

Pharmacokinetics and Dose Proportionality of Sublingual Sufentanil NanoTab in Healthy Volunteers

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Treatment of Acute Pain

- ARX-01: Sufentanil NanoTab PCA System

- *Indication: Acute Post-Operative Pain*
- Better tolerated than IV PCA morphine
- No IV – improved mobility, fewer complications
- Pre-programmed – reduced risk of errors



ARX-01

- ARX-02: Sufentanil NanoTab BTP Management System

- *Indication: Cancer Breakthrough Pain (BTP)*
- Timing/PK matches breakthrough episode
- Safer than transmucosal fentanyl



ARX-02

- ARX-03: Sufentanil/Triazolam NanoTab

- *Indication: Procedural Analgesia & Sedation*
- Rapid onset of sedation and analgesia
- Safe – no monitoring requirement



ARX-03

Sufentanil: A Superior Opioid

- Approved for IV and epidural administration
 - *Minimal clinical risk*
- High therapeutic index¹
 - *Broad, safe dosing range*
- No active metabolites
 - *Well tolerated*

Opioid	Therapeutic Index ¹
Methadone	12
Meperidine	28
Morphine	70
Hydromorphone	232
Fentanyl	300
Sufentanil	25,000

Therapeutic index = median lethal dose (LD₅₀) / lowest median effective dose (ED₅₀)

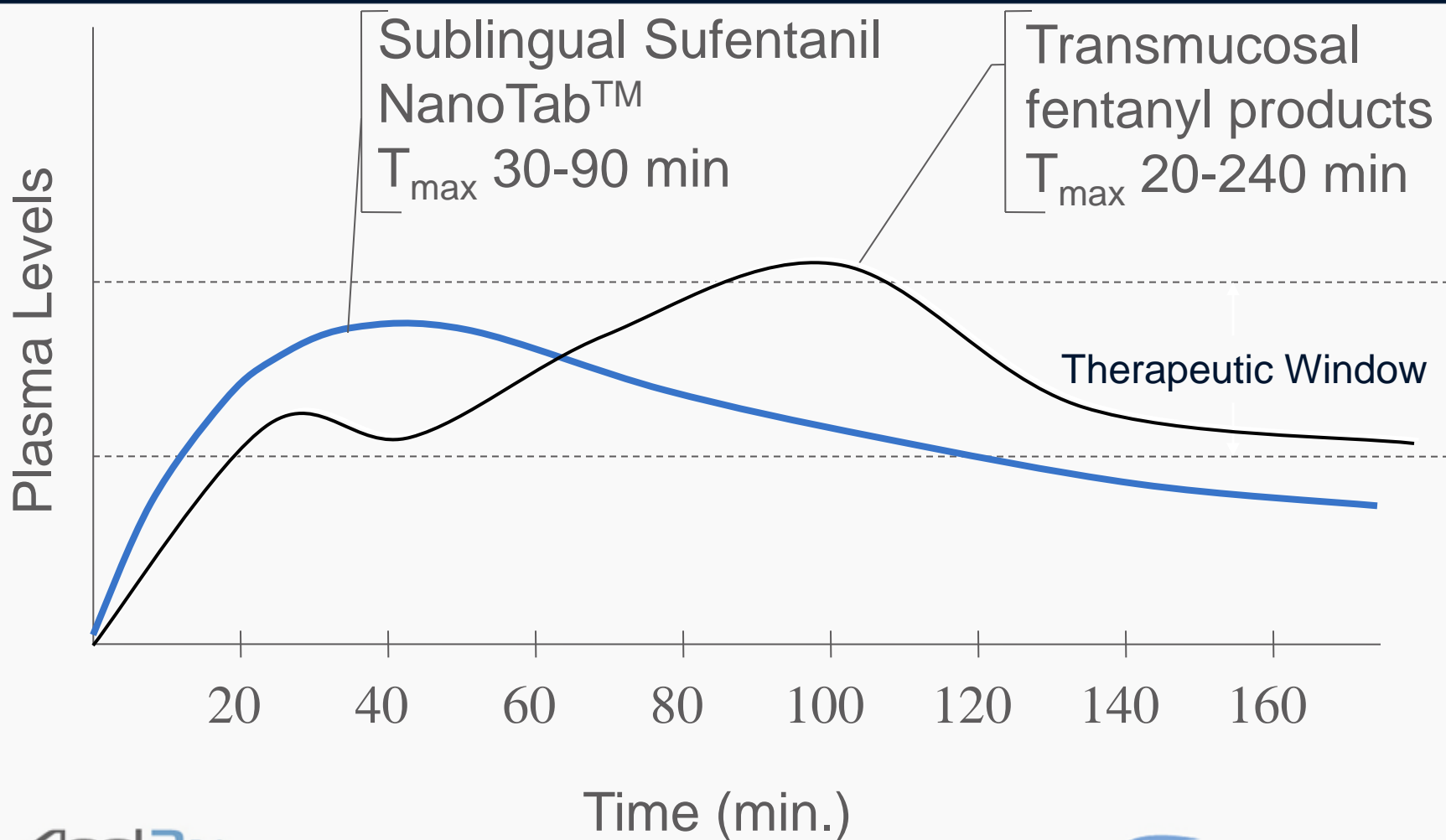
¹ De Castro J: Practical applications and limitations of analgesic anesthesia: a review. *Acta Anaesthesiol Belg* 1976; 27: 107-28.

