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# Zolmitriptan versus sumatriptan for the acute oral treatment of migraine: a randomized, double-blind, international study

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This randomized, double-blind, parallel-group study compared the efficacy and tolerability of zolmitriptan (2.5 or 5 mg) and sumatriptan (50 mg) in the acute oral treatment of up to six moderate-to-severe migraine attacks. The intention to treat (ITT) population comprised of 1522 patients: 500 treated with zolmitriptan 2.5 mg (2671 attacks), 514 with zolmitriptan 5 mg (2744 attacks) and 508 with sumatriptan 50 mg (2693 attacks). Overall, the 2-h headache response rates in these groups were 62.9, 65.7 and 66.6%, respectively. There were no statistically significant differences between sumatriptan 50 mg and zolmitriptan 2.5 mg ($P = 0.12$) or 5 mg ($P = 0.80$). Approximately 40% of patients in each group reported a 2-h headache response in ≥ 80% of attacks. There were no statistically significant differences between the groups in the rates of headache response at 1 h (zolmitriptan 2.5 mg 36.9%, zolmitriptan 5 mg 39.5% and sumatriptan 50 mg 38.0%) or 4 h (70.3, 72.9 and 72.2%, respectively) or in the rates of meaningful migraine relief at 1, 2 or 4 h or sustained (24-h) pain relief. All treatments were well tolerated. In conclusion, zolmitriptan (2.5 or 5 mg) proved similarly efficacious compared with sumatriptan (50 mg), both in terms of response rates and consistency across attacks.

## Introduction

Migraine is a common neurological condition with an estimated prevalence of 15–18% in women and 6% in men (Stewart *et al*., 1992, 1994). It is a chronic disorder involving episodic attacks characterized by headache and often other symptoms (e.g. nausea, vomiting, phonophobia, photophobia) (Headache Classification Committee of the International Headache Society, 1988). As such, migraine can result in severe debilitation and reduced quality of life for patients (Osterhaus *et al*., 1994; Stewart and Lipton, 1994; Dahlöf and Dimenäs, 1995).

The first 5-$HT_{1B/1D}$ receptor agonist, sumatriptan, was a major advance in antimigraine therapy when it was introduced in 1991 (Dechant and Clissold, 1992; Plosker and McTavish, 1994; Perry and Markham, 1998). Zolmitriptan ('Zomig') is a selective 5-$HT_{1B/1D}$ receptor agonist with improved bioavailability (Seaber *et al*., 1998) and a dual central and peripheral action on the trigeminovascular system (Martin, 1997). These properties may provide greater and more consistent efficacy than sumatriptan. Zolmitriptan has proved highly efficacious and well tolerated in the acute oral treatment of migraine in placebo-controlled trials (Rapoport *et al*., 1997; Solomon *et al*., 1997). Long-term studies have established its effectiveness and tolerability in treating multiple attacks over a period of up to 12 months (The International 311C90 Long-Term Study Group, 1998; Tepper *et al*., 1999). Studies indicate that a zolmitriptan dose of 2.5 mg provides the optimal balance between efficacy and tolerability, although some patients may benefit from a 5-mg dose Rapoport *et al*., 1997; Schoenen and Sawyer, 1997).

The primary objectives of this trial were to assess whether zolmitriptan (2.5 and 5 mg) were equivalent in terms of efficacy to sumatriptan for the treatment of the first migraine headache and to assess the efficacy of zolmitriptan 2.5 and 5 mg compared with sumatriptan 50 mg in the acute treatment of six migraine attacks. The secondary objective was to compare the tolerability profiles of the two agents.

## Methods

### Study design

This was a randomized, double-blind, parallel-group, multicentre trial conducted on an outpatient basis in 21 countries throughout the world. The trial was designed and conducted in accordance with the ethical principles

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of Good Clinical Practice and the Declaration of Helsinki. The study was approved by local ethics committees and, where applicable, local regulatory authorities.

### Patients

Male and female patients aged 18–65 years with an established diagnosis of migraine (Headache Classification Committee of the International Headache Society, 1988) were recruited. Patients were required to have: a history of migraine symptoms of at least 1 year duration, an age of migraine onset $< 50$ years; a history of 1–6 attacks per month in the 2 months prior to the study and the ability to distinguish non-migraine headaches from typical migraine without aura. Eligible patients were able to comply with all trial procedures, including the completion of diary cards, and all provided written, informed consent.

