Real-world data analysis of genomic profiling-matched targeted therapy outcomes in patients with advanced fusion-positive NSCLC

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INTRODUCTION

- Clinical oncology societies recommend the use of Comprehensive Genomic Profiling (CGP) to identify patients eligible for matched targeted therapy, yet full utilization of the potential benefits of CGP has not occurred in routine clinical practice.
- Here we assess the adherence to ESMO matched targeted therapy recommendations and associated outcomes for CGP-based *ALK*, *RET*, *ROS1*, and *NTRK* fusions detected in a large real-world, observational dataset of advanced NSCLC patients.

METHODS

Data Sources:
- De-identified stage IV or metastatic NSCLC records from the Tempus database were retrospectively analyzed.
- The database encompasses molecular and clinical data from hundreds of clinics across the United States sequenced with the Tempus xT assay (DNA and whole exome capture RNA) from 2018 - 2022.

Definitions and Statistical analysis:
- Real-world overall survival (rwOS) was defined as the interval from start of medication prescribed after sequencing to date of death, censored on the last known physician encounter.
- A cox proportional hazards model was fit to evaluate the relationship between matched targeted therapy compliance and rwOS in fusion-positive patients.
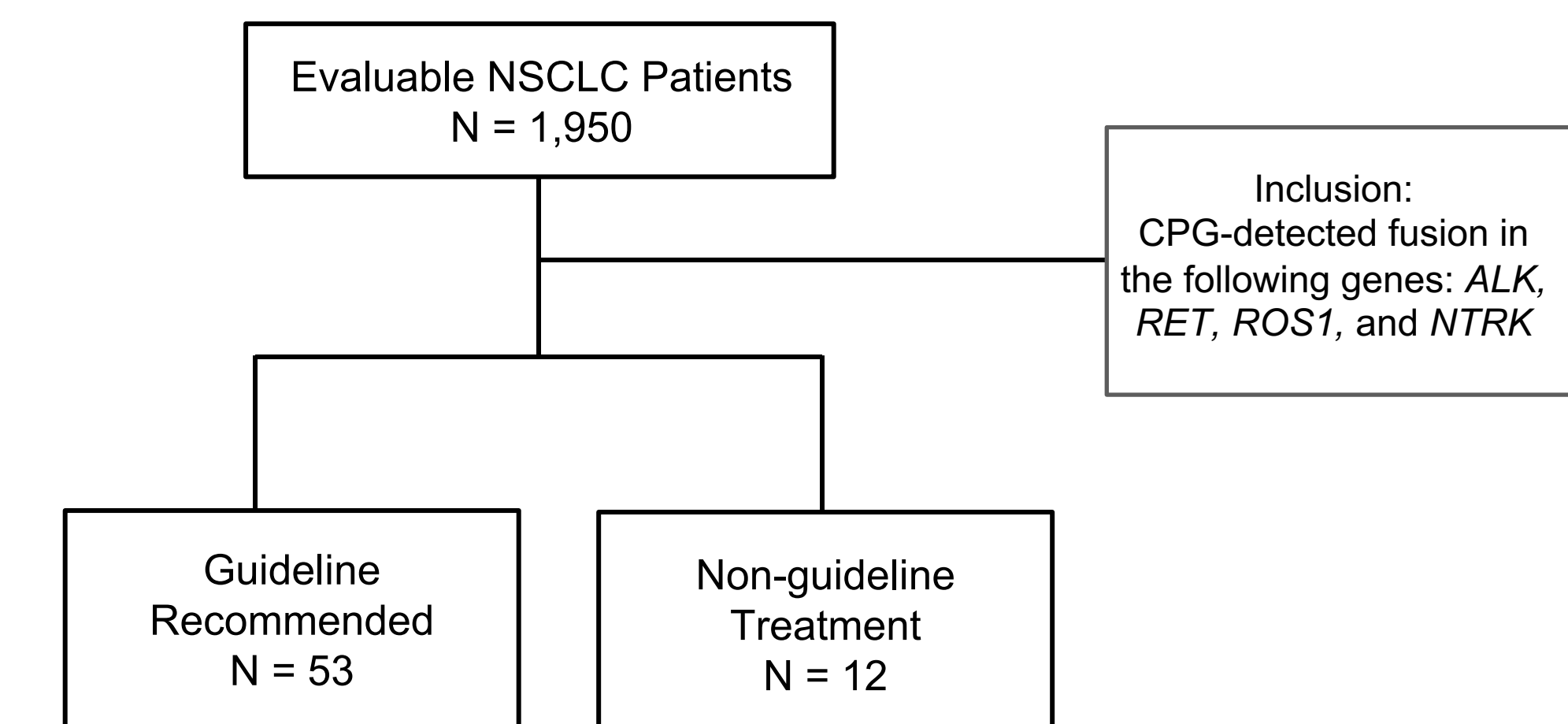
Cohort Selection:

Figure 1. CONSORT Diagram. Among 1,950 evaluable patients that met study inclusion criteria, 65 (3.3%) had a CGP-detected fusion: *ALK* (N=38), *RET* (N=15), *ROS1* (N=11) and *NTRK* (N=1).

