

PHARMACOKINETIC PROFILE OF SUMATRIPTAN RT TECHNOLOGY™ AND NAPROXEN SODIUM—NEW SINGLE-TABLET FORMULATION

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OBJECTIVE

Evaluate the PK of sumatriptan formulated with RT Technology™ (SumaRT) 85mg and naproxen sodium 500mg given as a single-tablet formulation (SumaRT/Nap).

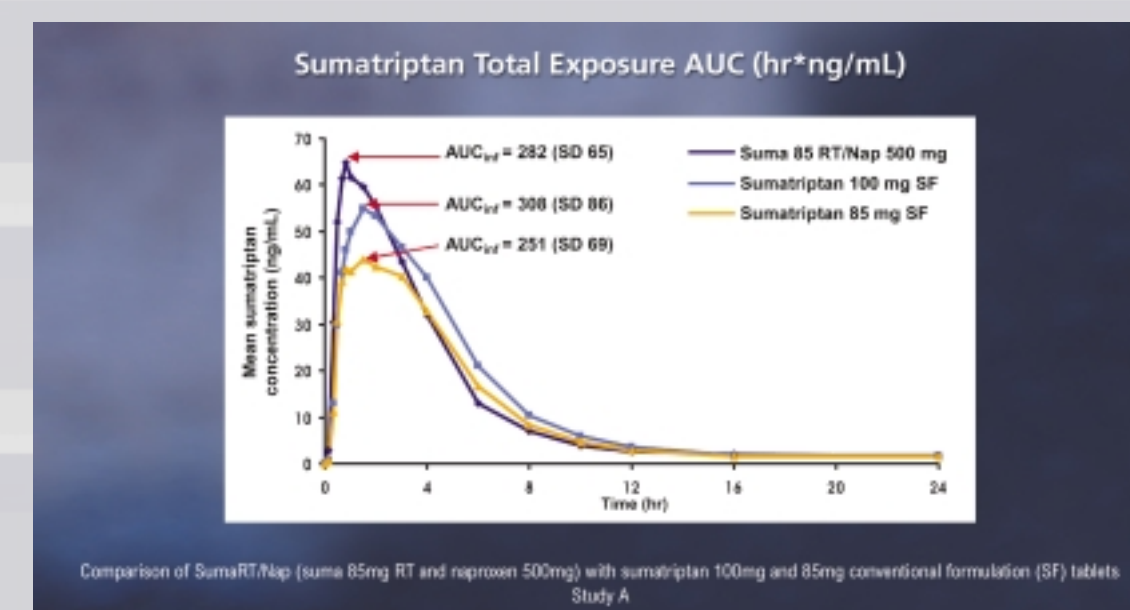
BACKGROUND

Targeting multiple sites of action in the migraine cascade has not been studied in prospective trials. Mechanistic and clinical data support early intervention with triptans to improve outcomes (Levy et al, *PNAS* 2004; Winner et al, *Mayo Clin Proc* 2003). RT Technology improves dissolution, gastric emptying, and early absorption of oral sumatriptan (Walls et al, *Curr Med Res Opin* 2004). Combining multimechanism therapy with RT Technology may improve therapeutic benefit in patients with migraine.