Patients with basilar, ophthalmoplegic or hemiplegic migraine headache or non-migraine headache on more than 10 days per month over the preceding 6 months were excluded. Other exclusion criteria included: pregnancy, lactation or inadequate contraception in female patients; ischaemic heart disease (or other vascular disease, including Prinzmetal angina), dysrhythmias or cardiac accessory pathway disorders (e.g. Wolff–Parkinson–White syndrome); uncontrolled hypertension (systolic blood pressure $\geq 160$ mmHg or diastolic blood pressure $\geq 95$ mmHg); use of monoamine oxidase inhibitors, methysergide, or methylergonovine within 2 weeks of randomization; an abnormal clinical laboratory result, recent history of alcohol or drug abuse, hypersensitivity to study treatments, previous unacceptable adverse event following use of 5-$HT_{1B/1D}$ receptor agonists, participation in another clinical trial during or within 30 days prior to this study and risk of transmitting HIV, any other sexually transmitted disease or hepatitis B. Patients could only be admitted to the trial once.

### Treatment

Patients were randomly allocated to treatment with zolmitriptan 2.5 mg, zolmitriptan 5 mg or sumatriptan 50 mg (1 : 1 : 1 ratio) in balanced blocks of three using a computer-generated random numbers scheme. Zolmitriptan was supplied as 2.5 mg tablets; patients randomized to a 5-mg dose took two zolmitriptan tablets for each dose. Sumatriptan was supplied as 50 mg tablets. Blinding was maintained using the double-dummy method, by which patients were given placebo tablets matching zolmitriptan and/or sumatriptan according to their randomization.

Patients initially received three treatment packs each containing medication for a single migraine headache. Each pack comprised two strips. Patients used the first strip for the initial treatment of a migraine headache of moderate or severe intensity, provided they had been free of any previous migraine for 24 h and the headache was not of $> 12$ h duration (or, if present on waking, present for $> 12$ h since waking). Patients could use the second strip (containing identical medication to the first) to treat recurrent headache 2 h after the initial dose, if required. Patients returned to the clinic within 2 weeks of any treated attack, where they were assessed and given additional medication if necessary until they had been treated for a total of six migraine headaches.

Patients were requested not to sleep between dosing and the 4-h post-dose assessment. They were instructed not to take any ergot derivative, sumatriptan or opiate within 24 h before study medication or any other form of analgesic within 6 h. Patients could take escape medication (e.g. analgesics, non-steroidal anti-inflammatory agents, antiemetics or sedatives) to treat persistent migraine headache provided it was approved by the investigator and administered at least 2 h after study medication. Patients were requested not to take ergotamine derivatives within 6 h after treatment. Other medications were permitted at the discretion of the investigator.

### Assessments

Patients were provided with calendars on which they recorded details of all migraine attacks and, if appropriate, details of menstrual flow. They were also given diary cards on which they recorded information about the following before and 1, 2 and 4 h after a dose of study medication: headache intensity, meaningful migraine relief (MMR), migraine recurrence, nausea, photophobia, phonophobia and use of escape medication. MMR is a subjective global evaluation of treatment made by patients which encompass all migraine symptoms and overall treatment satisfaction. At each clinic visit, the investigator reviewed the diary card and recorded the use of concomitant and escape medications, the occurrence of adverse events and the patients' global impression of treatment.

The primary efficacy endpoint for the interim first attack analysis was headache response at 2 h after administration of trial medication. The primary efficacy end-point for the six migraine attacks was the proportion of patients with a headache response at 2 h after the first dose of study medication across all attacks treated. Headache response was defined as a reduction in headache severity from 'severe' or 'moderate' to 'mild' or 'none'. Secondary end-points included

headache response rates 1 and 4 h after treatment and the consistency of headache responses, as assessed by the proportion of patients with 1-, 2- and 4-h responses in ≥ 80% of attacks and in 100% of attacks.