NanoTab™ Benefits

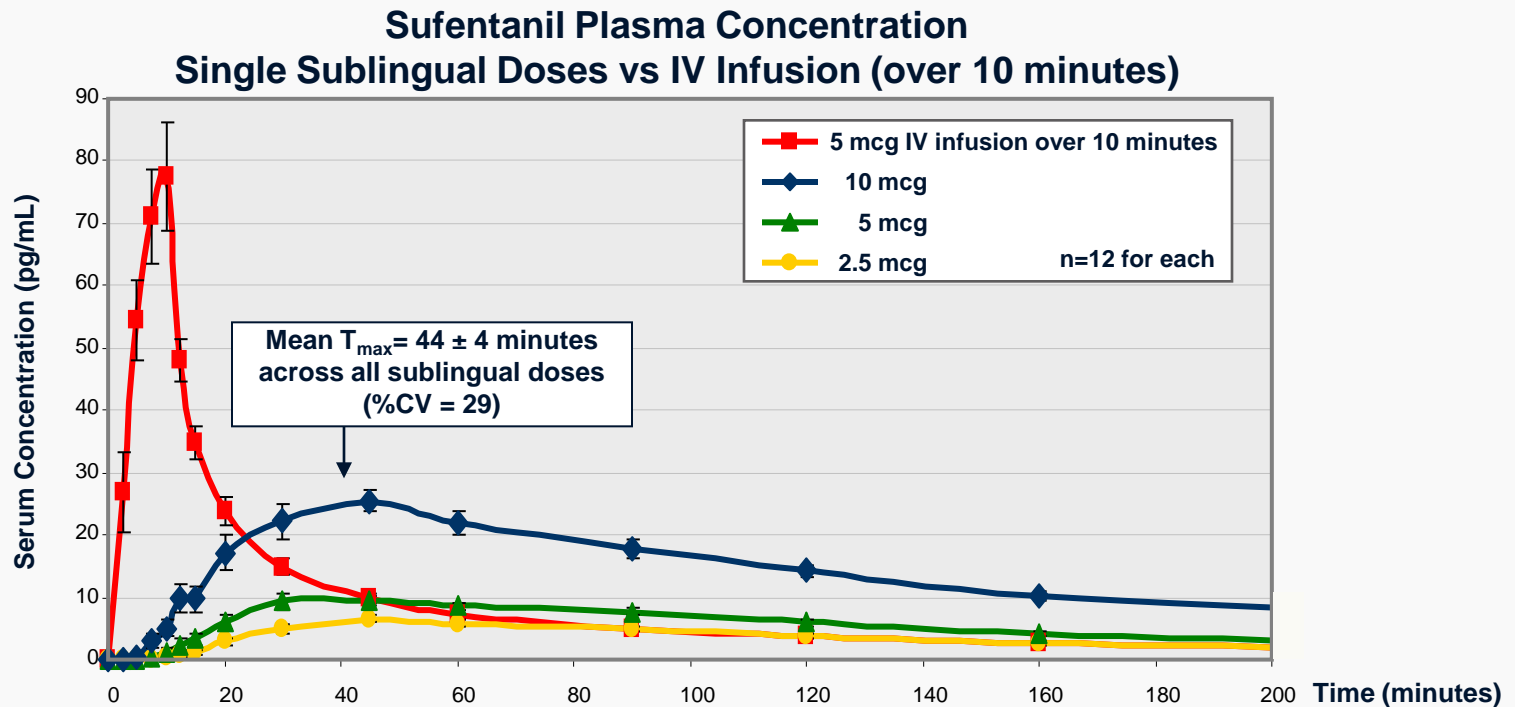
- Minimizes saliva production
- Enhanced transmucosal uptake
- Consistent PK
- High bioavailability



