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**Fentanyl Pectin Nasal Spray Provides
Clinically Meaningful Pain Relief and a
More Rapid Onset of Analgesia Compared with
Immediate-Release Morphine Sulphate in
Breakthrough Cancer Pain**

M. Fallon, A. Gatti, A. Davies, E. A. Lux,
K. Kumar, R. Galvez, on behalf of the
Fentanyl Nasal Spray Study 044 Investigators Group

Breakthrough Cancer Pain (BTCP)

- BTCP affects 60%–95% of all cancer patients with pain¹⁻³
- Although variable, a typical BTCP episode is rapid in onset (median onset to peak pain intensity [PI], 1-3 minutes) and short-lived (median duration, 30-45 minutes)^{1,3}
- Oral immediate-release morphine sulphate (IRMS) is the most common treatment for BTCP. However, its time to effectiveness can be too slow (≥ 30 minutes) to be consistent with the profile of a typical BTCP episode^{4,5}
- Shortening the time to meaningful pain relief, delivering consistent efficacy, optimising patient acceptability and tolerability are likely to improve treatment outcomes

1. Portenoy RK, Hagen NA. *Pain*. 1990;41:273-281.

2. Svendsen KB et al. *Eur J Pain*. 2005;9:195-206.

3. Portenoy RK et al. *J Opioid Manage*. In press.

4. Zeppetella G. *Eur J Cancer Care*. 2009;18:331-337.

5. Collins et al. *J Pain Manage*. 1998;16:388-402.

Optimising BTCP Management

- Conventional nasal products are convenient as simple aqueous solutions delivered as sprays but may not be the most appropriate solution given potential problems with nasal drip and unpredictable drainage from the nose, which may also impact consistency of dosing¹
- Fentanyl pectin nasal spray (FPNS) has been developed with PecSys[®] delivery technology to produce a rapid but controlled delivery of fentanyl across the nasal mucosa¹
- FPNS has been shown to have a rapid onset of effect in BTCP (5 minutes), provide clinically meaningful pain relief (10 minutes) and have consistent efficacy in FPNS-treated episodes compared with placebo²

1. Watts P, Smith A. *Expert Opin Drug Deliv.* 2009;6:543-552.

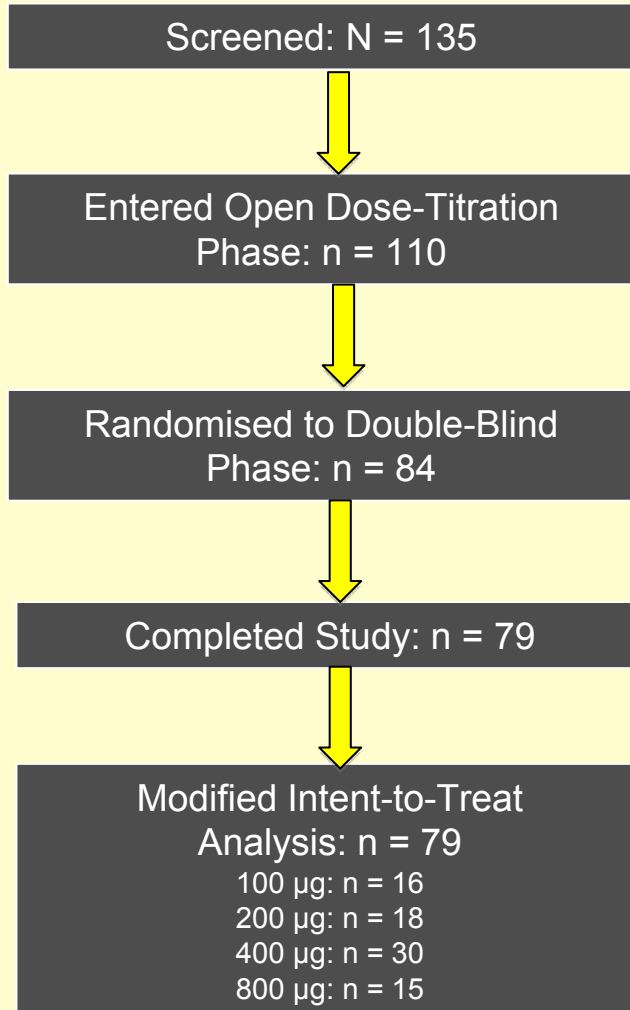
2. Portenoy RK et al. *Pain.* Manuscript submitted.

