Intranasal Sumatriptan Powder Delivered with a New Device is as Effective as 6 mg SC Sumatriptan in Preventing Glyceryltrinitrate (GTN) Challenge Induced EEG Changes in Migraineurs

ng'mL

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Background

Current nasal delivery devices are suboptimal in reaching target sites beyond nasal valve1

DtNose

- > Nasal sprays deliver predominantly to the non-ciliated anterior region where it is readily sniffed along the nasal floor and swallowed
- > The bi-directional OptiNose nasal devices improves delivery to the highly vascularized respiratory mucosa beyond the nasal valve²
- > GTN challenge induces migraine attack in 75% of patients in absence of pretreatment³

Objectives

- >To compare, by quantified wake EEG (qEEG), effects of IN sumatriptan succinate delivered using the OptiNose powder delivery device with SC sumatriptan on GTN-induced migraine
- > To compare the pharmacokinetics (PK) and tolerability of IN and SC sumatriptan.

Study design

- > 12 patients with moderate or severe migraine without aura
- > Controlled, randomized 3-way cross-over study.
- Pretreatment with SC sumatriptan (6mg) and IN 10mg and 20mg (2 x 10mg) delivered 15 minutes before the GTN-challenge (0.9mg sublingual)
- Assessment of pharmacokinetics, quantitative wake EEG (gEEG) and migraine/pain scores



Capsule

delivered doses are ≈7,5mg and ≈15mg

Air Inlet

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6 mg Subcutaneou 20 mg OptiNose 10 mg OptiNose 100 90 20 (15) mg 6mg sumatriptan 80 10 (7.5) mg sumatriptan sumatriptan 70 intranasal intranasa SC 964+254 60 Cmax 108 ± 71 Tmax* (Median)(min) 20 20 10 50 AUC_{Ber} (Mean±SD)(ng/mL) 2219.9±1605.2 2888.2±946.9 6400.1±1823.8 40 30 20 Graph is showing Mean ± SEM 100 1 Time /minutes 150 No migraine attacks occurred

Results - Pharmacokinetics

Sumatriptan powder delivered with the OptiNose device is as efficient as 6mg SC in preventing migraine attacks in migraineurs receiving GTN challenge despite much lower bioavailability

Much faster absorption than Imitrex IN



Similar qEEG-profile for IN sumatriptan powder and 6mg SC in patients receiving GTN challenge EEG - Median maps - Relative Energy Per Protocol Population INP : sumatriptan intranasal powder)-10 10- 20- 30- 40- 50-in 20 30 40 50 60 ain ain ain ain ain Time Point. line Theta (%) 20 mg N=11 IN 20 mg Theta (%) 10 ng N=1; IN 10 mg Theta (4) SC 6mg a.c. 6 mg N-12

Results - Median gEEG maps

Conclusions

- > IN sumatriptan powder is safe and well tolerated. No reports of bad aftertaste
- > IN sumatriptan powder delivered with the OptiNose device is much faster absorbed from the nose than marketed nasal product
- > As effective as SC in preventing migraine attacks after GTN challenge
- Mean gEEG changes for OptiNose IN Sumatriptan powder are similar to SC
- Results support that CNS effects correlates with the rate, not extent, of drug absorption⁶
- Phase II results will be available in 2008

References

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