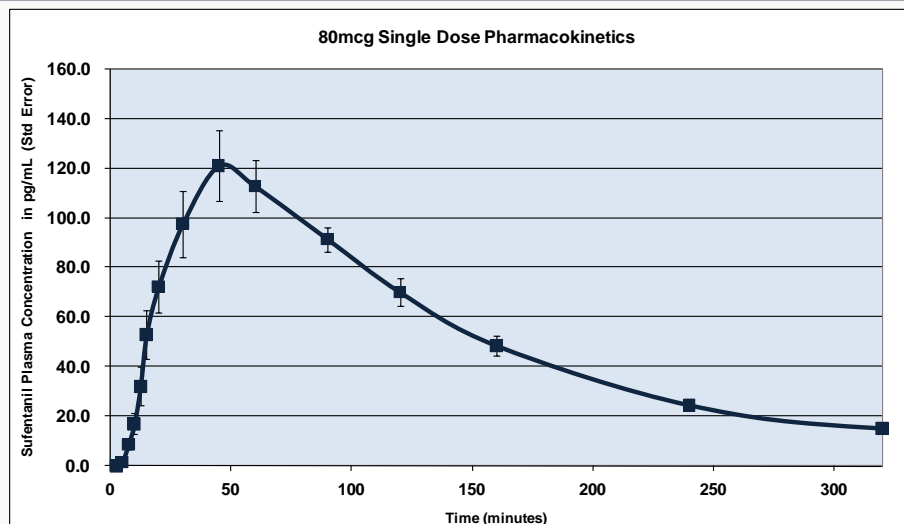
Low GI uptake = Consistent T_{max}



NanoTab Oral Transmucosal Delivery: Turning Sufentanil AUC on its Side



Sufentanil NanoTab™ 80 mcg Dose



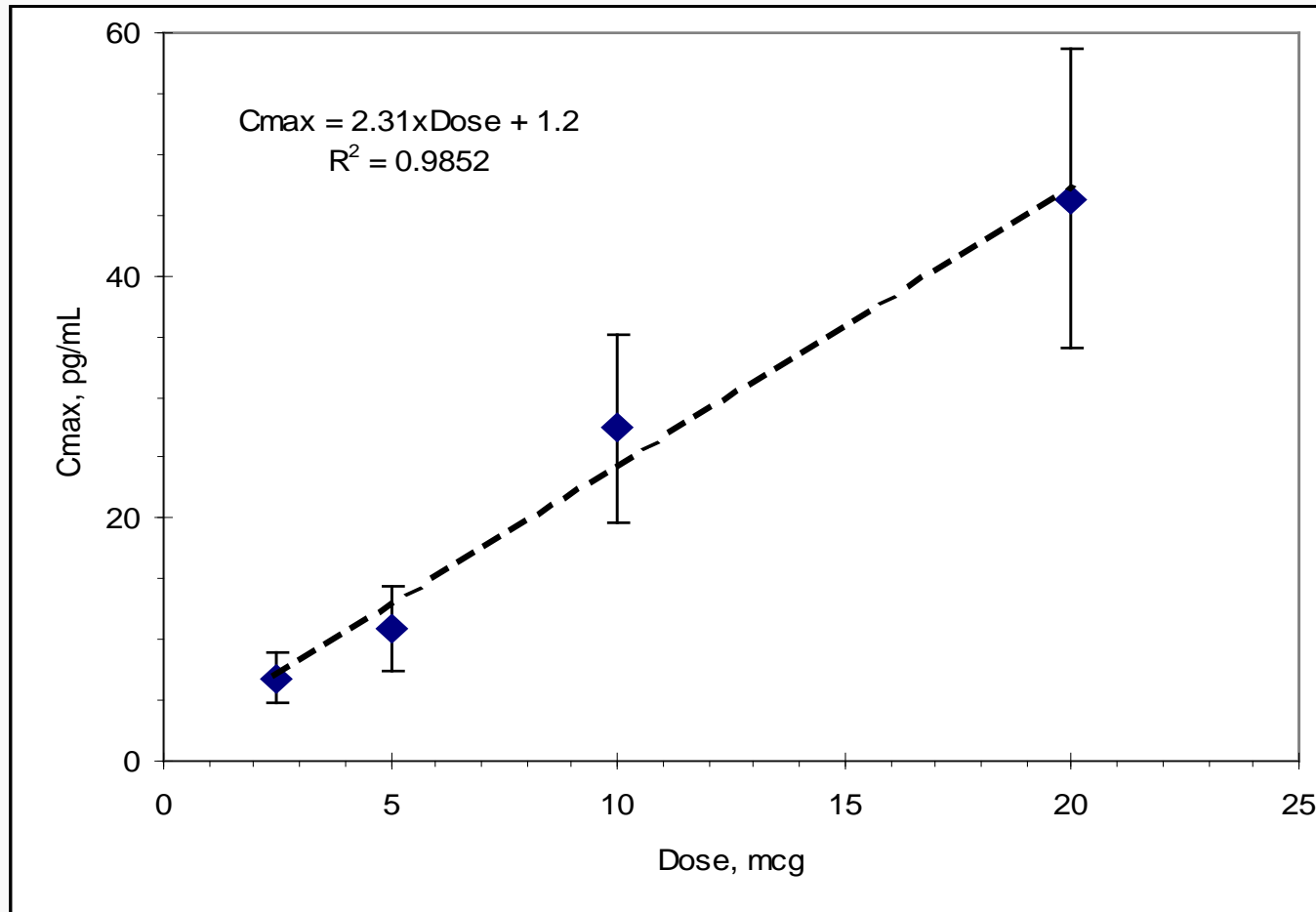
	ARX-02 80 mcg	Fentora 400 mcg	Actiq 400 mcg	Onsolis 800 mcg	Abstral/Rapinyl** dose not specified
Active Ingredient	Sufentanil	Fentanyl	Fentanyl	Fentanyl	Fentanyl
Mean T_{max} in minutes (range)	53 (30 – 90)	47 (20 - 240)	91* (35 - 240)	60 (45 – 240)	57*** (22 - 240)
t_{1/2} in hours (range) (coefficient of variation)	4.23 (2.89 – 5.79) (21%)	11.09 (4.63 - 20.59) (not specified)	6.43 (not specified) (115%)	14 (not specified) (not specified)	~20 (11.5 - 25) (not specified)

*Actiq T_{max} data was dose adjusted (800 mcg to 400 mcg) per Fentora Package Insert Table 1

