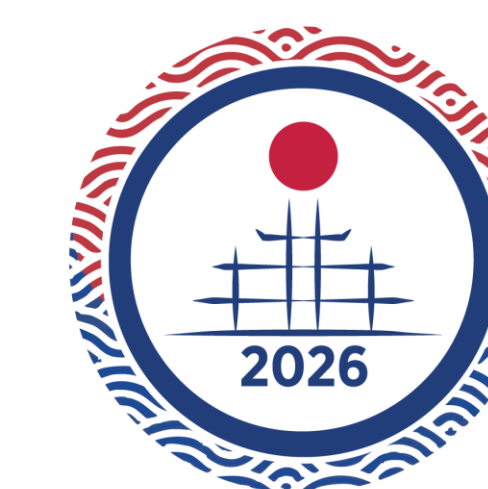


Clinical Trials Confer Greatest Benefit in Later-Line, Non-Driver NSCLC: Real-World Evidence from an Urban Academic Program

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Background

Clinical trial participation is critical to advancing lung cancer care, but real-world outcomes associated with trial enrollment compared to standard-of-care (SOC) therapy remain incompletely characterized. This is particularly relevant across molecular subgroups and lines of therapy, where the relative benefit of investigational therapies may differ. We evaluated progression-free survival (PFS) associated with clinical trial enrollment within a large academic thoracic oncology program that serves a racially and socioeconomically diverse patient population.

Methods

We performed a retrospective cohort study of 221 patients with lung cancer treated at the University of Illinois Chicago from 2021 to 2023. Patients were stratified by clinical trial enrollment versus SOC and further subdivided by stage (I–III vs IV), presence of actionable genomic alteration (AGA), and line of therapy (1L, 2L, 3L, ≥4L). Descriptive statistics were conducted on demographic characteristics of the study cohort. Median PFS (mPFS) was estimated for each subgroup and compared using Kaplan-Meier methodology and log-rank testing.