FPNS versus IRMS

Double-blind, double-dummy, randomised controlled trial

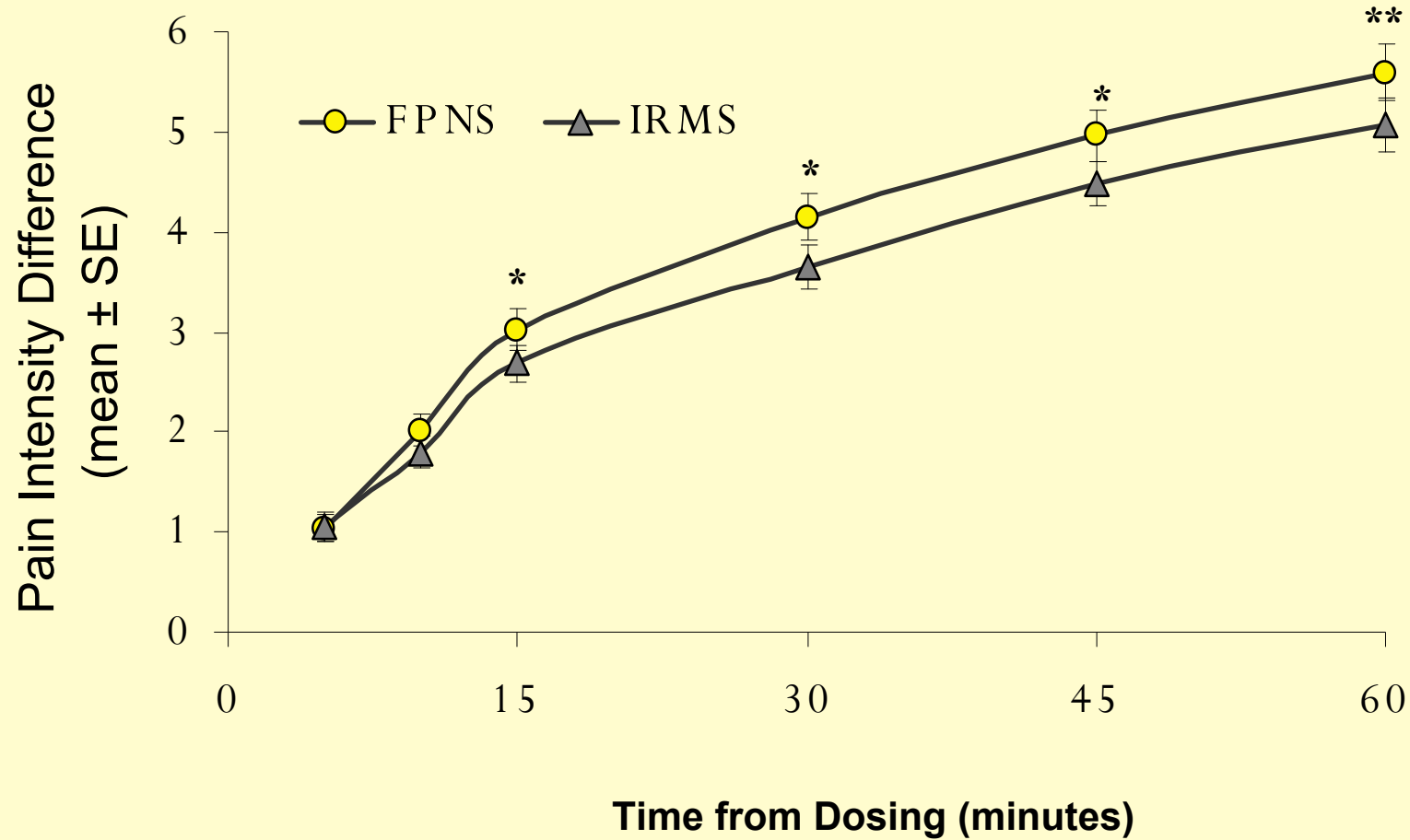
- Primary objective
 - To demonstrate the superior efficacy of FPNS (100–800 µg) compared with IRMS in the treatment of BTCP in opioid-tolerant cancer subjects
 - o Primary clinical end point: pain intensity difference at 15 minutes (PID15)
- Secondary objectives
 - To demonstrate the onset of action, time to clinically meaningful PR, acceptability, safety and tolerability of FPNS compared with IRMS
 - o Secondary efficacy end points: PI, PID, summed PID, PR
 - o Patient acceptability and satisfaction
 - o Adverse events (AEs)
 - o Tolerability profile