The profile of headache relief over 24 h post-dose was evaluated using three categories of response: 'no response' (patients with attacks of moderate to severe intensity who had no response to treatment at 2 h), 'partial response' (patients had a 2-h headache response and then experienced headache recurrence or used escape medication or additional study medication within 24 h) or 'full response' (patients had a 2-h headache response which was maintained for 24 h without having a recurrent headache or without taking escape medication or additional study medication within 24 h). Two secondary end-points considered pain relief over the 24 h post-dose period: 'sustained headache response over 24 h' (defined as a headache response at 2 h, no recurrence and no use of escape medication) and 'sustained pain-free response over 24 h' (defined as a pain-free response at 2 h, no recurrence and no use of escape medication). Other secondary end-points were the rates of MMR at 1, 2 and 4 h post-dose (for each patient over all attacks) and the patients' global impression (i.e. their overall satisfaction with treatment), graded as 'poor', 'fair', 'good' or 'excellent'.

### Statistical analysis

It was calculated that 450 patients in each treatment group would provide a 90% chance of showing equivalence between zolmitriptan 2.5 or 5 mg and sumatriptan 50 mg based on the proportion of patients with a 2-h headache response for the first headache treated. Allowing for withdrawals and unevaluable data, a total of 500 patients per group had to be recruited. For the six-attack analysis, a minimum of 450 evaluable patients per group gave a 98% chance to detect a 12% difference in overall 2-h headache response rate between zolmitriptan 2.5 or 5 mg and sumatriptan 50 mg (2% significance level). Using the estimated response rate cited in the sumatriptan regulatory package of 53% (US prescribing information) there would be a 90% chance of detecting a 12% difference between treatments. A 2% significance level was used in this analysis because a first-attack analysis was completed before all patients had completed the trial. This stricter criterion allows for the repeated analysis of data after both the first and sixth attack and helps to protect against type I (false positive) errors.

The six-attack efficacy analysis was conducted on the intention-to-treat (ITT) population of all patients who were treated for at least two headaches. All analyses used SAS (SAS®-SAS Institute Inc, Cary, NC, USA). Rates of headache response, MMR, sustained headache response and sustained pain-free response were analysed using the generalized estimating equations (GEE) approach for binary data. The consistency of headache response and the global impression end-point were analysed using logistic regression. The analysis allowed for the factors of: treatment, baseline headache intensity and country. For the GEE approach, attack number was also included. The estimated treatment odds ratios (comparing each zolmitriptan dose with sumatriptan 50 mg) were presented for each comparison, together with confidence intervals (CIs) and associated *P*-values. The odds ratio for a dose of zolmitriptan versus sumatriptan is the odds of a response on zolmitriptan divided by the odds of a response on sumatriptan. An odds ratio which is $>1$ implies that the probability of a response is greater following zolmitriptan than sumatriptan.

## Results

### Patients

One thousand seven hundred and eighty seven patients were recruited from 166 centres in 21 countries and randomized to treatment. During the trial, 620 patients were withdrawn from the randomized population (no differences were apparent between the groups) for reasons summarized in Table 1. The ITT population comprised of 1522 patients who was treated at least two migraines: 500 with zolmitriptan 2.5 mg, 514 with zolmitriptan 5 mg and 508 with sumatriptan 50 mg. This population treated a total of 8108 migraine attacks: 2671 with zolmitriptan 2.5 mg, 2744 with zolmitriptan 5 mg and 2693 with sumatriptan 50 mg. The safety analysis population included 1666 patients who received at least one dose of study medication.

The three ITT treatment groups were similar with respect to their demographic and baseline migraine characteristics (Table 2). Overall, the average age was 41.9 years and 85.3% (1299/1522) of patients were female. The mean age of onset of migraine was 21.1 years and the mean number of migraine attacks per month was 2.9.

The groups were similar with respect to the distribution of patients according to the number of attacks treated. The majority (75–76%) of patients in each group treated six migraines. The majority of attacks treated (61.2–64.9%) were of moderate intensity. Approximately 20% of attacks in each treatment group were menstrually related (occurring not more than 2 days before or 3 days after the onset of menses).

