A Comparative Trial of Zolmitriptan and Sumatriptan for the Acute Oral Treatment of Migraine

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Objective.–This randomized, double-blind, parallel group multicenter study compared response rates and tolerability of zolmitriptan with sumatriptan in the acute treatment of migraine.

Methods.–A sample consisting of 1445 outpatients with an established diagnosis of migraine was randomized to zolmitriptan, 2.5 mg or 5 mg, or sumatriptan, 25 mg or 50 mg. Patients took 1 tablet for moderate/severe migraine and a second identical tablet, if necessary, for recurrent headache of moderate/severe intensity 4 to 24 hours after the initial dose. Up to six attacks were treated during a 6-month period. The primary outcome measure was headache response 2 hours after the initial dose. Secondary end points included 1-hour and 4-hour headache response and pain relief over 24 hours.

Results.–A headache response at 2 hours was noted in 67.1% of patients taking zolmitriptan, 2.5 mg, and 64.8% of those taking zolmitriptan, 5 mg, versus 59.6% of patients taking sumatriptan, 25 mg, and 63.8% of those taking sumatriptan, 50 mg. At 2 and 4 hours, the differences between zolmitriptan, 2.5 mg, and sumatriptan, 25 mg, were statistically significant (odds ratio=1.49 and 1.67, respectively; both $P<.001$). Statistically significant differences between zolmitriptan, 2.5 mg, and sumatriptan, 50 mg, were seen at 2 and 4 hours post dose (odds ratio=1.21 and 1.23, respectively; both $P<.05$). At 1 hour post dose, the headache response rate for zolmitriptan, 2.5 mg, was numerically higher than response rates for sumatriptan, 25 mg and 50mg (odds ratio=1.16, odds ratio=1.06, though they failed to reach statistical significance; $P=.061$, $P=.461$ respectively). Differences between zolmitriptan, 5 mg, and sumatriptan, 25 mg, were statistically significant at 1, 2, and 4 hours (odds ratio=1.43, 1.46, and 1.78, respectively; all $P<.001$) and at 1 and 4 hours versus sumatriptan, 50 mg (odds ratio=1.28, $P=.002$; odds ratio=1.29, $P=.012$, respectively). Although not statistically significant at 2 hours, more patients responded to zolmitriptan, 5 mg, than to sumatriptan, 50 mg (odds ratio=1.16, $P=.064$). Patients receiving zolmitriptan, 2.5 mg or 5 mg, achieved more pain relief over 24 hours than patients receiving sumatriptan, 25 mg (odds ratio=1.47, and 1.54 respectively, both $P<.001$) or sumatriptan, 50 mg (odds ratio=1.17, $P=.021$; odds ratio=1.22, $P=.005$, respectively). All treatments were well tolerated.

Conclusions.–Zolmitriptan, 2.5 mg and 5 mg, was at least as effective as sumatriptan, 25 mg or 50 mg, for all parameters studied. Zolmitriptan, 2.5 mg, was significantly more effective than sumatriptan, 50 mg, in terms of headache response at 2 and 4 hours. Patients taking zolmitriptan were significantly more likely to have pain relief over 24 hours than those taking sumatriptan.

Key words: headache, migraine, sumatriptan, zolmitriptan

Abbreviations: 5-HT serotonin, BP blood pressure, OR odds ratio

(*Headache* 2000;40:119-128)

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Accepted for publication August 13, 1999.

An estimated 10% to 15% of people worldwide suffer from migraine,[1] and more than 80% of these sufferers experience some disability directly related to their migraines.[2] The introduction of selective serotonin (5-HT) receptor agonists provided effective choices for treating acute migraine attacks. Sumatriptan (Imitrex), the first 5-$HT_{1B/1D}$-specific receptor agonist available for the acute treatment of migraine, was an improvement over the older antimigraine medications, such as ergotamine. Reported efficacy rates for oral sumatriptan, 50 mg, range from 54% (2 hours post dose) to 77% (4 hours post dose).[3–5] Experimental studies in animals, however, suggest that sumatriptan does not access the CNS unless the blood-brain barrier is disrupted experimentally, which is not the case for the newer generation of triptans.[6] Sites within the CNS may provide additional targets for antimigraine actions, such as the trigeminal nucleus caudalis.[7]