Patient Disposition



- 76% successfully titrated
- Demographics
 - Mean age (\pm SD): 55.9 \pm 12.3
 - 53.8% male; 46.2% female
- 94% completed the double-blind phase of the study
- Only 4.7% of patients withdrew from titration (2.4% in DB/DD phase) due to AEs and 5.5% due to lack of efficacy
- 740 BTCP episodes were analysed (372 treated with FPNS, 368 treated with IRMS)

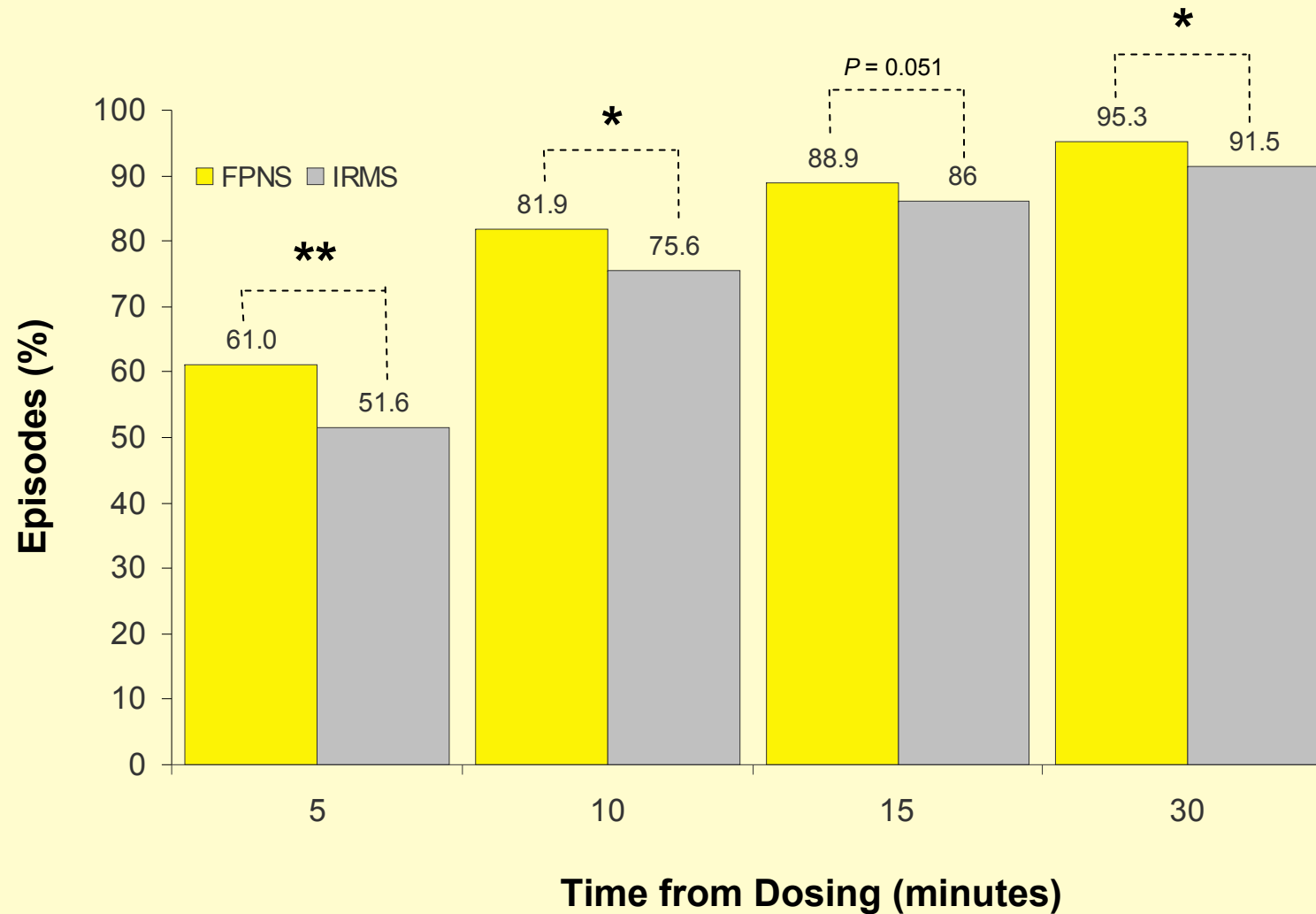
Primary End Point: PID15



* $P < 0.05$, FPNS vs. IRMS.

** $P < 0.01$, FPNS vs. IRMS.

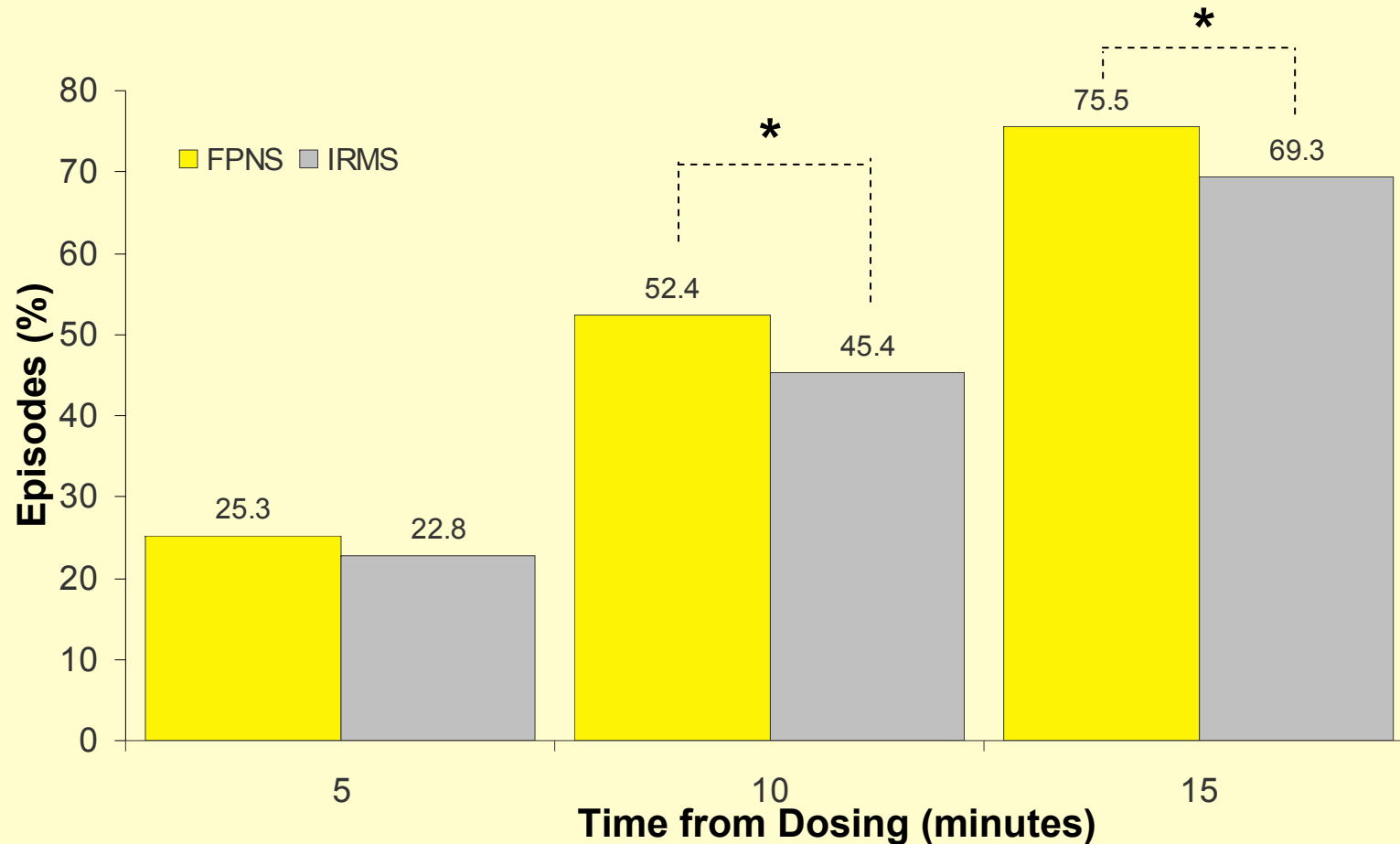
Onset of Pain Improvement (≥ 1 -point change in PR)