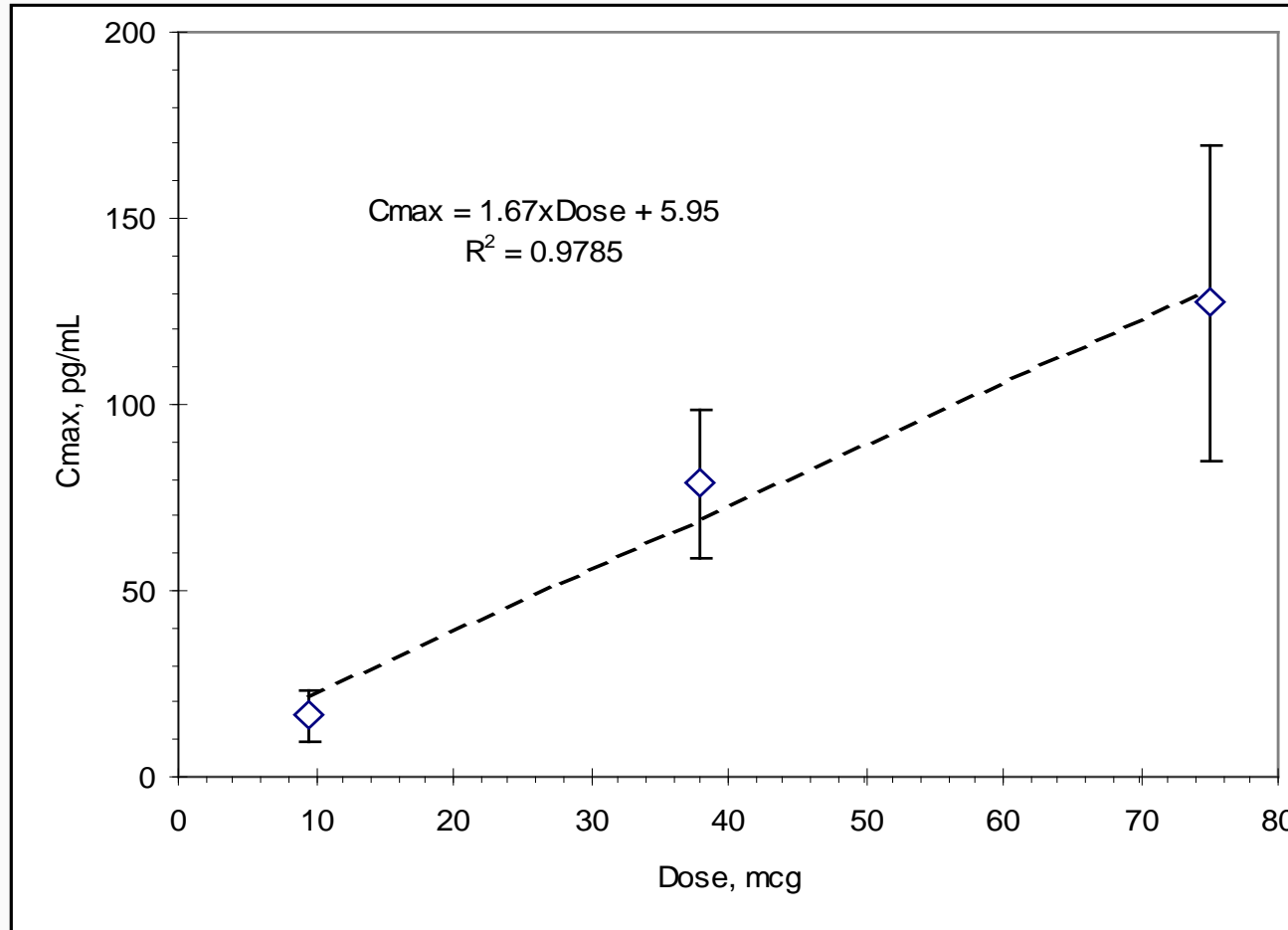
**Data (except T_{max}, see below) taken from EMEA document describing product characteristics and package labeling http://www.emea.europa.eu/pdfs/human/referral/rapinyl/rapinyl_annexl_IV_en.pdf