Zolmitriptan (Zomig), a relatively new 5-HT_1 receptor agonist, has a different pharmacological[7] and pharmacokinetic profile[8] from oral sumatriptan. Zolmitriptan has dual peripheral and central action and rapid absorption.[7,8] It has an oral bioavailability of approximately 40%[9] compared with 14% for oral sumatriptan.[10] Together, these characteristics offer the potential for additional clinical benefits for migraine sufferers. Sufferers seek rapid and effective pain relief, but they also seek a treatment that provides consistent efficacy, low headache recurrence, and minimal adverse events.[11,12] The central action and increased bioavailability of zolmitriptan may provide improved and more consistent clinical efficacy than sumatriptan, a rationale that underpinned the current study.[7,13]

The results of double-blind, placebo-controlled clinical trials of zolmitriptan show that when used to treat a single attack, 2-hour headache response rates for zolmitriptan, 2.5 mg, range from 62% to 65%,[14,15] rising to 85% in an open-label, long-term trial.[16]

Although the clinical effects of 5-HT agonists have been compared with placebo, there exists a continued need for comparative trials. To compare the relative response rates and assist clinicians in determining the most appropriate medication for their patients with migraine, zolmitriptan and sumatriptan were compared directly. The current study evaluates the headache response rate at 1, 2, and 4 hours in patients using either zolmitriptan or sumatriptan to treat up to six moderate/severe migraine attacks during a 6-month period. In addition, the study evaluated meaningful migraine relief 1, 2, and 4 hours after the first dose and pain relief over 24 hours in patients using zolmitriptan compared with sumatriptan.

METHODS

This was a randomized, double-blind, parallel design study comparing zolmitriptan, 2.5 mg and 5 mg, with sumatriptan, 25 mg and 50 mg. It was conducted on an outpatient basis with patients recruited from primary care offices, neurology offices, and research clinics in the United States. All patients provided written informed consent, and the study protocol was approved by the Institutional Review Board associated with the individual study centers.

Patients enrolled into the study had established diagnoses of migraine according to the criteria of the IHS[17] with a history of migraine attacks for at least 1 year. Women were asked to use a reliable method of contraception.

Patients were excluded from the study if they had evidence or history of ischemic heart disease, arrhythmia, or accessory conduction pathway disorders (eg, Wolff-Parkinson-White syndrome); hypertension (systolic BP $\geqslant$160 mm Hg or diastolic BP $\geqslant$95 mm Hg); or any condition that may have put them at increased risk on exposure to study medication or that may have interfered with efficacy or safety assessments. Patients with a history of basilar, ophthalmoplegic, or hemiplegic migraine; with nonmigraine headache for 10 or more days per month in the previous 6 months; or who were using monoamine oxidase inhibitors, methysergide, methylergonovine, fenfluramine, or dexfenfluramine were also excluded. Other exclusion criteria included drug or alcohol abuse, clinically abnormal laboratory results at screening, lactation, unacceptable adverse events (in the opinion of the investigator) following previous use of any 5-$HT_{1B/1D}$ receptor agonist, simultaneous participation in another clinical trial, or treatment with another investigational drug within 30 days before screening.

Once entered into the trial, patients used either zolmitriptan, 2.5 mg or 5 mg, or sumatriptan, 25 mg or 50 mg, to treat their first migraine. A second dose identical to the first was available to treat any recurrent migraine occurring 4 to 24 hours after the initial dose. Escape medications for the treatment of persistent headache (ie, a migraine that did not respond to study medication by 2 hours after treatment) were allowed no sooner than 2 hours after the last dose of study medication; nonsteroidal anti-inflammatory agents, analgesics, or sedatives were permitted, but acute antimigraine treatments such as sumatriptan, ergotamine, dihydroergotamine, and isometheptene were not permitted as escape medications.

Following treatment of the first migraine headache with randomized medication, patients returned to the center with a completed diary card and any unused medication. They were then given additional blinded medication identical to the treatment used for their first attack to treat the next migraine. This cycle was repeated for the treatment of six migraine attacks or until the study ended.

