

Nasal Delivery of Sumatriptan Powder with a Novel Bi-Directional Device is Highly Effective in Treating a Single Migraine Attack

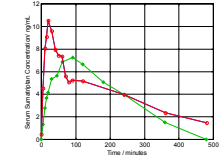
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Background

A Phase I study with the novel nasal powder bi-directional delivery device delivering sumatriptan powder showed excellent results.

Mean PK curves for OptiNose 10 (7.5 mg) and Imitrex 10 mg

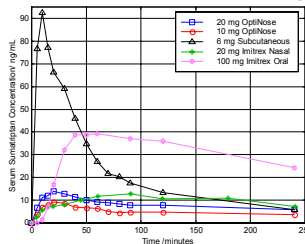


- Rapid absorption with t_{max} of 20 min compared to 90 min for Imitrex nasal spray.
- As effective as 6mg SC in preventing migraine attacks after GTN challenge.

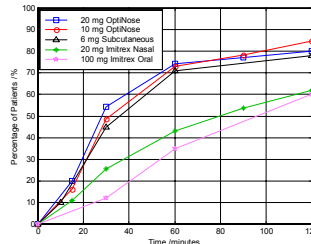
Luthringer R et al. AAN. Poster P07.039, April 2008

Highly effective: similar to SC with minimal systemic exposure and few side effects

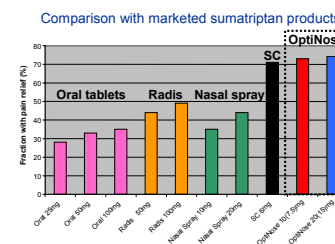
Pharmacokinetics of sumatriptan



Relief of Headache



Pain relief at 60 minutes



Fast and efficient pain relief

Relief of headache was greater for both doses compared with placebo from 60 minutes:

- 30 minutes (10 mg, 48.6% vs 31.3% NS; 20 mg, 54.3% vs 31.3% $p=0.0841$)
- 60 minutes (10 mg, 73.0% vs 37.5% $p<0.004$; 20mg, 74.3% vs 37.5% $p<0.004$)
- 90 minutes (10 mg, 78.4% vs 40.6% $p<0.003$; 20 mg, 77.1% vs 40.6% $p<0.003$)
- 120 minutes (10 mg, 83.8% vs 43.8% $p<0.0008$; 20mg, 80.0% vs 43.8% $p<0.003$)

Objectives

- To evaluate the efficacy, safety and tolerability of intranasal sumatriptan succinate powder at doses of 10 and 20 mg administered by a new bi-directional delivery system during a single migraine episode.

Methods

- Double-blind, parallel group Phase II study
- Ten centers in the Czech Republic.
- Migraine patients with or without aura (18-65 years $n=117$) were randomized (1:1:1) to receive treatment of a single migraine episode of moderate or severe intensity:
 1. 10mg (single dose to side of migraine)
 2. 20mg (administration to each nostril)
 3. Placebo (migraine side or both sides)

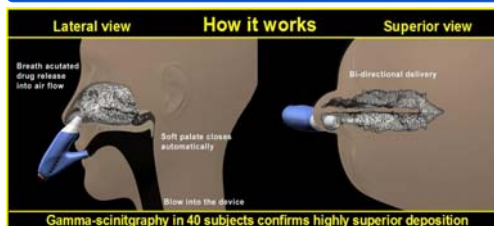
A high proportion of patients pain-free at 2 hrs and sustained pain-free at 48 hours

Pain-free A significantly greater proportion of subjects in both the 10mg (54.1%, $p=0.0261$) and 20mg (57.1%, $p=0.0127$) groups were pain-free at 120 minutes compared with placebo (25%). A significantly greater proportion of patients

were **sustained pain-free** up to 48 hours (10 mg 47.4%, $p=0.05$), 20 mg (48.6%, $p<0.05$), placebo (21.9%).

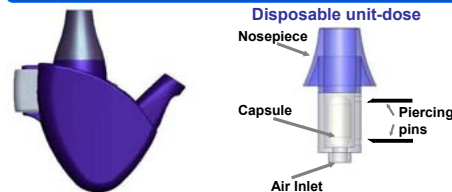
Significant improvements in functional disability compared with placebo. (90 minutes:10 mg $p<0.02$; 20 mg $p<0.02$ and 120 minutes:10 mg $p<0.02$; 20 mg $p<0.004$).

Bi-directional nasal delivery



Bi-directional nasal devices improve delivery to the highly vascularized respiratory mucosa beyond the nasal valve.

OptiNose powder delivery device



Emitted dose from each capsule is $\approx 75\%$ of the nominal filled dose of 10mg. The actual mean delivered doses are $\approx 7.5\text{mg}$ and $\approx 15\text{mg}$ for the nominal 10 and 20mg doses respectively.

Treatment very well tolerated

Both sumatriptan doses were well tolerated with no withdrawals due to adverse events.

A bitter or metallic taste was reported by only 4 (10.3%) and 5 subjects (12.8%) in the 10 mg and 20 mg groups, respectively.

Conclusions

- OptiNose delivery of nasal sumatriptan powder provides rapid and highly effective treatment of a single migraine attack.
- The fraction of patients pain-free and with pain relief is higher than marketed oral and nasal formulations and similar to SC injection.
- Direct effects via the trigeminal nerve have been suggested as a possible mechanism of action.

References

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