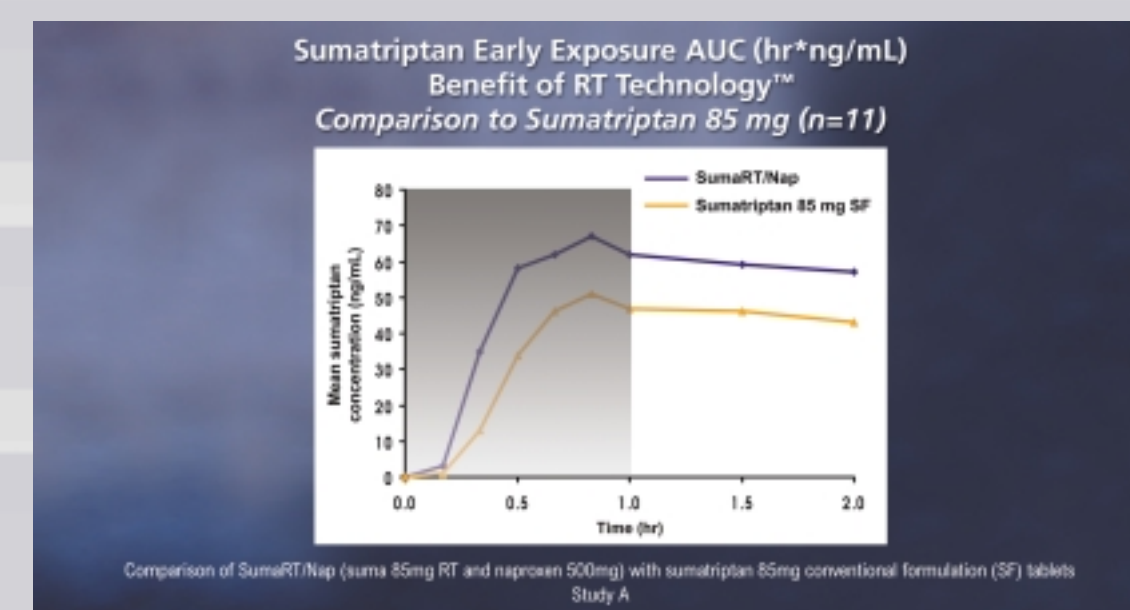
METHODS

Two separate randomized, single center, open-label, incomplete block, 3-way crossover studies were conducted in healthy volunteers. Study A included 5 groups (n=24): SumaRT/Nap (single tablet), sumatriptan 85mg non-RT, sumatriptan 100mg non-RT, commercial naproxen sodium 550mg, and naproxen sodium 500mg. Study B included 4 groups (n=29): SumaRT/Nap, SumaRT 85mg plus naproxen sodium 500mg (2 tablets), sumatriptan non-RT 85mg plus naproxen sodium 500mg (2 tablets), and sumatriptan non-RT 50mg plus naproxen sodium 500mg (2 tablets).

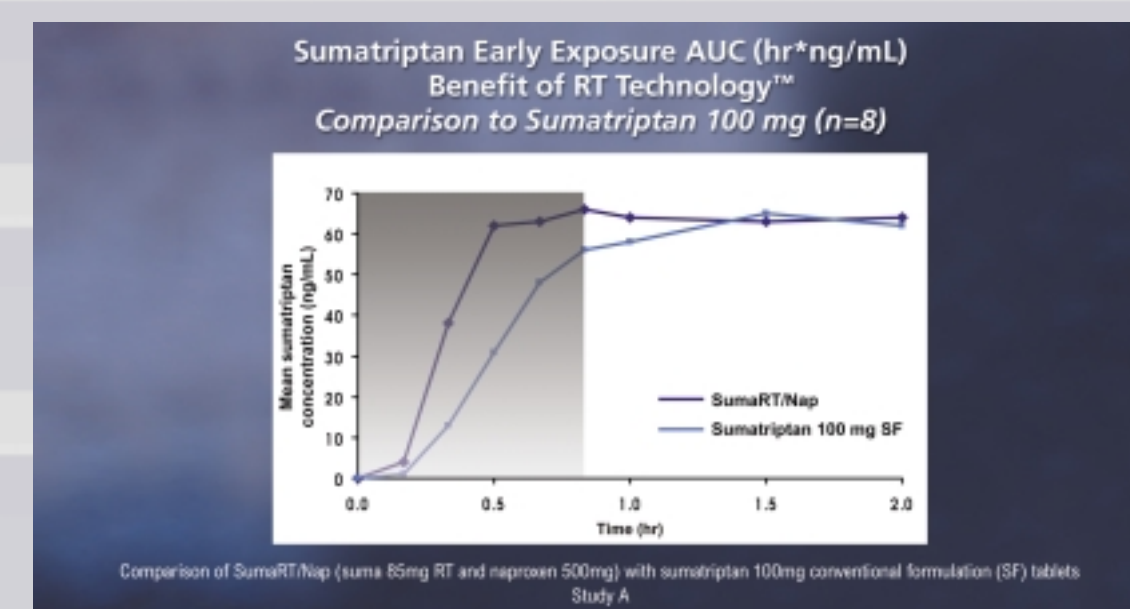
RESULTS FOR SUMATRIPTAN



- Overall exposure of sumatriptan (AUC_{0-inf}) was similar among the treatment groups.
- C_{max} values are within the range of previously determined sumatriptan variability.