The primary efficacy end point was headache response 2 hours after initial treatment. Headache response was defined as a reduction in headache intensity from severe or moderate at baseline to mild or none at 1, 2, or 4 hours after treatment. The intensity of each migraine and the accompanying symptoms were recorded immediately before and 1, 2, and 4 hours after the initial dose. Recurrence was defined as a headache that initially responded to the first dose of trial medication by 4 hours and then recurred with moderate or severe intensity 4 to 24 hours after the first dose. The intensity of the headache recurrence was measured immediately before and 2 hours after treatment with the second dose.

The secondary end point of pain relief over 24 hours was assessed to provide a complete picture of migraine management following the initial dose. The categories for response were the following: full (patient had a headache response at 2 hours and maintained that response for 24 hours without having a recurrent headache or taking escape medication); partial (patient had a response at 2 hours and then had a recurrence or took escape medication); and none (patients with attacks of moderate-to-severe intensity who had no response to treatment at 2 hours). Pain relief over 24 hours provides a combined assessment of the proportion of patients with a full response and the proportion of patients with a full or partial response. Sustained pain relief over 24 hours was a full response, as defined above.

Meaningful migraine relief, which encompasses all migraine symptoms, and overall treatment satisfaction (ie, excellent, good, fair, poor) were subjective assessments recorded by patients on diary cards. Consistency of response was defined as the percentage of patients responding in 80% or more treated attacks. Patients who reported that they achieved a headache response or meaningful migraine relief were included in the analysis only if no escape medication had been taken prior to the assessment.

STATISTICAL ANALYSIS

To be included in the statistical analysis, patients had to treat at least two headaches. Headache response rates, meaningful migraine relief, and sustained pain relief over 24 hours were analyzed using the generalized estimating equations (GEE) method for ordinal data with the logistic mean link in SAS. Pain relief over 24 hours was analyzed using GEE for ordinal data with the cumulative logistic mean link in SAS. Global rating of treatment satisfaction was analyzed the same way using SAS logistic regression. The effects of treatment, region (combination of centers), and individual baseline severity were included in all the models except for global rating of treatment satisfaction where individual baseline severity was not included because it was an overall evaluation over multiple attacks (up to six). Consistency of headache response was analyzed using the chi-square test. Estimated treatment odds ratios (ie, the ratio of the odds for the two treatment groups being compared), *P* values, and 95% confidence intervals were obtained. Odds ratios were tested at the 5% level of significance. Statistical significance was obtained when $P \leqslant .05$.

The following secondary parameters were not subject to formal statistical analysis because they were not based on the original randomized sample. However, descriptive statistics were provided. These

parameters were the following: data relating to the incidence of headache recurrence, time to recurrence, use of additional medication to treat recurrence, improvement in associated baseline headache symptoms, and incidence of adverse events.

The intent-to-treat population (ie, patients treating at least two headaches) was the primary focus of efficacy.

RESULTS

A total of 1445 patients with migraine were enrolled from 61 centers. Of these patients, 1212 treated at least two migraine attacks (intent-to-treat population) and 1043 completed the study (ie, they treated two to six migraine headaches or remained in the trial for 6 months). The intent-to-treat population treated a total of 6187 migraine attacks. Demographic characteristics were similar among the four treatment groups (Table 1).

Overall, a higher percentage of patients who received either dose of zolmitriptan had a headache response at 2 hours than those who received either dose of sumatriptan. In the zolmitriptan treatment groups, 67.1% of those receiving the 2.5-mg dose and 64.8% of those receiving the 5-mg dose reported a 2-hour headache response, compared with 59.6% of those receiving sumatriptan, 25 mg, and 63.8% of those receiving sumatriptan, 50 mg.

The differences in response rates between patients using zolmitriptan, 2.5 mg or 5 mg, and those using sumatriptan, 25 mg, were statistically significant at 2 hours ($P<.001$, both zolmitriptan doses). Furthermore, patients taking zolmitriptan, 2.5 mg, had a significantly higher response rate at 2 hours when compared with those taking sumatriptan, 50 mg ($P=.017$) (Table 2). More patients responded at 2

