

P3.190: Polypharmacy, Drug-Drug Interactions and Cannabis Use among Patients with Oncogene-Driven NSCLC: A Real-World Analysis

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INTRODUCTION

- Patients with oncogene-driven NSCLC taking oral targeted therapies are at high risk for polypharmacy (taking ≥5 medications) and significant drug-drug interactions (DDIs) due to improved survival and prevalent comorbid conditions.
- Data on incidence and patterns of polypharmacy, severe DDIs and cannabis use in this population are limited. This study aimed to describe these patterns and examine the association between polypharmacy and DDI risk.

METHODS

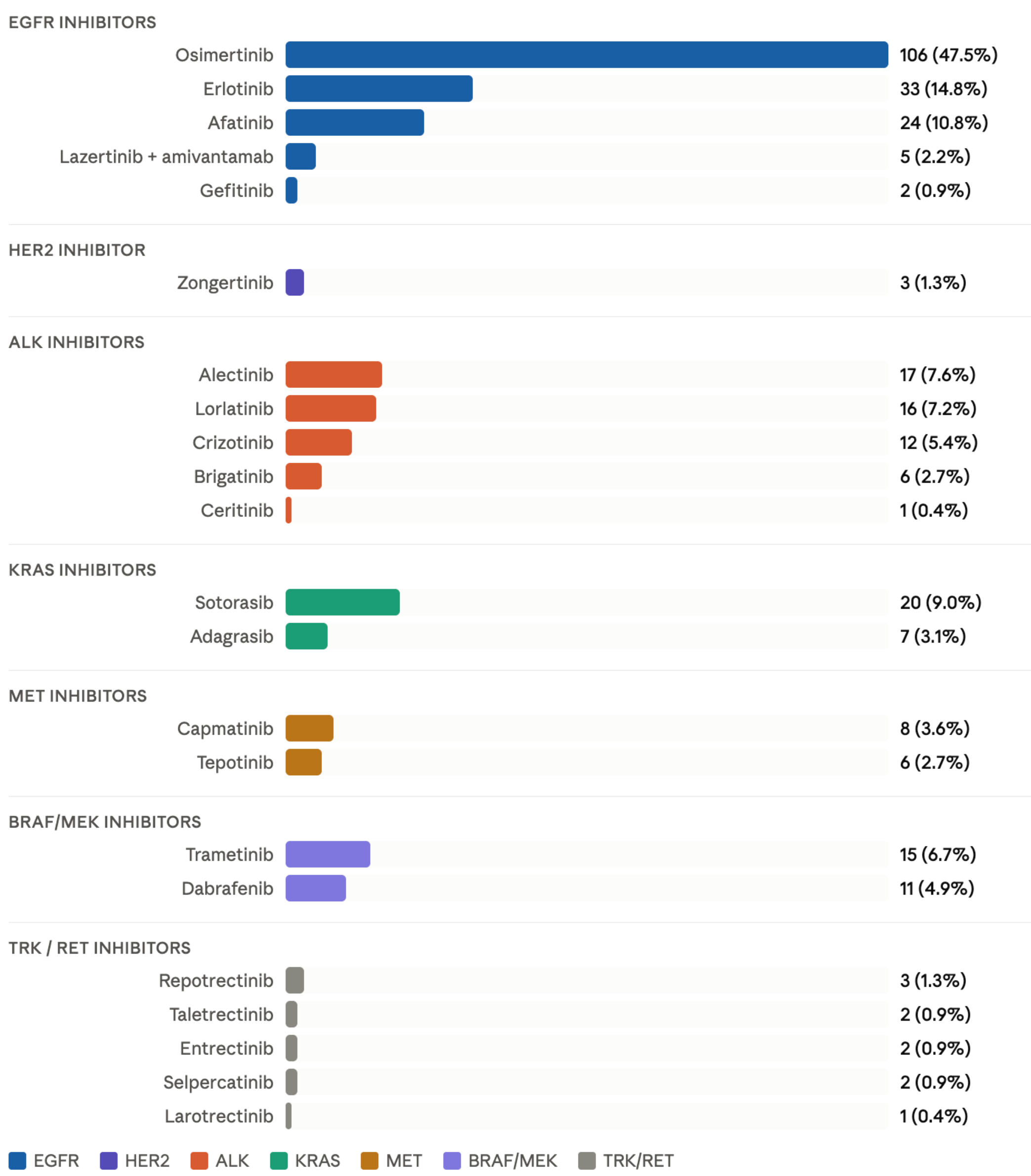
- We collected data pertaining to concurrent medication records and cannabis use of patients diagnosed with NSCLC taking oral targeted therapies, 2012 to 2025 at Rush University Medical Center, Chicago, IL. Eligible patients were identified via prescription and treatment plan records. Concurrent medications active at TKI initiation were extracted from the electronic health records.
- DDIs were identified by cross-referencing concurrent medications against FDA prescribing information and classified as contraindicated, major, or moderate per FDA label language. Cannabis/cannabinoid use was extracted from medical cannabis orders and social history. Analysis was performed using Chi-square test and Spearman rank correlation.