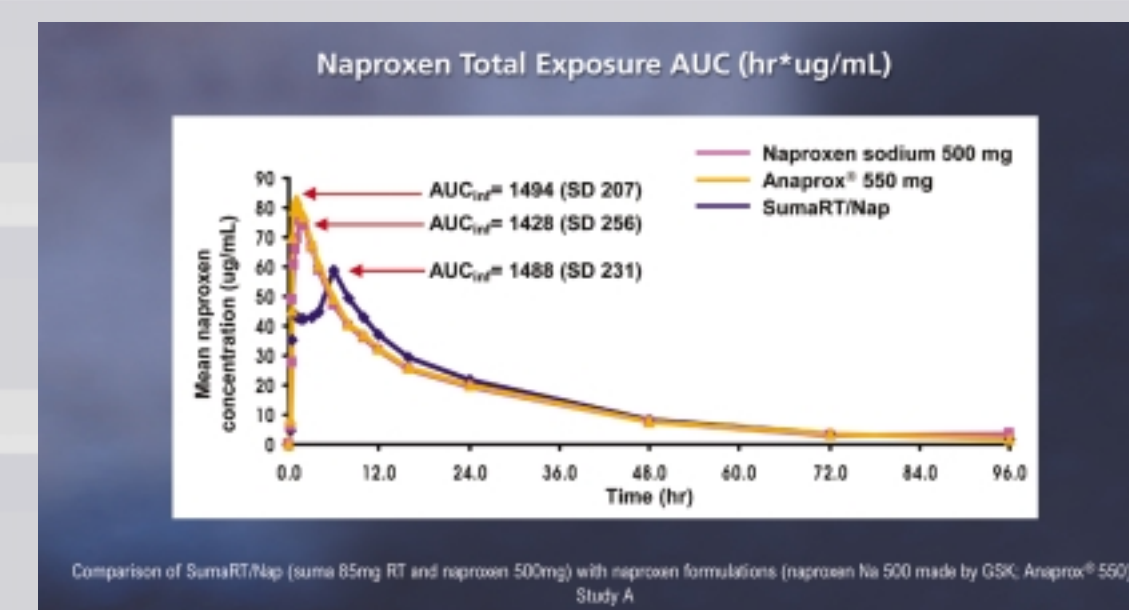


- AUC_{0-1hr} for sumatriptan given as SumaRT/Nap was 39.4 hr*ng/mL, which was 60% greater vs. sumatriptan non-RT 85mg (24.6 hr*ng/mL).