* $P < 0.05$, FPNS vs. IRMS.

** $P < 0.001$, FPNS vs. IRMS.

Episodes with Clinically Meaningful PR (≥ 2 -Point Reduction in PI¹)



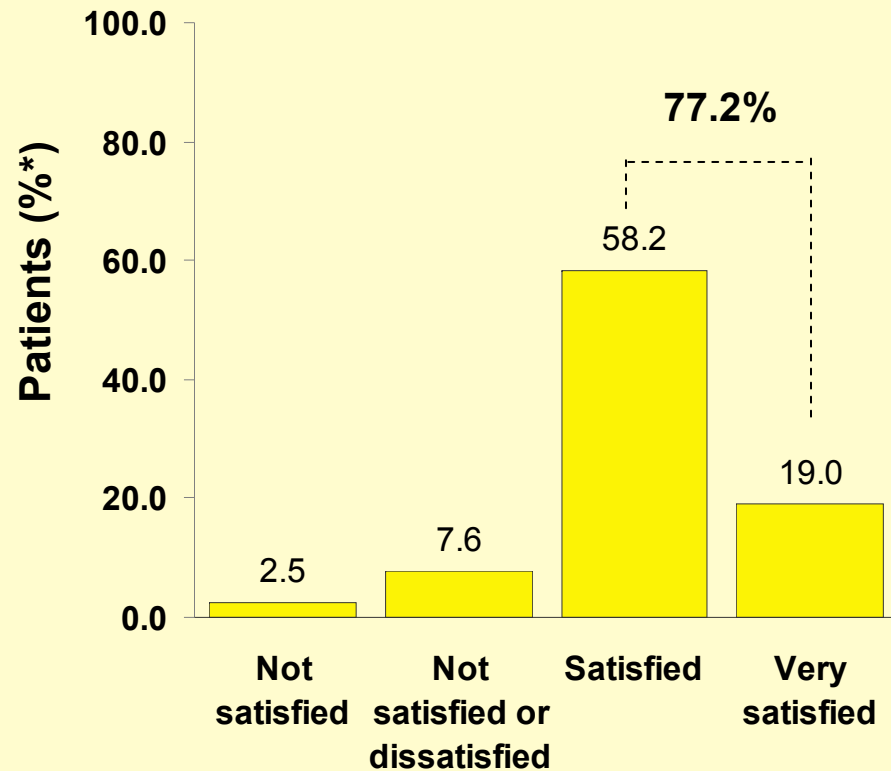
* $P < 0.05$, FPNS vs. IRMS.