**Table 1** Reasons for withdrawal of patients during the study

| Variable | Zolmitriptan (mg) | | Sumatriptan (50 mg) |
|---|---|---|---|
| | 5 | 2.5 | |
| No. of patients randomized | 593 | 597 | 597 |
| Number (%) withdrawn because of: | | | |
| Informed consent withdrawn | 44 (7.4) | 44 (7.4) | 45 (7.5) |
| End of study period before six attacks could be treated | 41 (6.9) | 38 (6.4) | 49 (9.3) |
| No treatable migraine attacks | 37 (6.2) | 35 (5.9) | 27 (4.5) |
| Lost to follow-up | 21 (3.5) | 14 (2.3) | 13 (2.2) |
| Adverse event/concurrent illness | 17 (2.9) | 21 (3.5) | 17 (2.8) |
| Protocol non-compliance | 10 (1.7) | 14 (2.3) | 10 (1.7) |
| Condition worse | 2 (0.3) | 2 (0.3) | 2 (0.3) |
| Others | 34 (5.7) | 39 (6.5) | 44 (7.4) |
| Total withdrawal | 206 (34.7) | 207 (34.7) | 207 (34.7) |

## Efficacy

The statistical interim analysis of the observed 2 h headache response rates after the treatment of the first migraine headache demonstrated that both zolmitriptan doses were equivalent to sumatriptan 50 mg, with the 90% CI for the odds-ratios lying wholly within the calculated limits required to demonstrate equivalence. This paper will consider the results from the six-attack analysis.

## Headache response

Zolmitriptan 2.5 mg produced a 2-h headache response in 62.9% of attacks, zolmitriptan 5 mg in 65.7% and sumatriptan 50 mg in 66.6% of attacks. There were no statistically significant differences between the response rates in the zolmitriptan and sumatriptan groups (Table 3). Similarly, there was no statistically significant difference between the response rates across the six attacks in the zolmitriptan 2.5 mg, zolmitriptan 5 mg and sumatriptan 50 mg groups at 1 h (36.9, 39.5 and 38.0%, respectively) or 4 h (70.3, 72.9 and 72.2%, respectively (Table 3). Moreover, the headache response rates at each time-point were generally similar between the groups for each attack from 1 to 6 (Fig. 1).

The consistency of headache response across attacks was also similar in the three groups. There were no statistically significant differences between the groups in the percentages of patients responding (at any of the time-points) in ≥ 80% or in 100% of attacks. Overall, 38.6% zolmitriptan 2.5 mg recipients obtained a 2-h headache response in ≥ 80% of attacks, compared with 44.4% of zolmitriptan 5 mg recipients and 43.1% of

**Table 2** Demographic and baseline migraine characteristics of patients (intention-to-treat population)

| Variable | Zolmitriptan (mg) | | Sumatriptan (50 mg, $n$ = 508) |
|---|---|---|---|
| | 5 ($n$ = 514) | 2.5 ($n$ = 500) | |
| Mean age (years) ± SD | 41.7 ± 10.6 | 42.1 ± 10.7 | 41.9 ± 10.7 |
| Age distribution, $n$ (%) | | | |
| ≥ 18–39 years | 205 (39.9)[a] | 192 (38.4) | 198 (39.0) |
| ≥ 40–65 years | 307 (59.7)[a] | 308 (61.6) | 310 (61.0) |
| Sex, $n$ (%) | | | |
| Male | 72 (14.0) | 73 (14.6) | 78 (15.4) |
| Female | 442 (86.0) | 427 (85.4) | 430 (84.6) |
| Race, $n$ (%) | | | |
| Caucasian | 483 (94.0) | 480 (96.0) | 487 (95.9) |
| Other | 31 (6.0) | 20 (4.0) | 21 (4.1) |
| Type of migraine, $n$ (%) | | | |
| With aura | 86 (16.7) | 77 (15.4) | 75 (14.8) |
| Without aura | 288 (56.0) | 285 (57.0) | 291 (57.3) |
| With and without aura | 140 (27.2) | 138 (27.6) | 142 (28.0) |
| Mean age at onset of migraine (years) ± SD | 20.9 ± 10.2 | 21.5 ± 9.9 | 21.0 ± 10.1 |
| Mean no. of migraine attacks/month ± SD | 2.9 ± 1.5 | 2.9 ± 1.4 | 3.0 ± 1.5 |
| Duration of typical untreated headache, $n$ (%) | | | |
| 0–12 h | 50 (9.7) | 45 (9.0) | 51 (10.0) |
| > 12 to ≤ 24 h | 102 (19.8) | 125 (25.0) | 129 (25.4) |
| > 24 to ≤ 48 h | 173 (33.7) | 163 (32.6) | 168 (33.1) |
| > 48 to ≤ 72 h | 150 (29.2) | 142 (28.4) | 129 (25.4) |
| > 72 h | 39 (7.6) | 25 (5.0) | 31 (6.1) |

[a] One patient < 18 years and one patient > 65 years of age. SD: standard deviation.