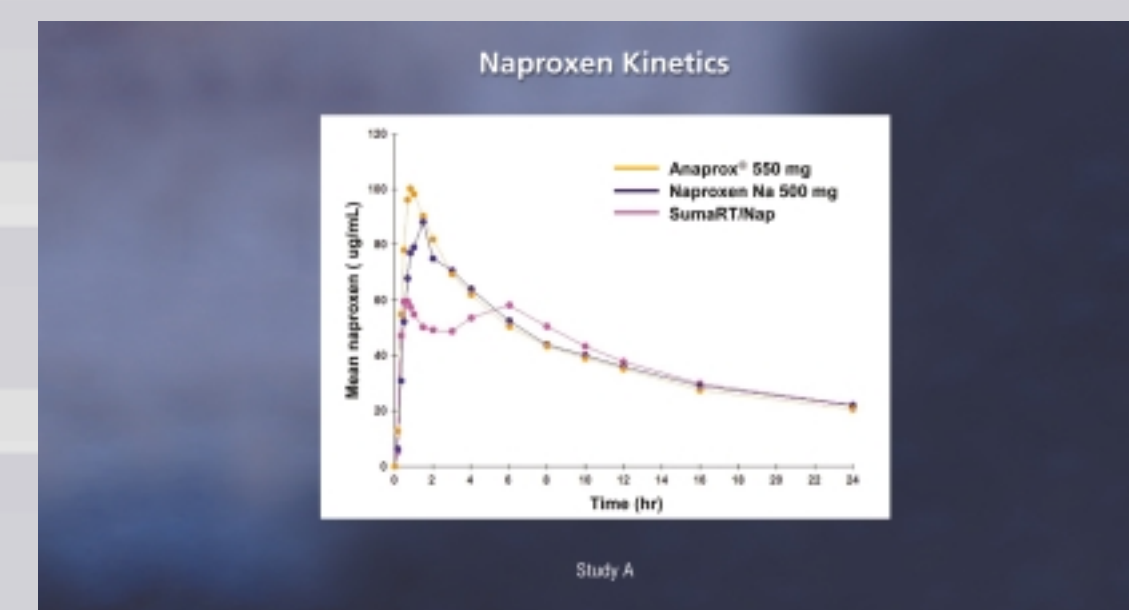


- AUC_{0-1hr} for SumaRT/Nap was 43.8 hr*ng/mL, which was 50% greater vs. sumatriptan non-RT 100mg (29.3 hr*ng/mL).
- As expected, AUC_{0-1hr} for SumaRT/Nap was 84% higher than sumatriptan 50mg non-RT plus naproxen (30.5 hr*ng/mL vs. 16.6 hr*ng/mL). (Study B)

RESULTS FOR NAPROXEN SODIUM



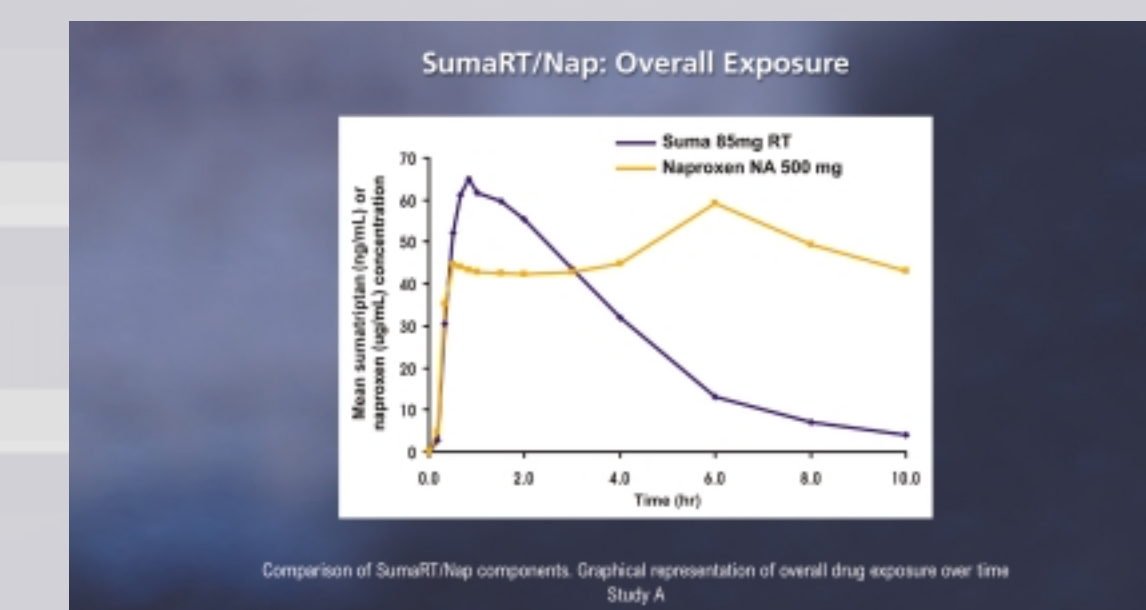
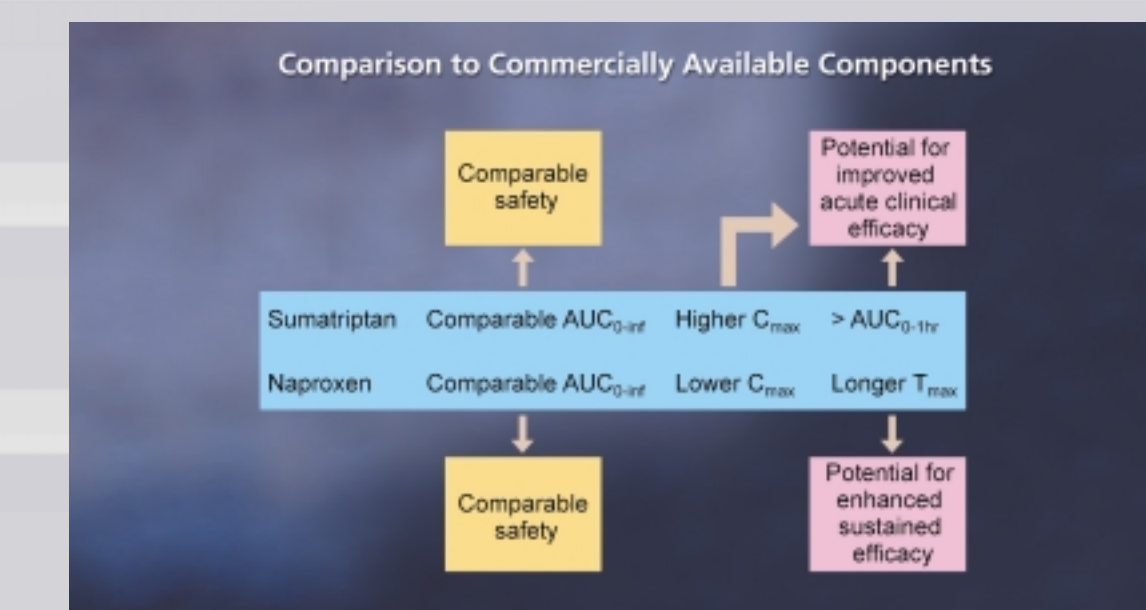
- Overall exposure of naproxen (AUC_{0-inf}) was similar among the treatment groups.