1. Farrar JT et al. *J Pain Symptom Manage*. 2003;25:406-411.

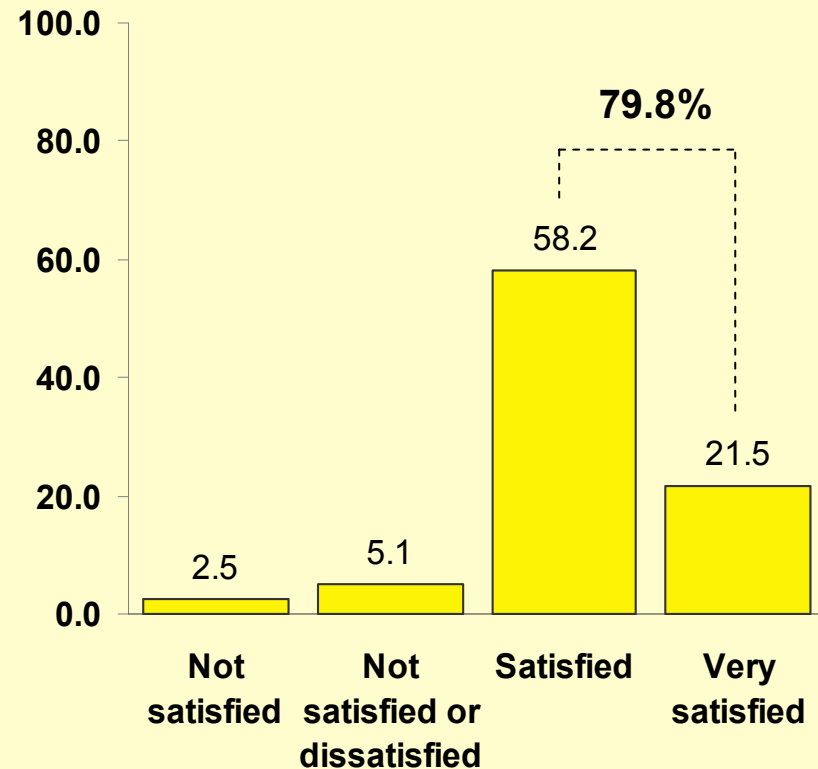


Satisfaction with Nasal Spray

Ease of Use



Convenience



*Missing values: 12.7%.

Acceptability with FPNS

- Higher rating of **overall satisfaction** with FPNS compared with IRMS
 - 30 minutes: 2.9 vs. 2.6, $P < 0.01$
 - 60 minutes: 3.0 vs. 2.7, $P = 0.01$
- Higher rating of **speed of relief** with FPNS compared with IRMS
 - 30 minutes: 2.9 vs. 2.6, $P < 0.01$
 - 60 minutes: 3.0 vs. 2.7, $P < 0.01$
- Higher rating of **reliability** with FPNS compared with IRMS
 - 3.0 vs. 2.7, $P = 0.01$