RESULTS

Patient demographics			
N = 223			
VARIABLE		N	%
Age at TKI initiation			
Median age, years (IQR)		66.1	(57.5–73.8)
Range (years)		29.2–97.0	
Vital status at analysis			
Alive		118	52.9%
Deceased		105	47.1%
Gender			
Female		137	61.4%
Male		86	38.6%
Race			
White		119	53.4%
Black or African American		52	23.3%
Asian		18	8.1%
Other / not reported		34	15.2%
Tobacco use status			
Never tobacco user		98	43.9%
Former tobacco user		108	48.4%
Current tobacco user		11	4.9%
Unknown / not assessed		6	2.7%

Oral targeted therapies by drug class

N = 223 patients; 22 unique agents; sorted by frequency within class



Drug-drug interactions at TKI initiation

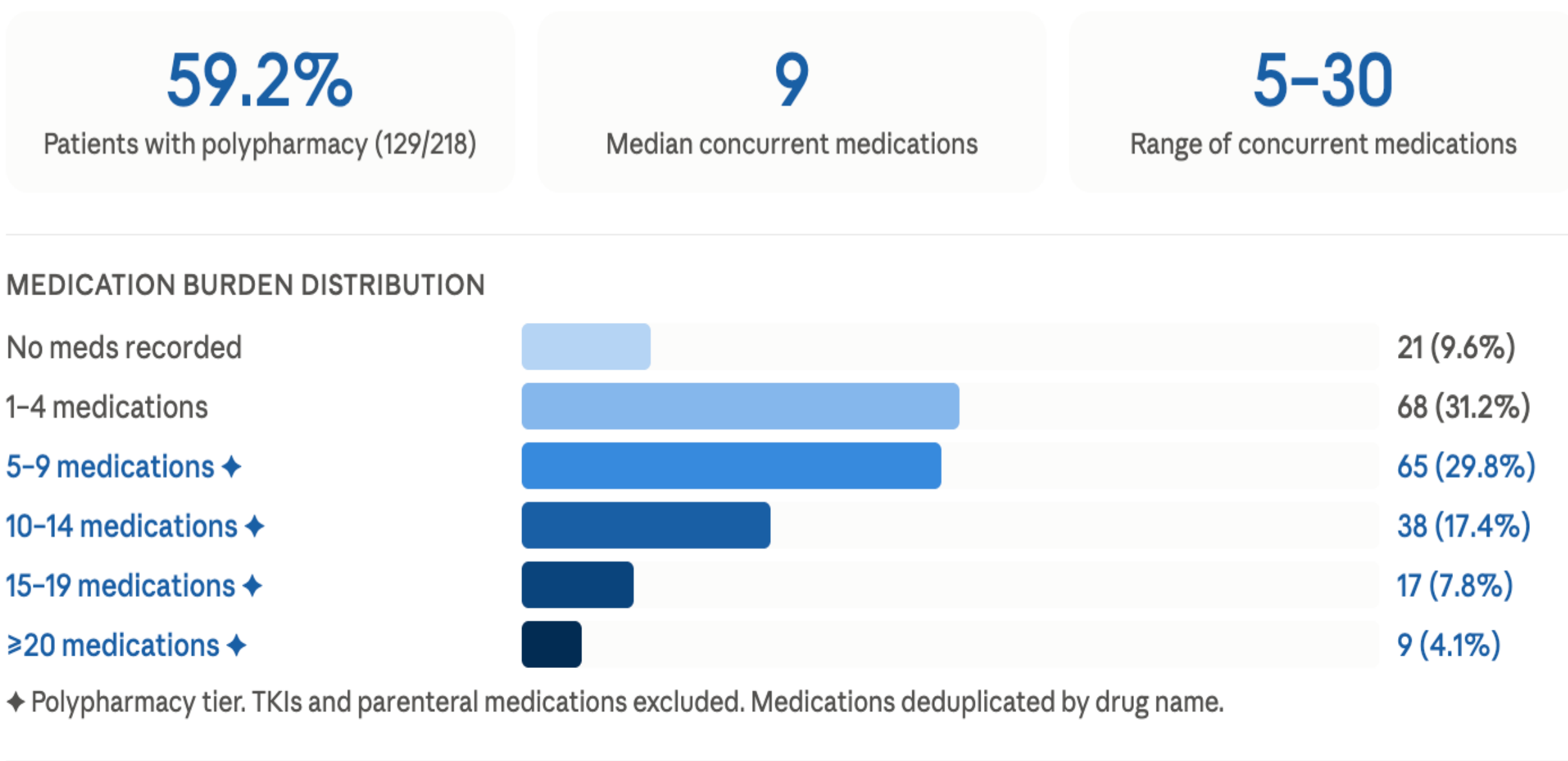
Per FDA prescribing information for each TKI; N = 218 evaluable patients

