

# Cefazolin-Induced Neutropenia Development: Preliminary Results From The BLIND-OHIO Trial

Nick Panchak, PharmD Resident; Jennifer Ross, PharmD, BCIDP; Jessica Das, PharmD, BCPS; Ryan McFarland, PharmD Candidate  
M Health Fairview, Minneapolis, MN

## BACKGROUND

Beta-lactam-induced neutropenia (BLIN) is a serious adverse and enigmatic reaction seen with beta-lactam antibiotics. The underlying mechanism is complex and varied, ranging from immune-mediated hypersensitivity, to direct toxic effects, to suppression of metalloprotein-mediated humoral immunity.<sup>1</sup> Proposed risk factors include high dose and long duration of beta-lactam treatments (>10 days).<sup>2</sup> One recent study showed a possible correlation between BLIN and faster administration rates.<sup>3</sup> patients receiving cefazolin. This study compares the incidence of neutropenia between IV push and intermittent

**Table 1. Properties of β-lactams**

Drug	BLIN Incidence <sup>2</sup>	Median time to onset (days) <sup>2</sup>
Cefepime	0.9 - 5.4%	26
Cefazolin	2.2 - 3.3%	3
Ceftriaxone	6%	21

infusion in patients receiving cefazolin in the home infusion setting.

## OBJECTIVES

1. Evaluate whether IV push administration of cefazolin increases the risk for BLIN compared to intermittent IV infusion in the home setting.
2. Explore additional risk factors for BLIN via logistic regression with the goal of developing an OPAT treatment algorithm to minimize the risk of this adverse event at Fairview Home Infusion (FHI).

## METHODS

This study was a single-center, retrospective cohort study of home infusion patients treated with cefazolin between 7/1/2019 and 7/1/2022. IV push and intermittent infusion administration was defined as being given over 10 minutes and 30 minutes, respectively. Data collection was conducted via manual chart review and electronic health record (EHR) data analytics reports. Identification of additional neutropenia risk factors via log-linked binomial regression is currently underway. Inclusion screening was conducted via automated data extraction and manual chart review.

### Inclusion criteria:

Age ≥18 y/o	Completed research authorization	Seen within the Fairview Health System	Admission history available within Epic
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### Exclusion criteria:

Baseline neutropenia prior to antibiotic therapy	Chemotherapy prior to antibiotic course	Inadequate lab or therapy data to assess for neutropenia
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## PRELIMINARY RESULTS: Cefazolin-Induced Neutropenia

**Table 2. Baseline Characteristics**

Patient Categories	Patients (n)	Age (years)		Baseline ANC (cells×1000/μL)		ANC Change (cells×1000/μL)		Duration (days)	
		Mean	SD	Mean	SD	Mean	SD	Mean	SD
No Events	413	57	16	9.1	5.4	-4.1	5.0	32	15
Infusion	76	72	12	9.6	5.2	-5.1	4.7	38	18
IV Push	337	54	15	9.0	5.4	-3.9	5.0	31	14
1+ Event(s)	18	58	19	5.6	2.9	-4.2	2.3	40	21
Infusion	4	73	14	5.4	2.5	-4.3	1.9	35	5
IV Push	14	54	18	5.7	3.1	-4.1	2.8	42	24
Grand Total	431	57	16	8.9	5.4	-4.1	4.9	32	16

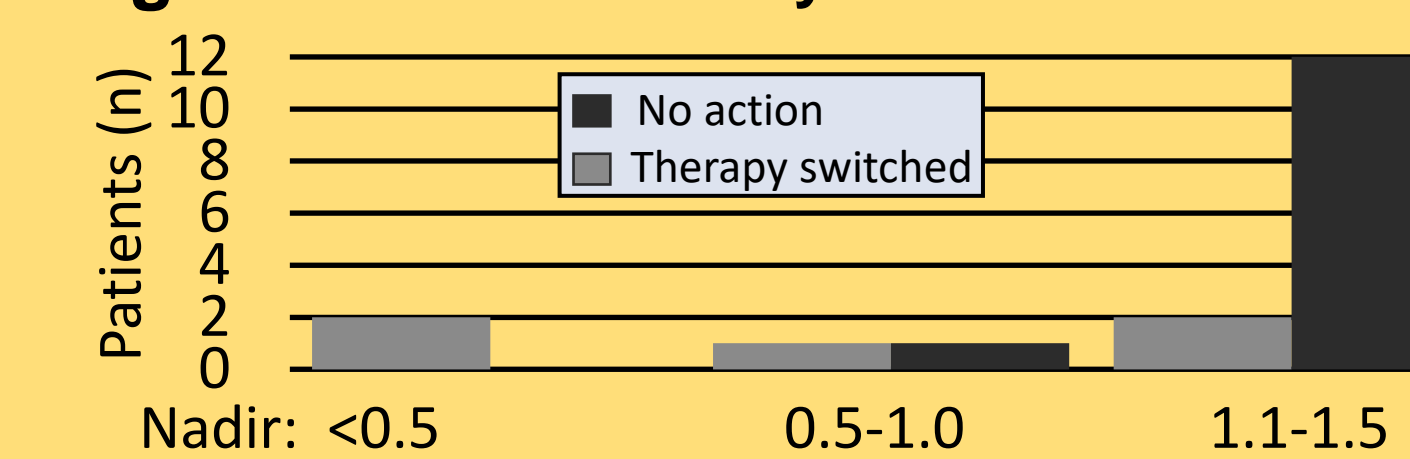
**Table 4. Preliminary Linear Regression Analysis**

Covariates	Standard Error	t Stat	P-value	Regression Statistics	
Total (intercept)	0.047	0.93	0.35	Multiple R	0.183
Baseline ANC	0.0021	-2.83	0.0049	R Square	0.034
Treatment Duration	0.00071	2.25	0.025	Standard Error	0.212
Patient Age	0.00068	0.16	0.87	F Significance	0.006

**Table 3. Primary Outcome: Neutropenia by Route of Admin**

Route	No Events	1+ Event(s)	Percent	P value
Infusion	76	4	5.0%	0.437
IV Push	337	14	4.0%	
Grand Total	413	18	4.2%	

**Figure 1. Event Severity and Interventions**



**Figure 2.** Modrian, Piet. Composition with Large Red Plane, Yellow, Black, Gray, and Blue, 1921.<sup>5</sup>



## DISCUSSION

- Our data did not show statistically significant differences in rates of cefazolin-induced neutropenia.
- Patients with Medicare at FHI received IV therapy on an ambulatory infusion (CADD) pump for homecare coverage. These patients tend to be older in age and make up a significant portion of the infusion arm.
- BLIN is rare and multifactorial; establishing a correlation with any one covariate is challenging.
- Linear regression is not ideal for this application but is an adequate preliminary illustration of the impact of covariates; log-linked binomial regression is currently underway.
- The incidence of BLIN with cefazolin is in line with previous literature, but the median onset is much longer.<sup>2</sup>

## CONCLUSIONS

- Additional studies are required to elucidate the impact of infusion rate on the incidence of BLIN. Data collection from cefepime and ceftriaxone arms is currently underway.
- A lower ANC at baseline appears to be the strongest predictor of BLIN. Treatment duration was also positively correlated. Age represents a substantial confounder.
- Institutional practices may account for the nonsignificant correlation of neutropenia with rate of administration.
- All events observed in this study were asymptomatic and most were mild (ANC 1.5-1.1), requiring no intervention. Key cutoffs for neutropenia necessitating intervention are not well established and may be patient-specific.

## REFERENCES

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