Table 1.–Demographics and Migraine Headache History

	Treatment Group			
	Zolmitriptan		Sumatriptan	
	2.5 mg	5 mg	25 mg	50 mg
Characteristic	(n=295)	(n=305)	(n=306)	(n=306)
Age, y				
Mean (SD)	39.9 (10.0)	40.2 (10.5)	39.6 (10.2)	40.6 (10.2)
Age distribution (%)				
⩾18–39 y	46.8	46.9	49.0	44.8
⩾40–65 y	53.2	53.1	51.0	55.2
Sex (%)				
Women	84.4	89.8	88.9	87.3
Men	15.6	10.2	11.1	12.7
Age at onset of migraine attacks, y				
Mean (SD)	21.2 (10.4)	22.3 (10.6)	21.4* (10.3)	21.4 (10.2)
Average no. attacks/month				
Mean (SD)	3.6 (1.3)	3.6 (1.3)	3.5 (1.4)	3.7 (1.5)
Type of migraine (%)				
With aura	17.0	18.7	19.6	16.0
Without aura	55.9	57.4	54.6	58.8
Both	27.1	23.9	25.8	25.2

*n=305.

Table 2.–Statistical Analysis of Headache Response and Meaningful Migraine Relief

		Analysis of Results					
		Headache Response			Meaningful Migraine Relief		
Treatment Comparison	Hours Post Treatment	Odds Ratio*	95% CI†	P Value‡	Odds Ratio*	95% CI†	P Value‡
Zolmitriptan 2.5 mg vs Sumatriptan 25 mg	1	1.16	0.99–1.36	.061	1.20	1.04–1.39	.014
	2	1.49	1.27–1.74	<.001	1.36	1.16–1.59	<.001
	4	1.67	1.38–2.02	<.001	1.61	1.34–1.95	<.001
Zolmitriptan 2.5 mg vs Sumatriptan 50 mg	1	1.06	0.91–1.24	.461	1.07	0.93–1.24	.325
	2	1.21	1.03–1.41	.017	1.23	1.05–1.45	.009
	4	1.23	1.01–1.50	.039	1.16	0.96–1.41	.129
Zolmitriptan 5 mg vs Sumatriptan 25 mg	1	1.43	1.22–1.68	<.001	1.35	1.17–1.56	<.001
	2	1.46	1.25–1.71	<.001	1.39	1.18–1.63	<.001
	4	1.78	1.47–2.16	<.001	1.74	1.44–2.11	<.001
Zolmitriptan 5 mg vs Sumatriptan 50 mg	1	1.28	1.09–1.35	.002	1.19	1.03–1.37	.017
	2	1.16	0.99–1.35	.064	1.25	1.07–1.48	.005
	4	1.29	1.06–1.58	.012	1.25	1.03–1.52	.026

*Odds ratio is the ratio of the odds for the 2 groups being compared: OR indicates odds of response with zolmitriptan divided by the odds of response with sumatriptan.
†CI=confidence interval of odds ratios.
‡Statistically significant at $P \leq .05$.

hours to zolmitriptan, 5 mg than to sumatriptan, 50 mg, although this failed to reach statistical significance (odds ratio [OR] =1.16, $P=.064$).

Patients taking zolmitriptan, 2.5 mg, had a significantly higher response rate at 4 hours (83.3%) compared with sumatriptan, 25 mg (75.8%; $P<.001$) and 50 mg (80.8%; $P=.039$) (Table 2). At 1 hour post dose, patients taking zolmitriptan, 2.5 mg, had a headache response rate of 35% compared with 32.9% for those taking sumatriptan, 25 mg ($P=.061$), and 34.7% for sumatriptan, 50 mg ($P=.461$). The differences in headache response rates were significant at 1 and 4 hours between zolmitriptan, 5 mg, and sumatriptan, 25 mg (37.4% versus 32.9% and 83.6% versus 75.8%, respectively; both $P<.001$), and between zolmitriptan, 5 mg, and sumatriptan, 50 mg, at 1 and 4 hours (37.4% versus 34.7%, $P=.002$ and 83.6% versus 80.8%, $P=.012$, respectively) (Table 2).