Any DDI (68/218 patients)			
31.2%			
Contraindicated combinations — avoid concomitant use			
INTERACTION TYPE	CLASS	N	%
Gastric pH / PPI (erlotinib, gefitinib)	Contraindicated	5	2.3%
QTc prolongation (crizotinib, ceritinib, adagrasib)	Contraindicated	4	1.8%
CYP3A4 induction (rifampin, rifabutin)	Contraindicated	1	0.5%
Major interactions — avoid or requires dose modification / monitoring			
QTc prolongation (ondansetron, fluoroquinolones)	Major	26	11.9%
Statin / OATP1B1/B3 transporter inhibition	Major	9	4.1%
Gastric pH / PPI (sotorasib, selpercatinib, dabrafenib)	Major	6	2.8%
Anticoagulant — warfarin + osimertinib, erlotinib	Major	4	1.8%
H2 blocker — famotidine + erlotinib	Major	3	1.4%
Opioid / CYP3A4 substrate (fentanyl, oxycodone)	Major	2	0.9%
Moderate interactions — use with caution, monitor			
CYP3A4 induction — dexamethasone (chronic use)	Moderate	36	16.5%
CYP3A4 inhibition (diltiazem, verapamil, fluconazole)	Moderate	8	3.7%
Anticoagulant — moderate (warfarin + afatinib, trametinib)	Moderate	4	1.8%