SUMMARY

- This study demonstrates that in a **real-world, retrospective cohort**, most oncologists utilized **CGP to timely treat** patients with ESMO-recommended genomic matched targeted therapy (82%) for fusion-positive advanced NSCLC.
- More importantly, CGP-matched guideline-recommended treatment is **associated with improved rwOS** for fusion-positive advanced NSCLC.
- Future studies are needed to understand the gap in compliance with matched targeted therapy.

RESULTS

Table 1. Cohort Demographics and Characteristics.

Characteristic	Guideline recommended, N = 53	Non-guideline treatment, N = 12	p-value
Age at Sequencing			
Median (IQR)	60 (54, 69)	69 (62, 76)	0.04[1]
Gender			
Female	31 (58.5%)	8 (66.7%)	0.12[1]
Male	22 (41.5%)	4 (33.3%)	
Race			
Asian	6 (11.3%)	1 (8.3%)	
Black	1 (1.9%)	0 (0%)	0.7[1]
Other	5 (9.4%)	0 (0%)	
White	28 (52.8%)	10 (83.3%)	
Unknown	13 (24.5%)	1 (8.3%)	
Smoking Status			
Non-smoker	30 (56.6%)	7 (58.3%)	
Smoker	22 (41.5%)	5 (41.7%)	0.31[1]
Unknown	1 (1.9%)	0 (0%)	
Histology			
Adenocarcinoma	43 (81.1%)	8 (66.7%)	
Adenosquamous carcinoma	1 (1.9%)	0 (0%)	
Malignant neoplasm, primary	1 (1.9%)	0 (0%)	
Mucinous adenocarcinoma	1 (1.9%)	0 (0%)	0.03[1]
Neuroendocrine tumor	0 (0%)	1 (8.3%)	
Non-small cell carcinoma	2 (3.8%)	1 (8.3%)	
Squamous cell carcinoma	2 (3.8%)	0 (0%)	
Unknown	3	2	
Diagnosis to Medication			
Median days (IQR)	95 (46.0, 334.0)	283.5 (105.0, 563.3)	0.99[2]
Diagnosis to Sequencing			
Median days (IQR)	28 (19, 43)	35.5 (15.8, 464.7)	0.99[2]
Sequencing to Medication Start			
Median days (IQR)	38 (18, 145)	87 (58, 167)	1.0[2]
Sequencing Date to Last Known Date			
Median days (IQR)	391 (223, 613)	219.5 (168.5, 274.8)	1.0[2]