- There was a 36% decrease in the naproxen C_{max} given as SumaRT/Nap (69.7 ug/mL) vs. commercially available naproxen sodium 550mg (109.2 ug/mL).
- Similarly, there was a 28% decrease in naproxen C_{max} given as SumaRT/Nap (69.9 ug/mL) vs. naproxen sodium 500mg (95.4 ug/mL).

- The naproxen T_{max} after administration of SumaRT/Nap was delayed (median 6.0 hr) vs. commercially available naproxen sodium 550mg (median 1.0 hr) or naproxen sodium 500mg (median 0.92 hr). (Study A)
- There was a delay in naproxen T_{max} given as SumaRT/Nap (median 6.0 hr) vs. naproxen when administered as a two-tablet dose with sumatriptan 85mg RT and naproxen sodium 500mg. (Study B)

DISCUSSION



- RT Technology™ offers higher sumatriptan C_{max} and shorter T_{max} that may lead to more rapid onset of action and enhanced efficacy.
- Extended PK profile of naproxen may provide a mechanism for enhanced sustained efficacy based on its longer T_{max}.
- All treatments in both studies were well tolerated and no serious adverse events were reported.

CONCLUSIONS

These studies show that the new single-tablet SumaRT/Nap exhibits a consistent and reproducible, enhanced early absorption of sumatriptan as seen in previous reports. The extended absorption of naproxen was enhanced when taken together as single tablet vs. separate tablets. Sumatriptan has been previously reported to delay gastric emptying (Moro et al., *Dig Liver Dis* 2004), which may partially explain these findings. This suggests that the unique PK profile of a single-tablet SumaRT/Nap may lead to extended clinical benefits resulting in an improved sustained pain relief profile with a lower risk of recurrence.

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