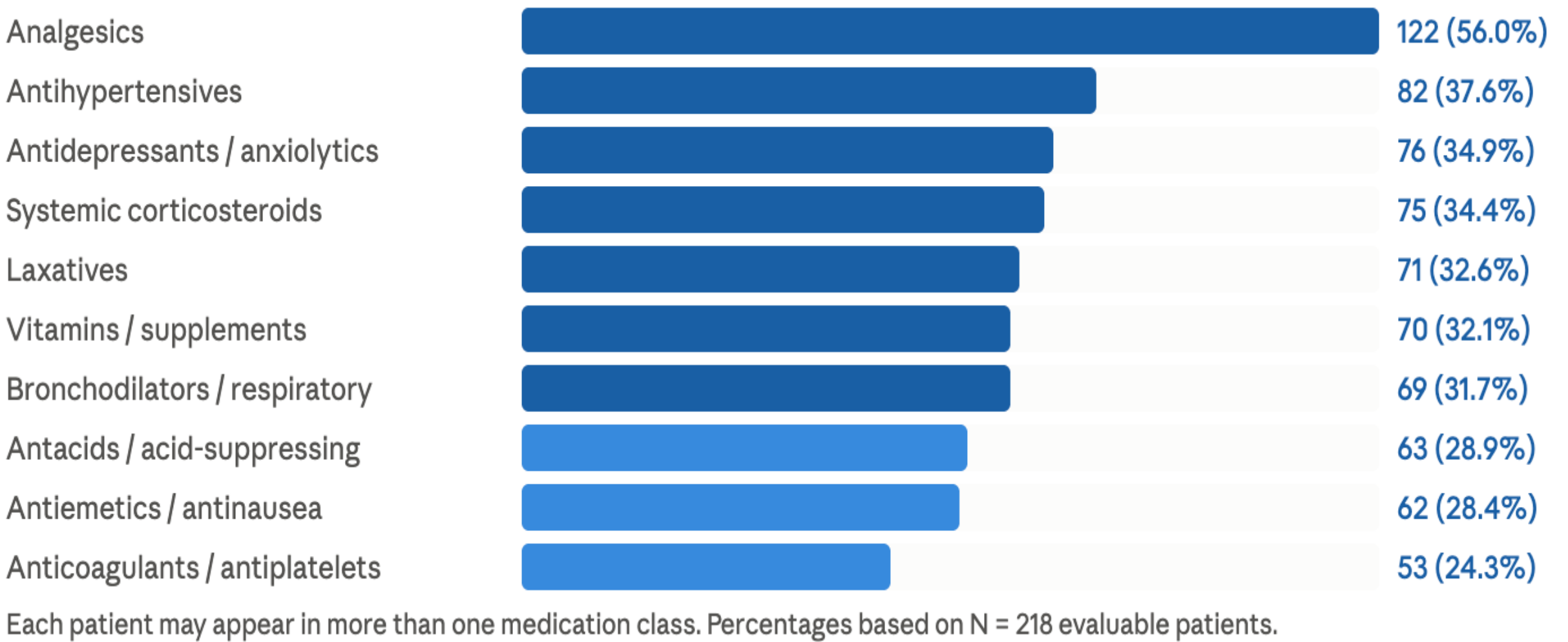
DDI = drug-drug interaction; OATP = organic anion transporting polypeptide; PPI = proton pump inhibitor. Patients may appear in more than one DDI category.

