

Newer Acute Migraine Specific Drugs May Provide Improved Sustained Relief and Freedom over 24 and 48 Hours Post Dosing

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INTRODUCTION

Migraine patients, in several surveys, have identified long-lasting relief without recurrences as a very important attribute for any acute migraine therapy. Many headache experts have advocated the inclusion of 2-24 hour sustained pain relief (SPR) and sustained pain freedom (SPF) as key end points in assessing the efficacy of acute migraine therapies. There is general consensus that the best way to compare the efficacy of different drugs in delivering the above results is to measure the Therapeutic Gain (TG), the difference between the rates for active drug and placebo, for the compounds studied. Several drugs in development claim to have better SPR compared to marketed drugs. Unfortunately TG for 2-24 hour and 2-48 hour sustained response or pain-free information is not available for many of the presently available acute migraine drugs. There are very few studies that attempt head to head comparisons of marketed drugs to emerging drugs.

During the period 2005-2007, at least four randomized, double-blind, controlled studies have been conducted and have reported TG for 2-24 hour sustained pain relief and pain-free rates. Even though these are not head to head comparisons, all these studies were conducted at about the same time, in similar geographical distribution, involving overlapping study centers potentially using same or similar patient population, similar study designs and study criteria. Three of these studies included triptans as active controls, thus also providing some actual head to head comparison data.

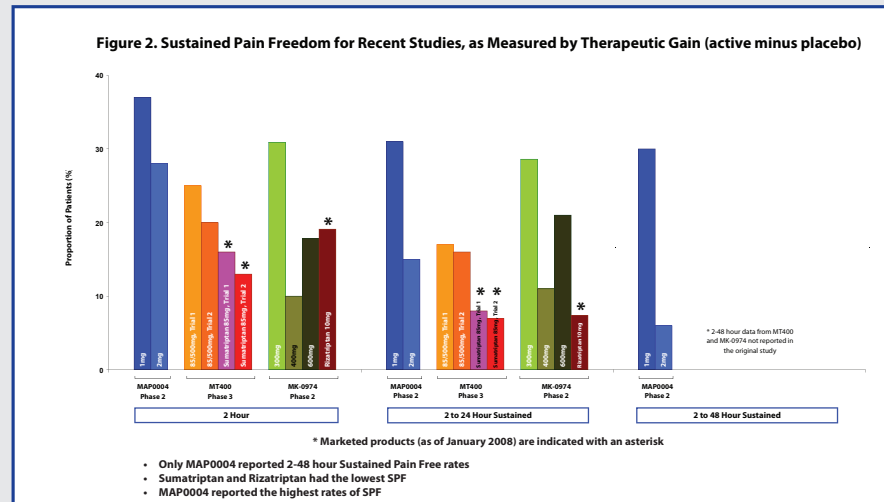
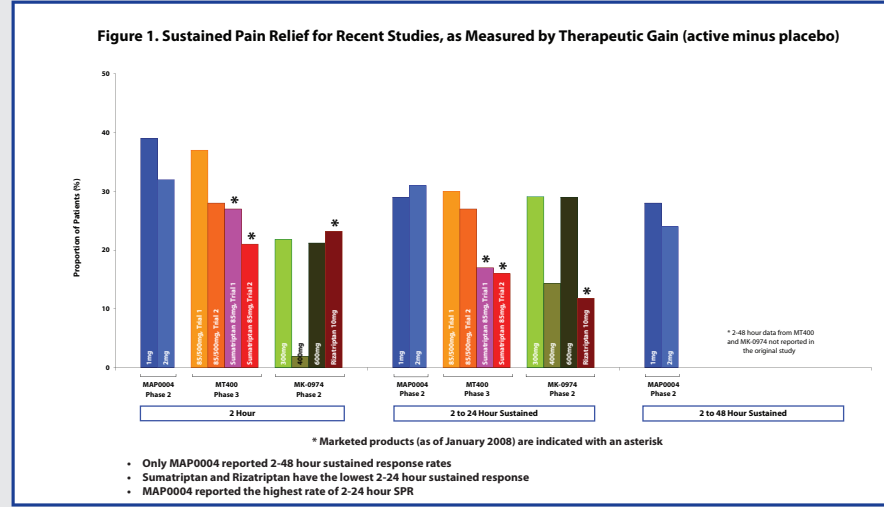
The present analysis was undertaken to compare the SPR and SPF results of eight different dosage forms of five acute migraine therapies.

METHODS

We compared SPR and freedom (SPF) responses of various drugs reported in four previously published randomized, placebo-controlled studies that were conducted contemporaneously, in similar geographies, with similar subject selection criteria and using similar study designs.

RESULTS

Four studies reported SPR and SPF rates for MAP0004, MT-400 sumatriptan/naproxen combination, MK-0974 CGRP inhibitor, sumatriptan and rizatriptan. **Figure 1** and **Figure 2** illustrate the Therapeutic Gains for the SPR and SPF data, respectively, that was reported from these recent studies.



RESULTS continued

The TG for 2-24hr SPF and SPR rates respectively were 31%, 29% for MAP0004 1 mg; 15%, 31% MAP0004 2 mg; 29%, 29% MK-0974 300 mg; 11%, 14% for MK-0974 400 mg; 21%, 29% MK-0974 600 mg; 17%, 30% suma/naproxen study 1; 16%, 27% suma/naproxen study 2; 8%, 17% sumatriptan study 1, 7%, 16% sumatriptan study 2; and 7%, 12% rizatriptan. The TG for 2-48hr SPF and SPR rates were 30%, 28% for MAP0004 1mg; 6%, 24% for MAP0004 2 mg; and were not reported for the other drugs.

DISCUSSION

Many clinicians and patients have observed that triptan therapy of acute migraine is limited by the high rate of recurrence of the headaches. Because there were no well controlled head to head studies in the past this could not be confirmed. In three studies included here newer acute migraine therapies MT400 and MK0974 were compared head to head with sumatriptan and rizatriptan, respectively. Both were clearly superior to the respective triptan in the 2-24 hour SPR and SPF. In a placebo-controlled study of similar design (but not head to head), MAP0004 appeared to deliver greater TG for SPR and SPF than that reported for the compounds in the above studies.

CONCLUSION

In analyzing data from four separate studies, each evaluating the efficacy of one compound and in three cases an active control, using similar patient selection criteria and similar study design, newer drug candidates MAP0004 and MK-0974 appeared to have greater TG for SPR and SPF end points compared to sumatriptan and rizatriptan. MAP0004 appeared to have 2-48hr SPF and SPR rates comparable to 2-24hr rates. These results need to be confirmed by direct head to head comparative studies.

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