Overall, more patients in the zolmitriptan treatment groups reported meaningful migraine relief, a subjective assessment recorded by patients on diary cards, at 1, 2, and 4 hours (43.4%, 72.2%, and 82.3% for zolmitriptan, 2.5 mg, respectively; 45.5%, 72.2%, and 83.1% for zolmitriptan, 5 mg, respectively) than patients in the sumatriptan treatment groups (39.2%, 66.2%, and 74.5%, respectively, for sumatriptan, 25 mg; 41.7%, 67.9%, and 80.1%, respectively, for sumatriptan, 50 mg). Patients receiving zolmitriptan, 2.5 mg, were significantly more likely to achieve meaningful migraine relief at 1, 2, and 4 hours after treatment compared with those taking sumatriptan, 25 mg ($P=.014$ at 1 hour, $P<.001$ at 2 and 4 hours), and at 2 hours after treatment compared with those taking sumatriptan, 50 mg ($P=.009$) (Table 2). At 1 and 4 hours post dose, patients taking zolmitriptan, 2.5 mg, were at least as likely to have meaningful migraine

relief as those taking sumatriptan, 50 mg (OR=1.07, P=.325 at 1 hour; OR=1.16, P=.129 at 4 hours). Patients taking zolmitriptan, 5 mg, were significantly more likely to achieve meaningful migraine relief at 1, 2, and 4 hours compared with sumatriptan, 25 mg and 50 mg (P<.001 at all time points for zolmitriptan, 5 mg, versus sumatriptan, 25 mg; P=.017 at 1 hour, P=.005 at 2 hours, and P=.026 at 4 hours for zolmitriptan, 5 mg, versus sumatriptan, 50 mg) (Table 2). A summary of all statistical comparisons is given in Table 3.

Both the 2.5-mg and 5-mg doses of zolmitriptan provide significantly better pain relief over 24 hours for up to six attacks treated (67.1% and 64.8%, respectively, with a full or partial response) compared with sumatriptan, 25 mg (59.4%; OR=1.47 and 1.54, respectively; P<.001), or sumatriptan, 50 mg (63.8%; OR=1.17, P=.021; OR=1.22, P=.005 respectively). Pain relief over 24 hours is a composite measure that takes into consideration 2-hour headache response, subsequent headache recurrence, and use of escape medications for headache over 24 hours.

Zolmitriptan, 2.5 mg and 5 mg, provided significantly better sustained pain relief over 24 hours for up to six attacks treated (40.7% and 42.5%, respectively) compared with sumatriptan, 25 mg (33.1%; OR=1.46 and 1.67, respectively; both P<.001). Sustained pain relief for zolmitriptan, 2.5 mg, was numerically greater when compared with sumatriptan, 50 mg, although failing to reach statistical significance (40.7% versus 38.1%; OR=1.15, P=.071). Zolmitriptan, 5 mg, provided significantly better sustained relief over 24 hours for up to six attacks treated, compared with sumatriptan, 50 mg (42.5% versus 38.1%; OR=1.31, P<.001).

Both doses of zolmitriptan had greater apparent consistency of response and, therefore, potentially greater reliability over multiple attacks than either dose of sumatriptan. The percentage of patients who responded at 2 hours post dose in 80% to 100% of attacks (ie, consistency of response) was higher for zolmitriptan, 2.5 mg and 5 mg, compared with sumatriptan, 25 mg and 50 mg. The consistency of response was

Table 3.–Statistical Comparison of Zolmitriptan, 2.5 mg and 5 mg, With Sumatriptan, 25 mg and 50 mg Treatment Groups

	Statistical Comparison With Sumatriptan Treatment Groups (Significance for Zolmitriptan vs Sumatriptan)			
Assessment	2.5 mg Zolmitriptan vs 25 mg Sumatriptan	2.5 mg Zolmitriptan vs 50 mg Sumatriptan	5 mg Zolmitriptan vs 25 mg Sumatriptan	5 mg Zolmitriptan vs 50 mg Sumatriptan
Primary				
2-h headache response	‡	*	‡	A
Secondary				
1-h headache response	A	A	‡	†
4-h headache response	‡	*	‡	*
MMR at 1 h	*	A	‡	*
MMR at 2 h	‡	†	‡	†
MMR at 4 h	‡	A	‡	*
Pain relief over 24 h	‡	*	‡	†
Sustained (24-h) pain relief	‡	A	‡	†
Consistency of response in ⩾80% of attacks	‡	A	†	A
Global treatment satisfaction	†	A	†	A

A indicates zolmitriptan is at least as effective as sumatriptan (ie, response rate is at least as high or odds ratio ⩾1); and MMR, meaningful migraine relief.
*P⩽.05.
†P⩽.01.
‡P⩽.001.

significantly higher for zolmitriptan, 2.5 mg (47.1%), and zolmitriptan, 5 mg (44.3%), compared with sumatriptan, 25 mg (33%; $P<.001$ and $P=.004$, respectively). The proportion of patients who responded to 80% of attacks or more at 2 hours was numerically higher for zolmitriptan, 2.5 mg (47.1%), and zolmitriptan, 5 mg (44.3%), than for sumatriptan, 50 mg (39.2%), although failing to reach statistical significance ($P=.051$, $P=.206$, respectively) (Figure 1).