Polypharmacy at TKI initiation

Defined as ≥5 concurrent non-oncologic medications; N = 218 evaluable patients

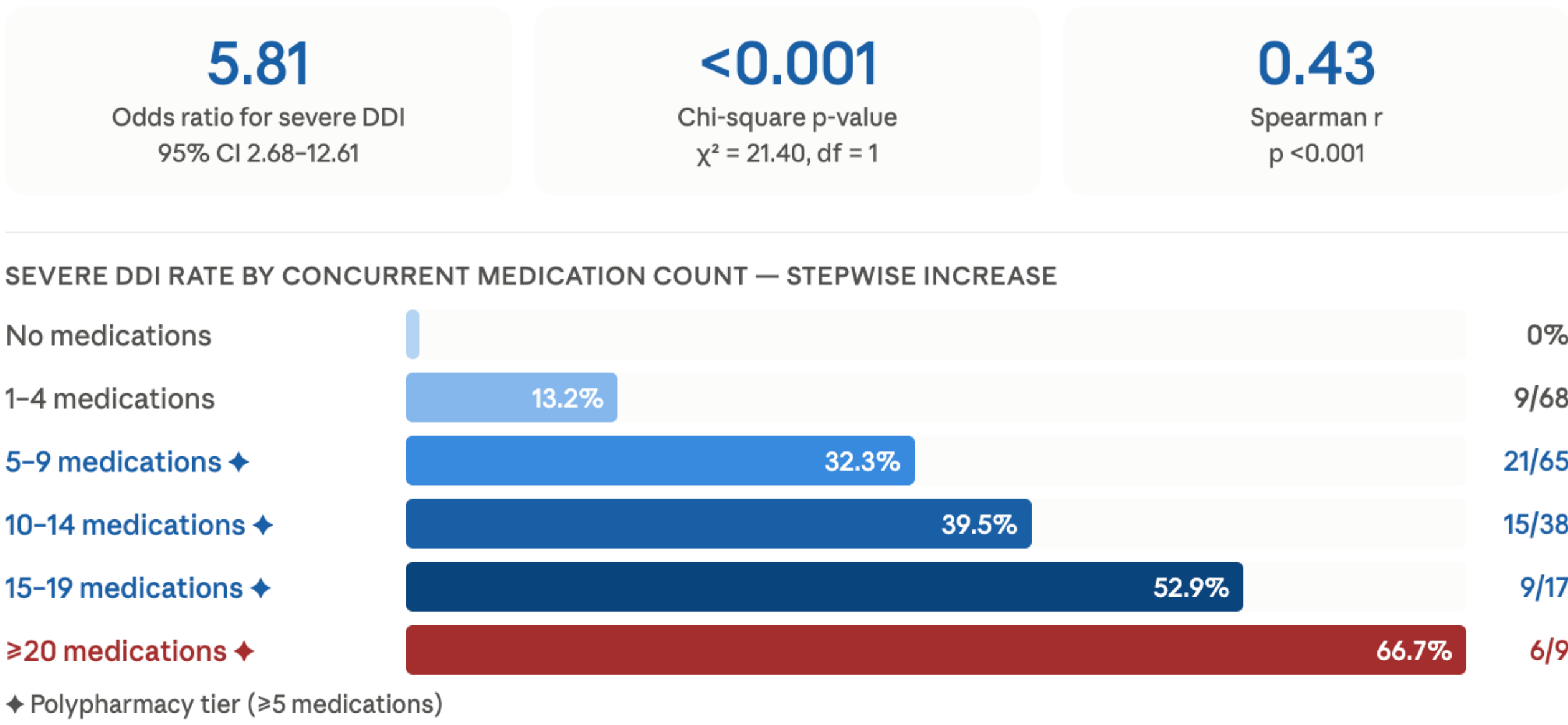


MOST PREVALENT CONCURRENT MEDICATION CLASSES (N = 218)



Polypharmacy and severe DDI risk — correlative analysis

Severe DDI = contraindicated or major per FDA prescribing information; N = 218



2×2 CONTINGENCY TABLE

GROUP	NO SEVERE DDI	SEVERE DDI	TOTAL
No polypharmacy (<5 meds)	80	9	89
Polypharmacy (≥5 meds)	78	51	129
Total	158	60	218

Polypharmacy patients: 39.5% severe DDI vs 10.1% in non-polypharmacy patients (p <0.001)

Cannabis / cannabinoid use

N = 223; identified from medical cannabis orders and social history documentation

Any use documented (13.0%)		
29		
Active at TKI initiation (4.5%)		
10		
Medical cannabis orders (10.8%)		
24		
VARIABLE	N	%
Source of documentation (N = 29)		
Medical cannabis order only	22	75.9%
Social history documentation only	5	17.2%
Documented in both sources	2	6.9%
Prescribed cannabinoid formulation (N = 24)		
Dronabinol (synthetic oral THC) — any dose	21	87.5%
Dronabinol 2.5 mg capsule	14	58.3%
Dronabinol 5 mg capsule	9	37.5%
Dronabinol 10 mg capsule	1	4.2%
Medical cannabis (unspecified formulation)	2	8.3%
Cannabidiol solution (patient's own, non-Epidiolex)	1	4.2%
Route of use — social history (N = 7)		
Edible — baked goods	2	28.6%
Edible — gummy / other	2	28.6%
CBD — route not specified	1	14.3%
Route not documented	2	28.6%
TKI at time of cannabis documentation — social history (N = 7)		
Osimertinib	2	28.6%
Adagrasib	1	14.3%
Zongertinib	1	14.3%
Erlotinib → osimertinib (sequential)	1	14.3%
Alectinib → lorlatinib (sequential)	1	14.3%
Capmatinib	1	14.3%

Dronabinol is a synthetic oral delta-9-tetrahydrocannabinol (THC) FDA-approved capsule. Some patients had orders at multiple doses reflecting titration; dose percentages are calculated among dronabinol patients (n = 21). Percentages for route of use and TKI calculated among social history patients (n = 7).

CONCLUSION

- Polypharmacy is highly prevalent in patients with oncogene-driven NSCLC, underscoring the importance of medication reconciliation to mitigate the risk of DDIs at treatment initiation and during follow-up.
- Notably, 4.6% of patients were identified as receiving concurrent medications that are contraindicated with their TKI per FDA prescribing information. Our findings highlight the importance of pharmacist-led comprehensive medication and substance use review, including cannabis and cannabinoids. Prospective studies are needed to investigate the association between polypharmacy, DDIs, and cannabis/cannabinoid use with patient-reported outcomes, time on therapy, and targeted toxicities.
- The observed association between polypharmacy and severe DDIs is a hypothesis-generating finding that warrants prospective validation.

CONTACTS AND DISCLAIMERS

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References available upon request.

Claude AI was used to assist with creation of some visuals.