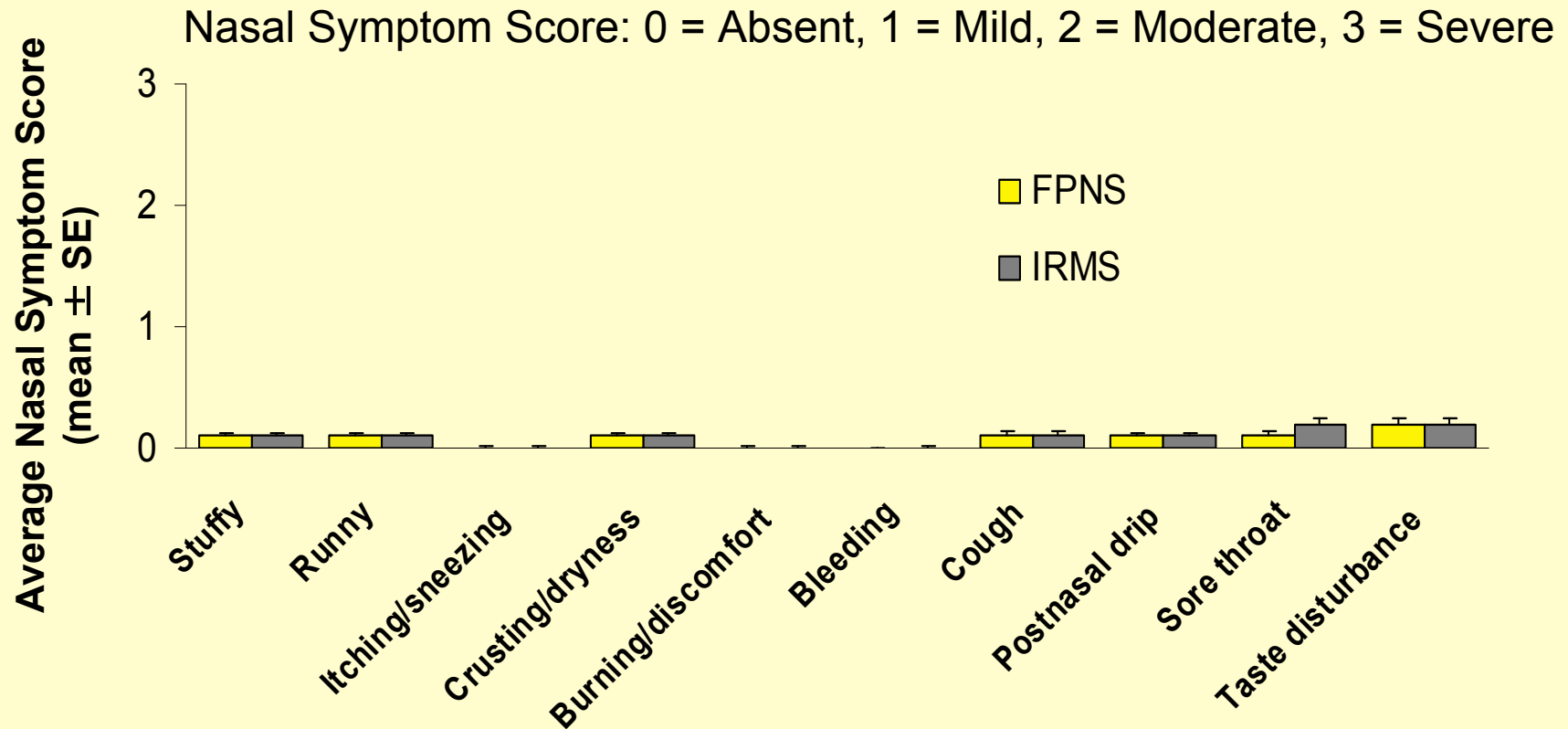
Treatment-Related Adverse Events by Severity (all phases, by patient)

Severity	FPNS, n (%)					IRMS n = 80 n (%)
	100 µg n = 105	200 µg n = 82	400 µg n = 60	800 µg n = 23	All n = 106	
Mild	8 (7.6)	6 (7.3)	5 (8.3)	1 (4.3)	14 (13.2)	0 (0)
Moderate	0 (0)	3 (3.7)	3 (5.0)	2 (8.7)	8 (7.5)	0 (0)
Severe	0 (0)	0 (0)	2 (3.3)	1 (4.3)	2 (1.9)	0 (0)
Total	8 (7.6)	9 (11.0)	10 (16.7)	4 (17.4)	24 (22.6)	0 (0)

Treatment-related adverse events

- Typical of opioids
- More frequent with FPNS
- Mainly mild to moderate
- Not dose related

Nasal Tolerability



Average nasal symptom score was assessed at 60 minutes after dosing for each episode during the double-blind period. Patients completed a nasal symptom score for 10 symptoms as follows: 0 = absent, 1 = mild, 2 = moderate and 3 = severe. The nasal symptom score was averaged over all episodes treated during the double-blind treatment phase.

Summary and Conclusions

- First clinical study to show the superiority of a new-generation fentanyl-based BTCP product over the most widely used standard treatment, IRMS
- Confirms and extends previous findings that FPNS provides rapid onset of action from as early as 5 minutes after dosing and early clinically meaningful levels of PR from 10 minutes after dosing
 - Significantly greater number of episodes showed improvement in PR scores within 5 minutes compared with IRMS
 - Significantly greater number of episodes treated with FPNS showed clinically meaningful PR (≥ 2 -point reduction in PI) by 10 minutes compared with episodes treated with IRMS

Summary and Conclusions (cont)

- FPNS had significantly higher acceptability and satisfaction scores than did IRMS at both 30 and 60 minutes
- FPNS was safe and well tolerated and resulted in no significant symptoms or clinical findings related to nasal administration
- In conclusion, this study demonstrates superior outcomes with FPNS compared with IRMS in the treatment of BTCP that better match the rapid onset and relatively short duration of the typical BTCP episode