More patients rated their treatment as "good" or "excellent" than as "fair" or "poor" across all treatment groups. Patients taking zolmitriptan, 2.5 mg or 5 mg, were more likely to give their treatment an overall higher rating when compared with patients taking sumatriptan, 25 mg (OR=1.64, $P=.002$; OR=1.68, $P=.001$, respectively). More patients taking zolmitriptan, 2.5 mg or 5 mg, rated their treatment higher than those taking sumatriptan, 50 mg, although the difference was not statistically significant (OR=1.19, $P=.265$; OR =1.22, $P=.199$, respectively).

The odds ratios for all the efficacy comparisons were greater than 1 in favor of both doses of zolmitriptan, showing zolmitriptan to be at least numerically superior to sumatriptan, 25 mg and 50 mg. The majority of the end points also reached statistical significance.

Headache recurrence, which can only occur in those patients who have had an initial headache response, was also assessed. Overall recurrence rates for attacks 2 through 6, combined (39.3% and 37.9%), were slightly lower and, in patients with recurrence, initial headache relief lasted slightly longer (13 to 15 hours) for patients taking zolmitriptan, 2.5 mg and 5 mg, than for patients taking sumatriptan, 25 mg or 50 mg (recurrence rates 45.6% and 43.9%, respectively; headache relief lasted 10 to 13.5 hours).

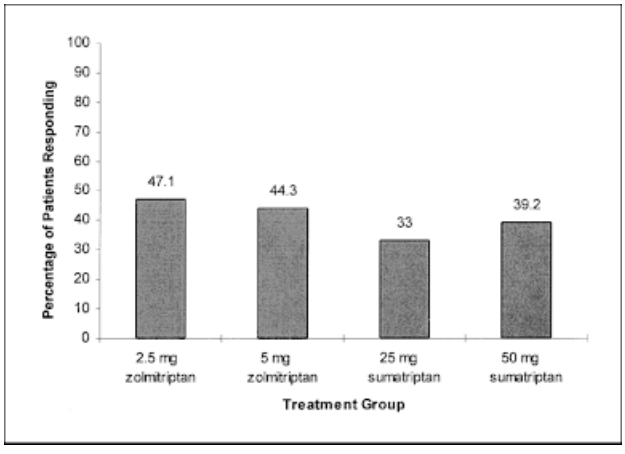

Fig 1.–Patients responding at 2 hours in 80% to 100% of attacks. Zolmitriptan 2.5 mg versus sumatriptan 25 mg, $P<0.001$; zolmitriptan 2.5 mg versus sumatriptan 50 mg, $P=.051$; zolmitriptan 5 mg versus sumatriptan 25 mg, $P=.004$; zolmitriptan 5 mg versus sumatriptan 50 mg, $P=.206$.

Roughly three quarters of the patients who experienced recurrence did not take additional medication for recurrence, even though patients were instructed that this was permitted. Patients in the zolmitriptan treatment groups were less likely to take additional medication for recurrence (15% and 20% for zolmitriptan, 2.5 mg and 5 mg, respectively) than patients in the sumatriptan, 25 mg, treatment group (30.2%). Additional medication for recurrent headache was taken by 21.4% of patients in the sumatriptan, 50 mg, treatment group.

In all treatment groups, nausea, photophobia, and phonophobia were substantially decreased to similar levels 2 hours after dosing compared with predose assessments. The percentage of patients across the four treatment groups with nausea before treatment ranged from 48% to 54%, decreasing to 24% to 26% 2 hours post dose. No apparent differences were observed across the 4 treatment groups. The percentage of patients with photophobia was reduced substantially from 75% to 80.4% across the treatment groups before treatment to 39.3% to 43.8% 2 hours post dose, as was the case for patients with phonophobia (range from 61.4% to 68.5% before treatment reducing to 29% to 33.7% 2 hours post dose). Sumatriptan, 25 mg, was associated with a slightly higher presence of photophobia and phonophobia post dose.

