

Pharmacokinetic Response after Subcutaneous Administration of Ceftriaxone

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Introduction

Subcutaneous administration of ceftriaxone may offer a more convenient and safer alternative to IV administration. This was a randomized, partially blinded, three-period crossover study in 18 healthy male and female subjects.

Three treatments were compared:

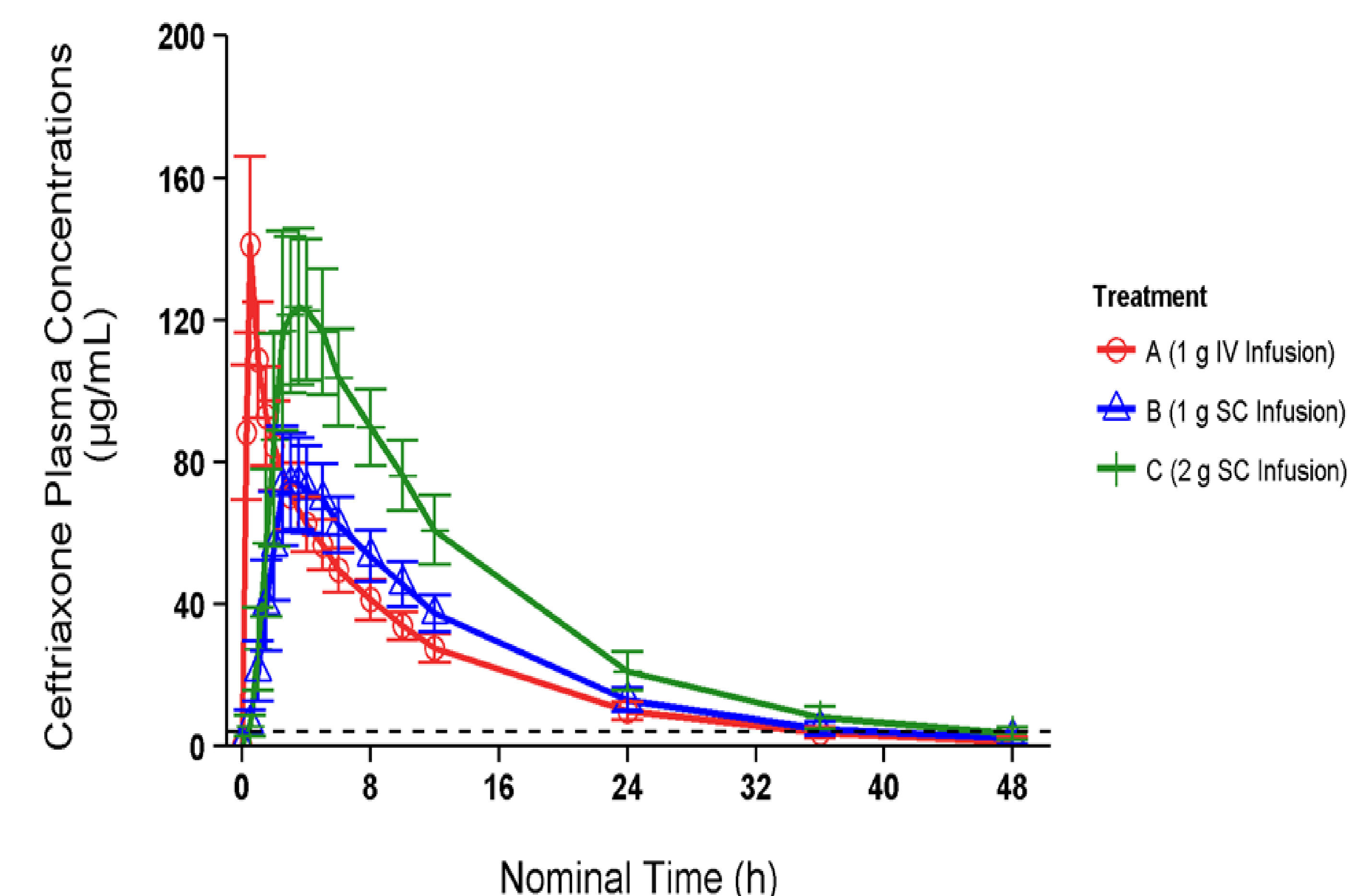
- 1 g administered subcutaneously over 2 hours
- 1 g administered IV over 30 minutes
- 2 g administered subcutaneously over 2 hours

The primary endpoint for the study was non-inferior antimicrobial coverage (time over MIC) when compared to the same dose given by intravenous infusion.

Table 1: Demographics

Characteristic	Statistic	All Subjects
Age (years)	N	18
	Mean (SD)	46.8 (11.3)
	Median (Min, Max)	49.0 (29.0, 63.0)
Sex: M	N (%)	8 (44.4%)
Sex: F	N (%)	10 (55.6%)
Race: White	N (%)	16 (88.9%)
Race: Black or African American	N (%)	2 (11.1%)

Figure 1: Mean Plasma Ceftriaxone vs. Time Plots



Results

Ceftriaxone exposure following subcutaneous 2-hour infusion of 1 gram was similar to that of the standard IV infusion over 30 minutes.

- Mean plasma concentrations after IV administration were comparable to concentrations reported in the package insert.
- The geometric mean absolute bioavailability following subcutaneous administration was 107.66%
- Antibacterial coverage (time of MIC) was equivalent with geometric mean ratio of 109.68%

These results support that the 1g subcutaneous infusion treatment of ceftriaxone is non-inferior to the currently approved 1 g IV infusion treatment.