***T_{max} taken from Lennernas, B. Br J Clin Pharm, 2004. 59:2; 249-253, 400 mcg dose; range from EMEA reference above

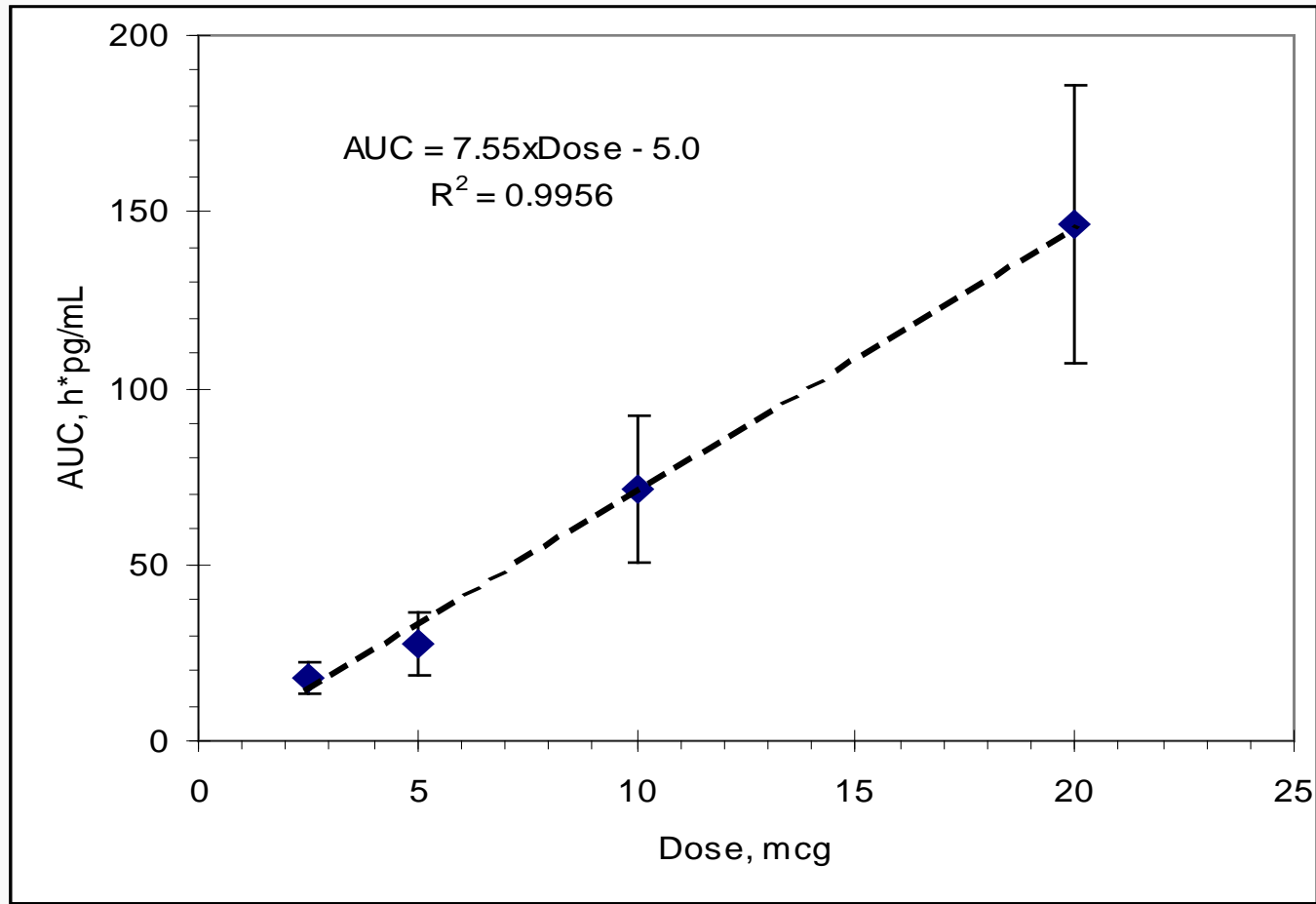
Mean (\pm SD) C_{\max} of Sufentanil vs. Dose



