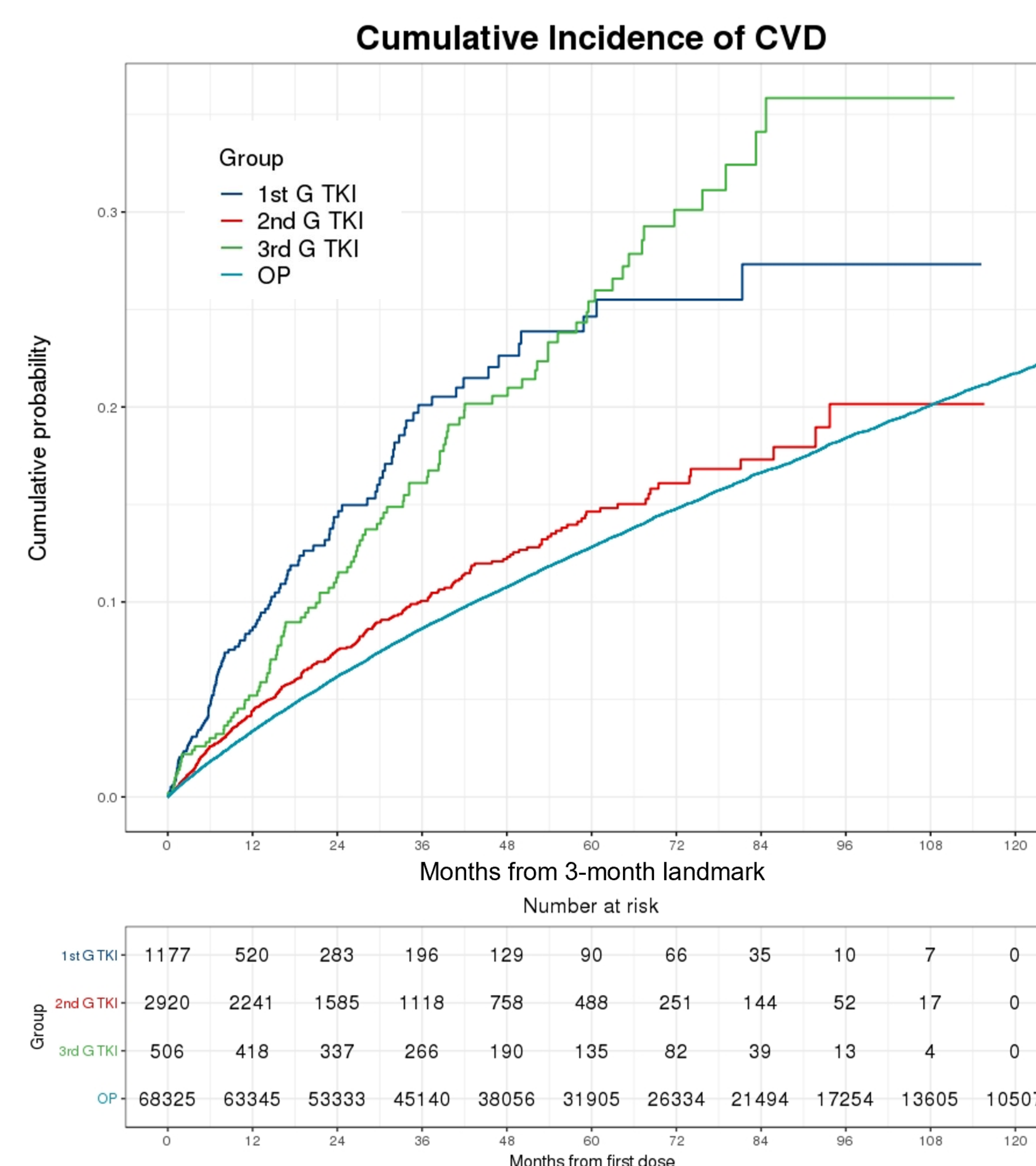


Figure 2. Risk of incident CVDs in each subgroup