[1]: Wilcoxon test
[2]: Chi-squared test

Figure 3. Proportion of Fusion Patients on CPG-matched Guideline Recommended Therapy.
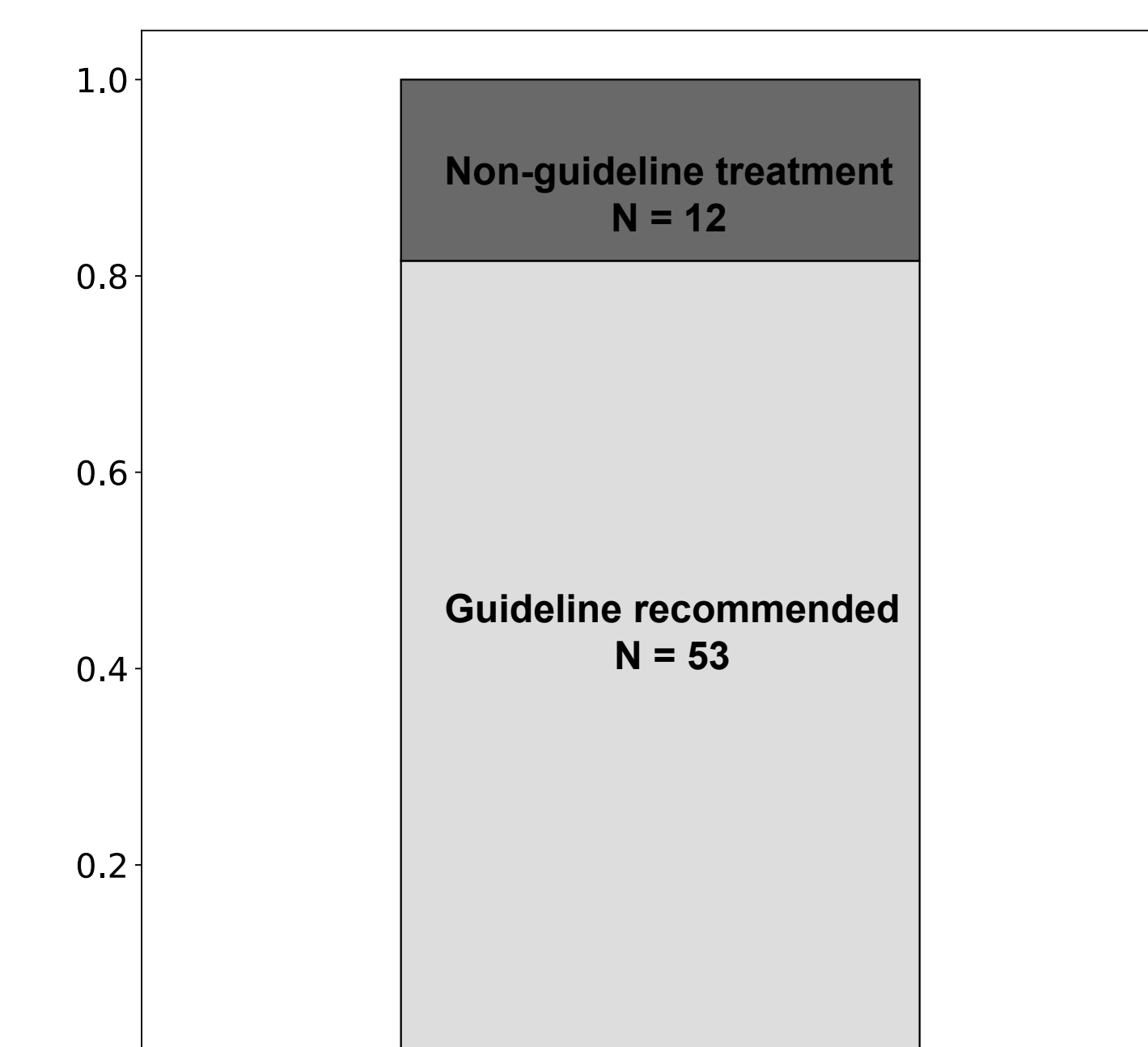
The overall compliance rate of targeted therapy was 82% (N=53).