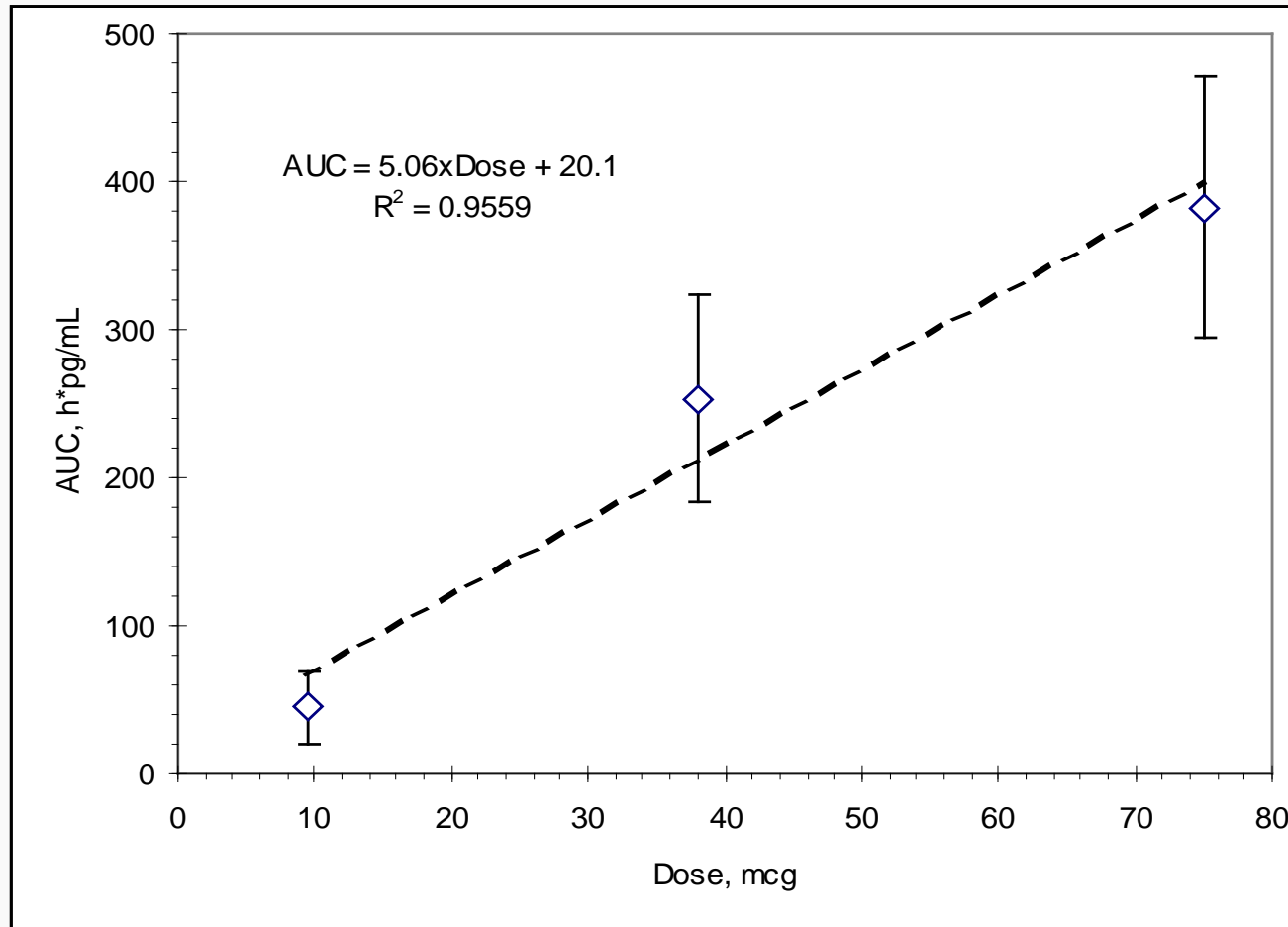
Mean (\pm SD) C_{\max} of Sufentanil vs. Dose



Mean (\pm SD) AUC_{inf} of Sufentanil vs. Dose



Mean (\pm SD) AUC_{inf} of Sufentanil vs. Dose



Sublingual Sufentanil NanoTab™

- First transmucosal formulation of sufentanil
- Highly consistent C_{\max} and T_{\max} – avoids dose stacking
- Shorter half-life than fentanyl products – allows more titratability in the treatment of acute pain episodes
- Small NanoTab™ size allows for compact Smart Dispensers to monitor dosing in both inpatient and outpatient settings

Thank You