SAFETY RESULTS

All patients who were randomized to treatment and who treated at least one headache (ie, 1338 patients treating 6315 attacks) were included in the safety analysis. Of these patients, 683 (51%) reported at least one adverse event across the attacks treated (up to six). The rate was similar among all treatment groups and decreased with number of attacks treated

Table 4.–Adverse Events by Treatment Group

	Percentage of Patients			
	Zolmitriptan		Sumatriptan	
	2.5 mg (n=327)	5 mg (n=337)	25 mg (n=336)	50 mg (n=338)
All adverse events (%)*	51.4	56.7	43.8	52.4
Adverse events reported by attack (%)†				
Attack 1	27.8	32.9	20.5	29.3
Attack 2	20.5	23.3	19.3	20.3
Attack 3	21.7	24.9	18.7	18.1
Attack 4	14.4	21.7	15.5	19.8
Attack 5	16.1	22.3	12.3	12.1
Attack 6	11.9	16.6	7.5	9.7
All adverse events (%)†				
Infection	5.8	4.2	1.8	5.6
Tightness†	2.1	6.5	0.9	2.7
Nausea	7.0	11.3	4.2	7.4
Vomiting	3.7	4.2	3.9	5.9
Dizziness	6.1	8.0	4.5	5.0
Paresthesia	4.9	8.0	3.6	4.4
Somnolence	4.3	7.7	3.6	3.8
Pharyngitis	7.0	7.7	5.1	4.1
Treatment-related adverse events (%)				
Dizziness	5.5	7.4	3.0	3.8
Nausea	5.5	6.8	3.0	5.9
Paresthesia	4.6	7.4	3.3	4.4
Somnolence	4.0	7.1	2.7	3.8
Tightness‡	1.2	5.6	0.9	2.7

*Proportion of patients reporting at least one adverse event at each attack.
†Patients may have more than one adverse event.
‡Sensation of tightness of the throat, chest, or jaw.

(Table 4). Descriptive statistics are provided for adverse events (Table 4).

Few patients withdrew from the trial because of adverse events (1.8%, 3.6%, 2.7%, and 2.1% for zolmitriptan, 2.5 mg and 5 mg, and sumatriptan, 25 mg and 50 mg, respectively), suggesting that the benefits outweighed the adverse events. As expected for 5-HT_1 agonists, the most frequently reported drug-related adverse events were dizziness, nausea, paresthesia, somnolence, and sensation of tightness of the throat, chest, or jaw (Table 4).

Ten patients (four in the zolmitriptan treatment groups and six in the sumatriptan treatment groups) reported 13 serious adverse events, none of which were considered by the investigator to be related to trial treatment. Twenty-one of the 74 adverse events leading to withdrawal were considered by the investigators to be of severe intensity; only 2 were considered serious and had no causal relationship to study treatment (moderate drug dependency [1 patient, sumatriptan, 25 mg] and severe eye hemorrhage [1 patient, zolmitriptan, 5 mg] in a patient who had a history of ophthalmic hemorrhage disorder since 1996).

COMMENTS

The development of zolmitriptan grew from a desire to provide an antimigraine therapy with an improved clinical profile in comparison with previously available treatments.[18] Zolmitriptan offers good oral bioavailability and dual central and peripheral action,

properties that theoretically may provide more consistent and higher efficacy, respectively.[18] The high efficacy rates and consistent response to zolmitriptan shown in this and prior studies[14–16,19] demonstrate the potential of zolmitriptan to address the important needs of migraine sufferers, namely, rapid, consistent, and effective pain relief.[11,12]

Patients taking zolmitriptan in this trial were more likely to have a headache response at 2 hours than those taking sumatriptan. The average 2-hour headache responses in this trial were 67.1% and 64.8% for zolmitriptan, 2.5 mg and 5 mg, respectively, compared with 59.6% for sumatriptan, 25 mg, and 63.8% for sumatriptan, 50 mg. In a previous trial with similarly sized groups, the percentages of patients with headache responses were 65% and 67% for zolmitriptan, 2.5 mg and 5 mg, respectively.[14]

