MannKind Corporation

Key Figures from Study MKC142

Demonstrating Bioequivalence of Medtone® Model C inhaler to the Next Generation Inhaler (2c) and Dose Equivalence of 2, 10 unit cartridges to 1, 20 unit cartridge

Objectives

- Test if 20U Gen2c is bioequivalent to 30U MedTone

and

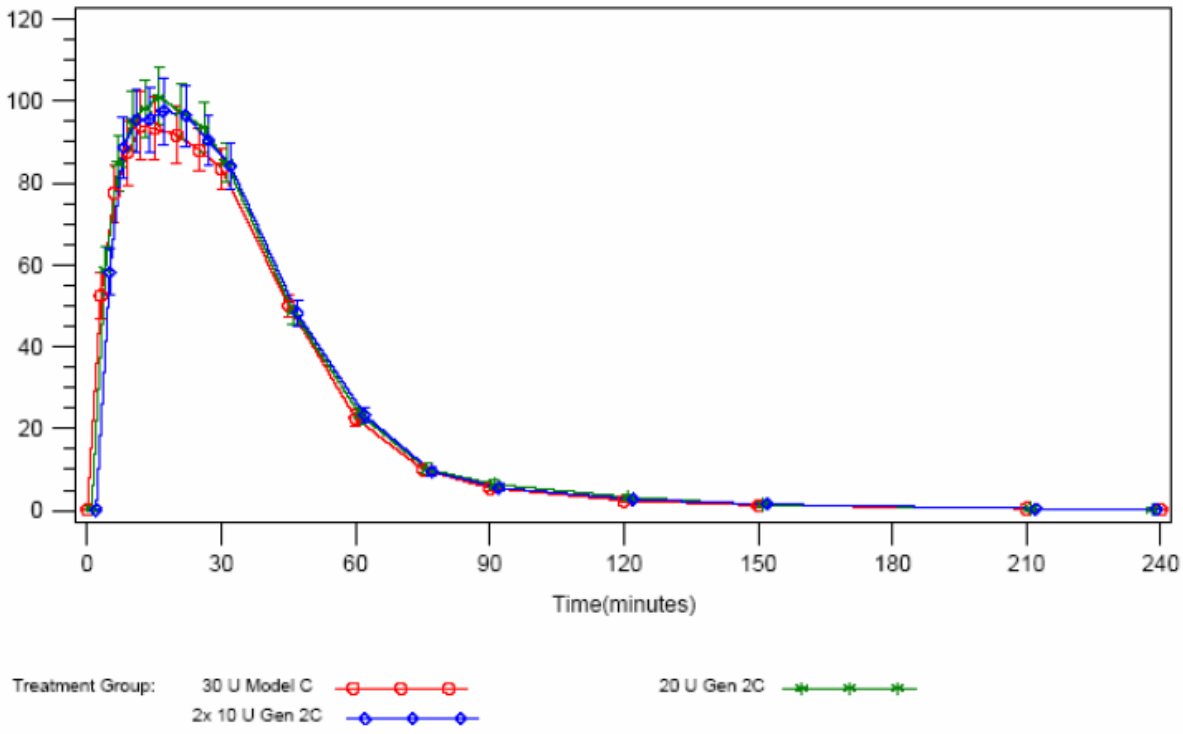
- Test if 2 x 10U Gen2c is bioequivalent to 20U Gen2

- Both an ECLIA and RIA assay were used with similar results

- Our analysis of both comparisons is that they are consistent with bioequivalence criteria

ECLIA (C peptide-corrected)

Figure 1. Mean C-peptide-Corrected Insulin Concentration Over Time (PK Population, n = 46)