Table 2: Summary of Absolute Bioavailability Results for Ceftriaxone Following IV and Subcutaneous Infusion

Parameter	Units	N	Geometric LSM (1gSC)	Geometric LSM (1gIV)	SC/IV (%)	90% Confidence Interval
AUC _{inf}	h*µg/mL	18	1079.53	1002.77	107.66	(104.35, 111.07)
AUC _{0-t}	h*µg/mL	18	1045.83	976.10	107.14	(103.89, 110.50)
C _{max}	µg/mL	18	77.05	139.03	55.42	(52.32, 58.69)

Conclusion

Subcutaneous infusion of 1 gram ceftriaxone over 2 hours results in complete bioavailability (107.66%) and equivalent antimicrobial coverage when compared to IV administration over 30 minutes. The study met predefined non-inferiority criteria for antimicrobial coverage (time over MIC). SC administration of ceftriaxone offers a novel delivery mode for treatment of susceptible infections without the need for vascular access.

Figure 2: Proportion of Time over MIC by Treatments

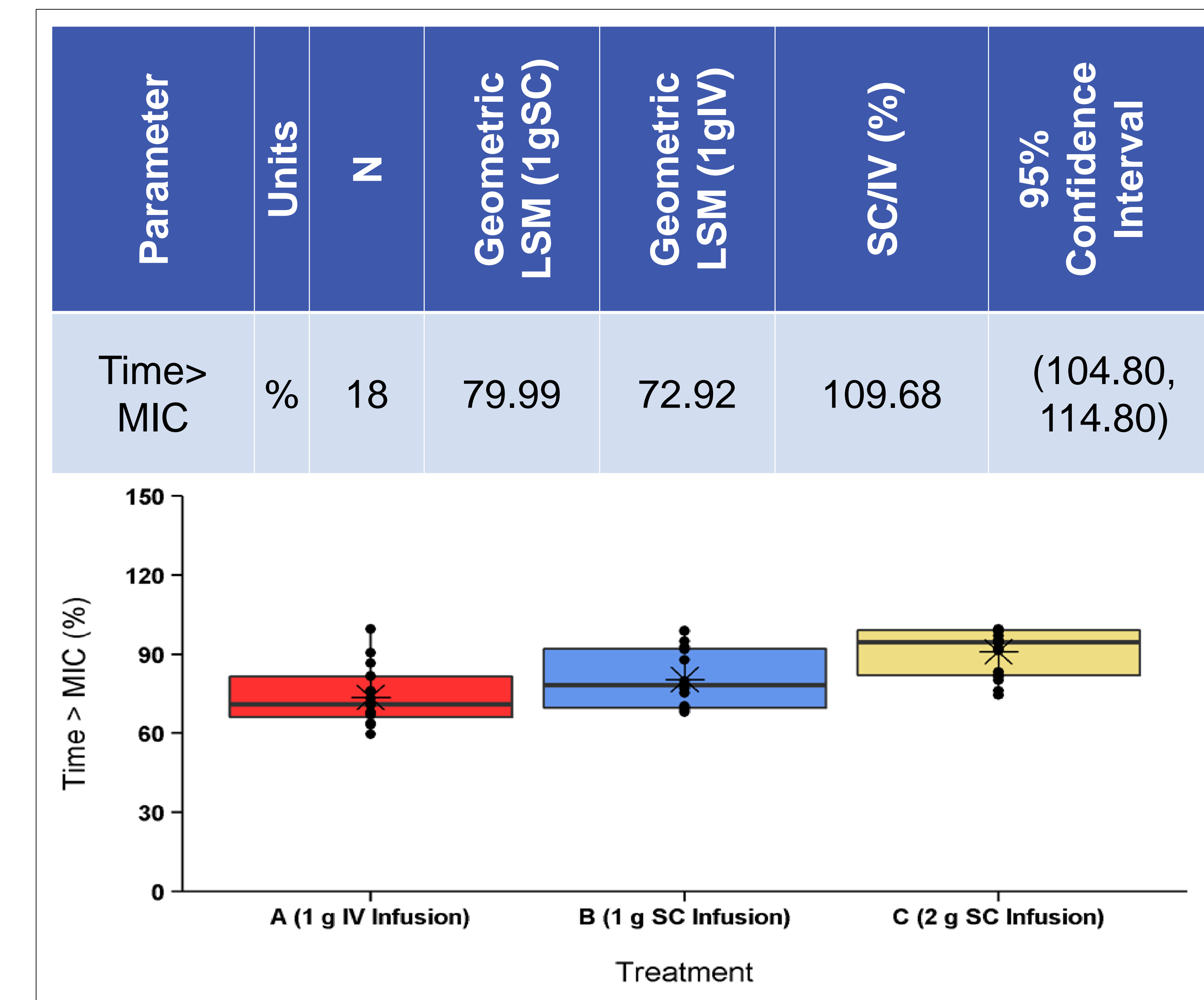


Table 3: Mean Ceftriaxone Plasma Concentration

Mean Plasma Concentration (mcg/mL)						
Group	T2h	T4h	T6h	T8h	T12h	T24h
1g SC*	56	72	62	53	37	13
2g SC	86	123	104	90	61	21
1g IV*	84	62	49	41	28	10
From Package Insert						
1g IV	88	67	53	43	28	9
1g IM*	76	68	56	44	29	ND

SC = subcutaneous, IV = intravenous, IM = intramuscular