Figures

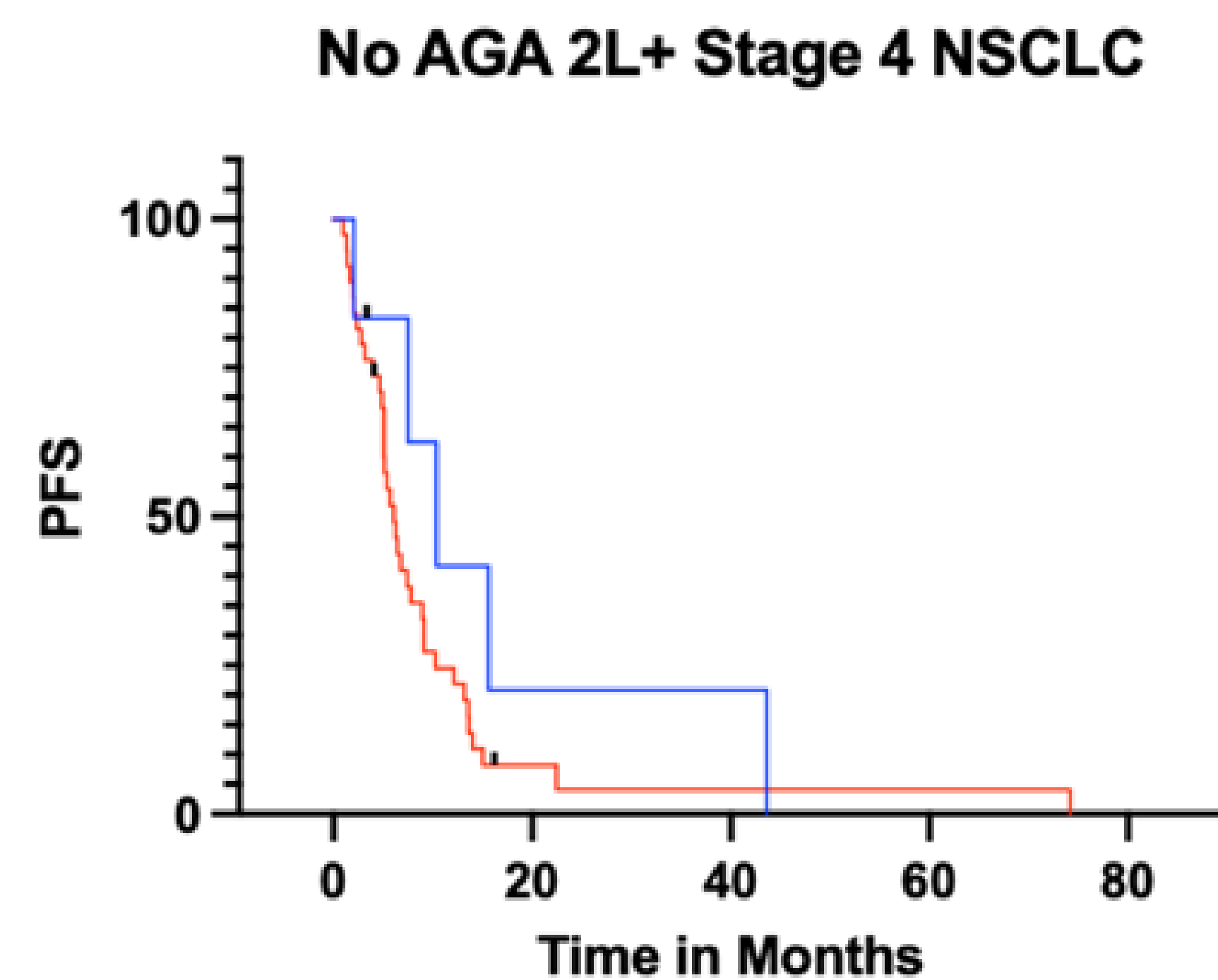


Figure 1: PFS in 2L+ Stage IV NSCLC without AGA

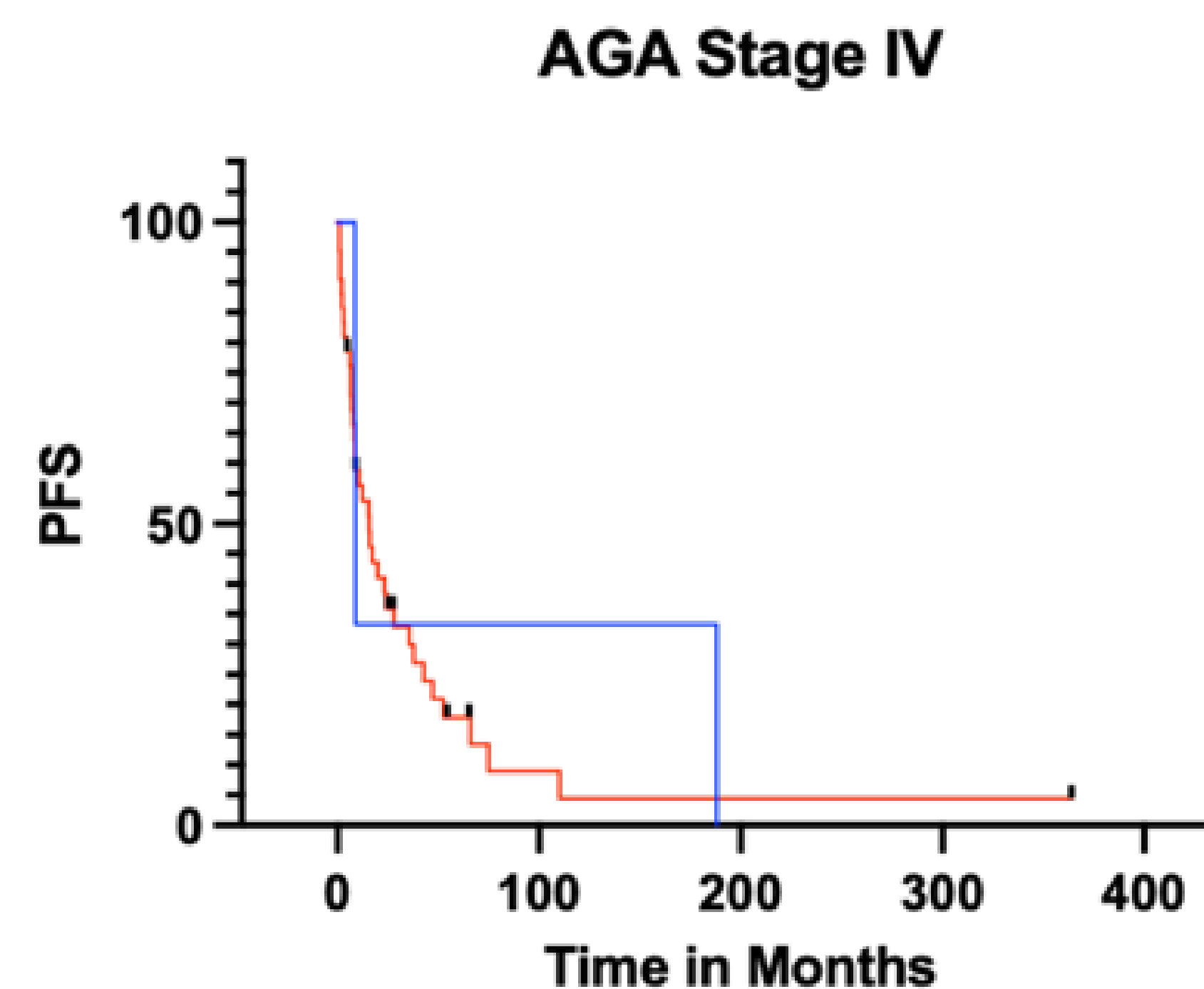


Figure 2: PFS in Stage IV NSCLC with AGA

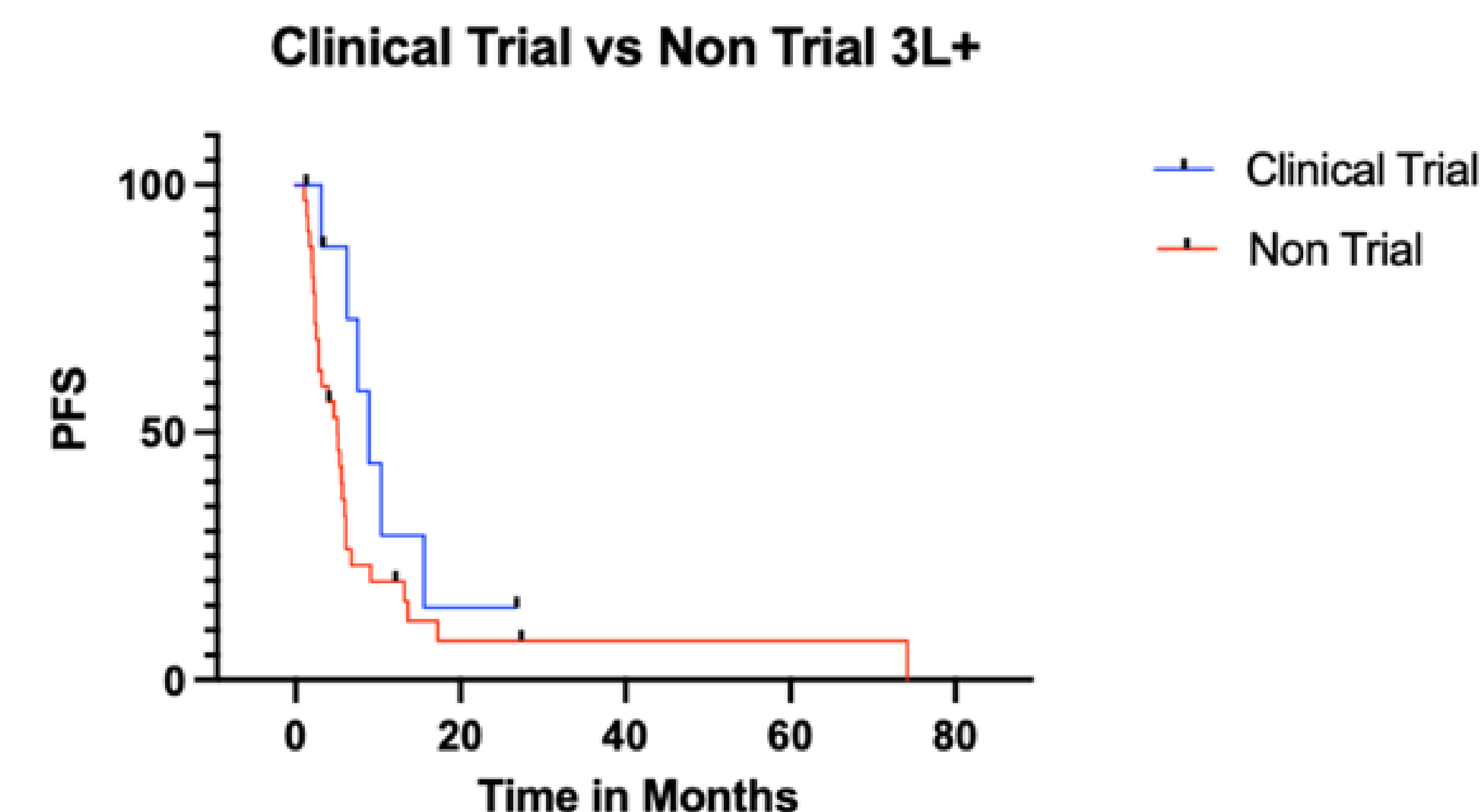


Figure 3: PFS in 3L+ NSCLC

Results

- 221 patients with average age at diagnosis of 64.79 (SD = 9.75)
- Majority of patients were Black (65.16%), followed by Non-Hispanic White (15.84%), Asian (10.41%), and Hispanic (8.14%)
- 85.97% of patients had known smoking history
- Most common stage at presentation was stage IV (40.72%)
- Most common histology type was adenocarcinoma (70.59%)
- 29.41% of patients had been enrolled in clinical trials
- In patients without AGAs, clinical trial enrollment was associated with numerically prolonged mPFS in later lines, most notably in 2L (686.5 vs 251 days), with similar directional trends observed in 3L and ≥4L settings
- For stage IV disease with AGAs, SOC demonstrated longer mPFS in earlier lines of therapy (2L: 601 vs 262 days; 3L: 518 vs 267 days)
- Across stages, clinical trial participation had comparable mPFS relative to SOC in 1L (330 vs 382 days), with a trend toward improved outcomes in later lines (3L: 289.5 vs 180 days; ≥4L: 226 vs 124 days)
- No comparisons reached statistical significance (all $p > 0.05$), likely reflecting limited sample size and heterogeneity of trial regimens

Discussion

In this real-world cohort, clinical trial enrollment was associated with outcomes comparable to SOC across all settings and demonstrated a consistent trend toward improved PFS in later-line therapy, particularly among patients without AGAs. These findings highlight the critical role of clinical trials as a therapeutic option in populations with limited standard treatment efficacy and support prioritizing trial enrollment in later-line and non-driver NSCLC.

Future directions include examining the impact of socioeconomic disparities on clinical trial enrollment and outcomes within this patient population.

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