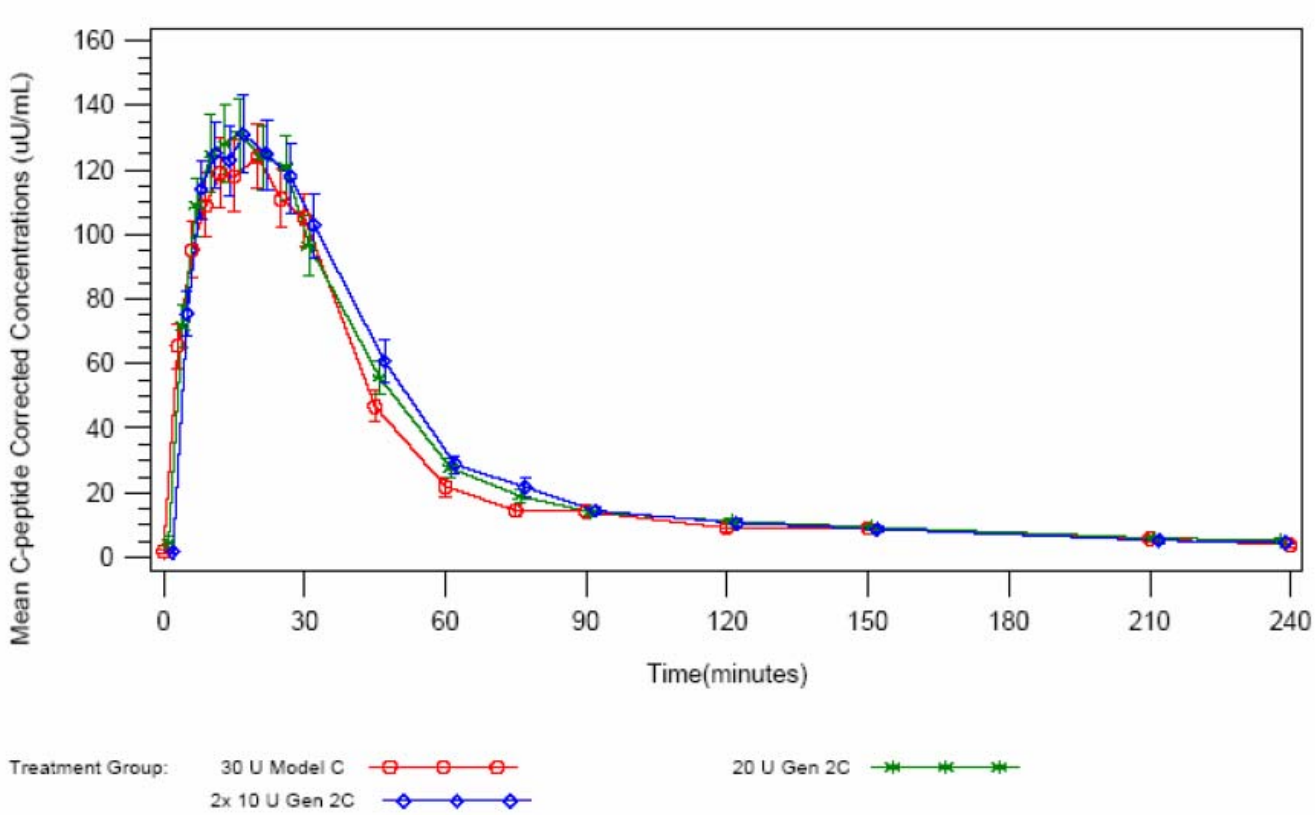


ECLIA results

Bioequivalence Assessment Based on C-peptide Corrected Insulin Concentration Values (PK Population, n = 46)				
PK Parameter	Statistics	30 U Model C	20 U Gen 2C	20 U Gen 2C vs. 30 U Model C
$AUC_{0\text{-}120\ min}$ (min x μU/ml)	Geometric Mean	4060.3	4294.5	
	Ratio			1.060
	90% CI			[0.981, 1.145]
C_{max} (μU/ml)	Geometric Mean	97.4	105.2	
	Ratio			1.082
	90% CI			[0.992, 1.180]
Bioequivalence Assessment Based on Baseline Corrected Insulin Concentration Values (PK Population, n = 46)				
PK Parameter	Statistics	30 U Model C	20 U Gen 2C	20 U Gen 2C vs. 30 U Model C
$AUC_{0\text{-}120\ min}$ (min x μU/ml)	Geometric Mean	6952.4	6964.5	
	Ratio			0.997
	90% CI			[0.940, 1.059]
C_{max} (μU/ml)	Geometric Mean	132.8	135.4	
	Ratio			1.017
	90% CI			[0.941, 1.099]
Bioequivalence Assessment Based on Raw Insulin Concentration Values (PK Population, n = 46)				
PK Parameter	Statistics	30 U Model C	20 U Gen 2C	20 U Gen 2C vs. 30 U Model C
$AUC_{0\text{-}120\ min}$ (min x μU/ml)	Geometric Mean	7759.6	7834.0	
	Ratio			1.006
	90% CI			[0.954, 1.060]
C_{max} (μU/ml)	Geometric Mean	139.7	142.8	
	Ratio			1.020
	90% CI			[0.948, 1.099]

RIA (C-peptide corrected)

Figure 2. Mean C-peptide Corrected Insulin Concentration Over Time
Pk population (n=46)



Error bars denote ± 1 standard error.

RIA results

Table 1. Bioequivalence Assessment Based on C-peptide-Corrected Insulin Concentration Values (PK Population, n = 46)

PK Parameter	Statistic	30 U MedTone Model C (n = 46)	20 U Gen2C (n = 46)	20 U Gen2C vs 30 U MedTone Model C
$AUC_{0\text{-}120}$ (min·µU/mL)	Geometric Mean	5008	5469	
	Ratio			1.096
	90% CI			[0.980, 1.226]
C_{max} (µU/mL)	Geometric Mean	137	139	
	Ratio			1.020
	90% CI			[0.922, 1.128]

Abbreviations: $AUC_{0\text{-}120}$, area under the serum concentration-time curve from time 0 to 120 minutes postdose; CI, confidence interval; C_{max}, maximum observed serum concentration; MedTone Model C, MedTone Inhaler Model C; PK, pharmacokinetic.

Geometric mean ratio and 90% confidence interval are model-adjusted values, derived from the mixed model with treatment, sequence, and period as fixed effect and with subject as random effect.