In this comparative study, zolmitriptan exhibited a higher headache response over multiple attacks compared with sumatriptan. Patients taking zolmitriptan for repeated attacks (up to six) responded more quickly with a significant difference between treatments seen by 1 hour (zolmitriptan, 5 mg, versus sumatriptan, 25 mg and 50 mg). Furthermore, zolmitriptan offers an additional benefit over sumatriptan in terms of pain relief over 24 hours. Considering that the median duration of untreated or unsuccessfully treated migraine headaches is 24 hours (mean 31 hours),[20] the ability of zolmitriptan to provide greater pain relief over 24 hours than sumatriptan is of clinical interest. The consistency of response over multiple attacks demonstrated by zolmitriptan in this trial was similar to that seen in other studies.[16,19]

Zolmitriptan and sumatriptan were both well tolerated, and few patients withdrew from the study because of adverse events.

CONCLUSIONS

Overall, a 2.5-mg or 5-mg dose of zolmitriptan was at least as effective as sumatriptan, 25 mg or 50 mg, for all parameters studied. A 2.5-mg dose of zolmitriptan was significantly more effective than sumatriptan, 50 mg, in terms of headache response at 2 and 4 hours. In addition, patients taking zolmitriptan were significantly more likely to have pain relief over 24 hours than those taking sumatriptan.

The tolerability of zolmitriptan, 2.5 mg and 5 mg, was similar to that seen in previous trials and, in conjunction with the efficacy profile, confirms zolmitriptan, 2.5 mg, as the optimal dose. The results from this comparative study suggest that zolmitriptan may be more efficacious than sumatriptan for the acute oral treatment of migraine.

ZOMIG is a trademark, the property of the Zeneca Group of Companies.

Acknowledgments: This trial was supported by a grant from Zeneca Inc., Wilmington, Delaware. Appreciation is expressed to Pam Fletcher, Project Leader, Zeneca Pharmaceuticals, Wilmington, Delaware, for assistance in the study design and analysis.

We would also like to thank the investigators who took part in this study: Alan Aarons, MD, Raleigh, NC; Jeffrey Apter, MD, Princeton, NJ; Paul Brownstone, MD, Boulder, Colo; Jacques Caldwell, MD, Gainesville, Fla; Elias Chalhub, MD, Mobile, Ala; James Dexter, MD, Columbia, Mo; Doug Dulli, MD, Madison, Wis; Keith Edwards, MD, Bennington, Vt; Donald England, MD, Eugene, Ore; John Ervin, MD, Kansas City, Mo; James Ferguson, MD, Salt Lake City, Utah; Benjamin Frishberg, MD, Rockville, Md; Hisham Hafez, MD, Nashua, NH; Jeffrey Robert Herbst, MD, Portland, Ore; Timothy Hodges, MD, Boise, Idaho; Robert Holloway, MD, Atlanta, Ga; Irving Kolin, MD, Winter Park, Fla; H. Edward Logue, MD, Birmingham, Ala; Peter Londborg, MD, Seattle, Wash; Scott London, MD, Denver, Colo; Antoinette Mangione, MD, Philadelphia, Pa; Dennis McCluskey, MD, Mogadore, Ohio; William McEntee, MD, Sarasota, Fla; Denis Mee-Lee, MD, Honolulu, HI; Charles Merideth, MD, San Diego, Calif; Donald Middleton, MD, Fairhaven, Mass; Felise Milan, MD, East Providence, RI; Barry Mishkin, MD, West Palm Beach, Fla; Jeffrey Morton, MD, Peoria, Ill; Linda Murray, MD, St. Petersburg, Fla; Eugenie Obbens, MD, Phoenix, Ariz; John Pappas, MD, Lexington, Ky; George Pyke, MD, Altamont Springs, Fla; Robert Riesenberg, MD, Decatur, Ga; Peter Ripley, MD, South Yarmouth, Mass; James Seltzer, MD, San Diego, Calif; John Sorensen, MD, Las Vegas, Nev; John Stafford, MD, St. Joseph, Mich; Susan Steen, MD, Tampa, Fla; Steven Targum, MD, Marlton, NJ; and Martin Throne, MD, Atlanta, Ga.

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