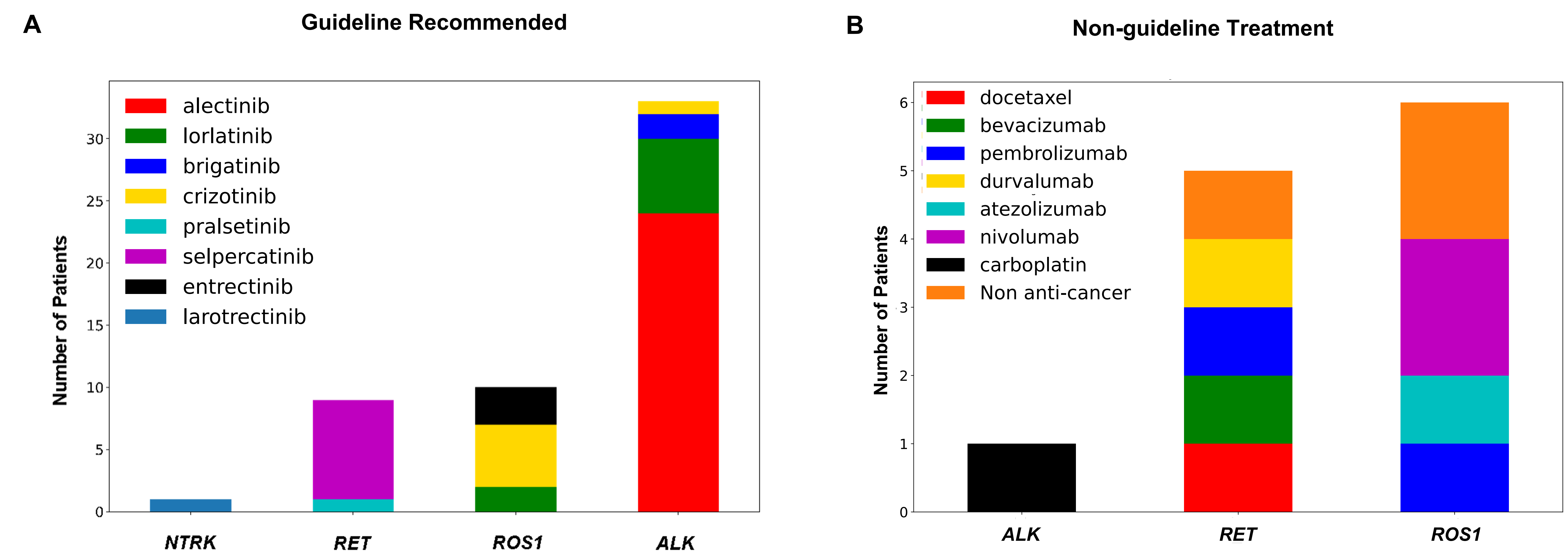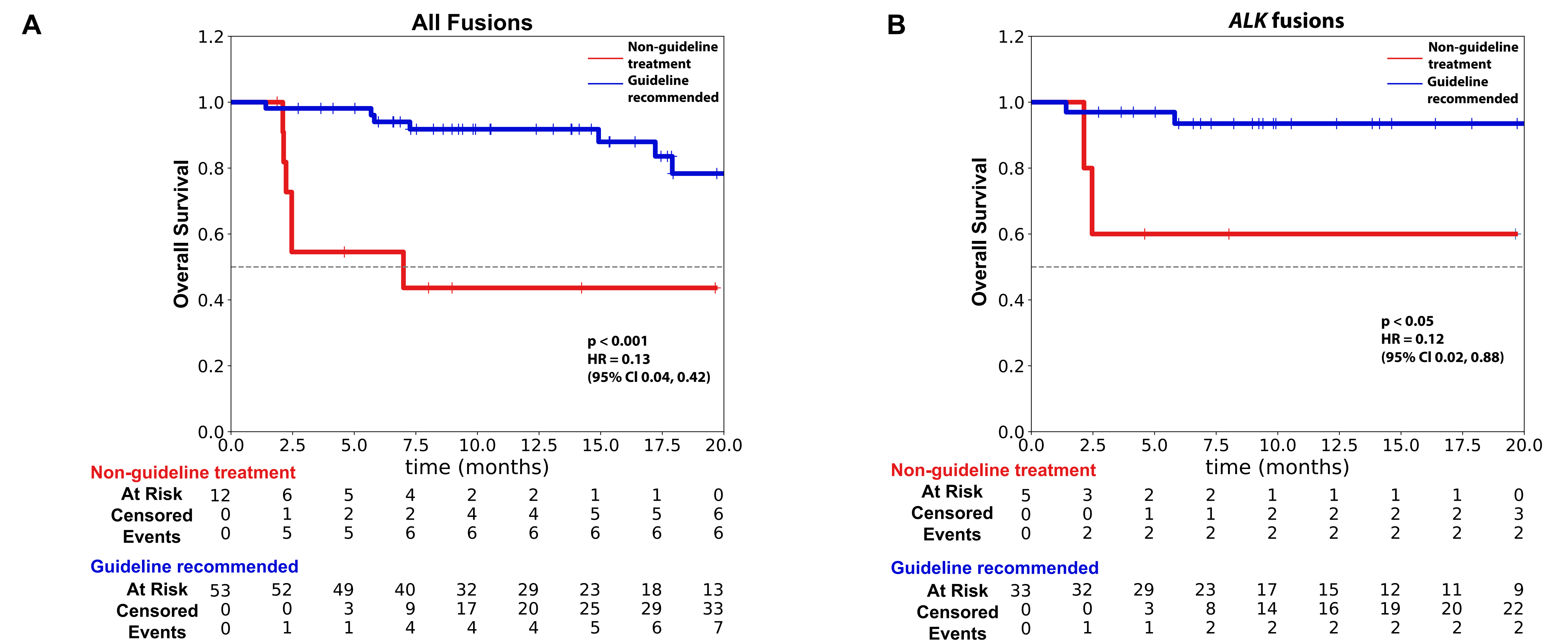**Figure 2. Distribution of Guideline Recommended Medications.**

Figure 4. Survival from Start of Medication.

[A] Fusion-positive patients receiving matched therapy had significantly longer rwOS than those that did not receive matched therapy. **[B]** ALK-positive patients receiving matched therapy had significantly longer rwOS than those that did not receive matched therapy.