**Table 3** Results of statistical comparisons of zolmitriptan 2.5 or 5 mg and sumatriptan 50 mg

| | Zolmitriptan 2.5 mg versus sumatriptan 50 mg | | | Zolmitriptan 5 mg versus sumatriptan 50 mg | | |
|---|---|---|---|---|---|---|
| Variable | OR | 98% CI | *P*-value | OR | 98% CI | *P*-value |
| Headache response | | | | | | |
| 1 h | 0.97 | 0.79–1.19 | 0.75 | 1.11 | 0.90–1.37 | 0.24 |
| 2 h | 0.87 | 0.71–1.07 | 0.12 | 1.02 | 0.83–1.26 | 0.80 |
| 4 h | 0.93 | 0.75–1.15 | 0.43 | 1.09 | 0.88–1.36 | 0.34 |
| MMR | | | | | | |
| 1 h | 0.87 | 0.71–1.07 | 0.13 | 1.08 | 0.88–1.33 | 0.36 |
| 2 h | 0.88 | 0.72–1.06 | 0.11 | 1.07 | 0.88–1.31 | 0.42 |
| 4 h | 0.88 | 0.71–1.10 | 0.18 | 1.11 | 0.88–1.38 | 0.29 |
| Sustained (24-h) pain-free response[a] | 0.90 | 0.73–1.12 | 0.26 | 1.09 | 0.88–1.36 | 0.34 |
| Sustained (24-h) headache response[b] | 0.94 | 0.78–1.14 | 0.47 | 1.07 | 0.89–1.29 | 0.37 |
| Global impression[c] | 1.09 | 0.83–1.44 | 0.46 | 1.20 | 0.91–1.58 | 0.13 |

[a] Pain-free at 2 h, no recurrence and no use of escape medication. [b] Headache response at 2 h, no recurrence and no use of escape medication. [c] Groups were compared in terms of the proportion of patients responding that treatment was ''excellent', and 'excellent' or 'good' and 'excellent' or 'good' or 'fair'. CI: confidence intervals; MMR: meaningful migraine relief; OR: odds ratio.

sumatriptan 50 mg recipients ($P = 0.14$ versus zolmitriptan 2.5 mg and $P = 0.55$ versus zolmitriptan 5 mg).

### Pain-free response

The pain-free response rates at 1 and 2 h were also comparable across the three treatment groups for each of the six attacks (Fig. 2a–c). Overall, a pain-free response at 1 h was achieved by 9.1, 12.0 and 11.4% of patients receiving zolmitriptan 2.5 mg, zolmitriptan 5 mg and sumatriptan 50 mg, respectively. Corresponding rates at 2 h were 32.4, 36.0 and 35.3%, and at 4 h 52.1, 55.5 and 54.9%.

### Meaningful migraine relief (MMR)

There were no statistically significant differences between the groups in the proportions of patients reporting MMR at any time-point (Table 3). MMR was reported at 2 h for 63.9% of attacks treated with zolmitriptan 2.5 mg, 68.2% of those treated with zolmitriptan 5 mg and 67.6% of those treated with sumatriptan 50 mg. There was little difference between the groups in the percentage of patients reporting MMR at 2 h in ≥ 80% of attacks (40.8, 45.7 and 44.5%, respectively) or in 100% of attacks (21.6, 28.8 and 27.4%, respectively).

### Twenty four hour pain relief

Similarly, there were no statistically significant differences between the groups in the relief of pain over 24 h (Table 3). Across the six attacks, 37.3–46.6% of zolmitriptan 2.5 mg recipients, 41.9–47.2% of zolmitriptan 5 mg recipients and 39.1–47.9% of sumatriptan 50 mg recipients reported a sustained headache response over 24 h. The corresponding rates of a sustained pain-free response over 24 h in the three groups were 20.5–26.5%, 24.6–28.9% and 23.7–28.4%, respectively (Fig. 2d).

### Global impression

In the global impression assessment, 65.8% of patients treated with zolmitriptan 2.5 mg, 69.7% with zolmitriptan 5 mg and 65.9% with sumatriptan 50 mg graded their treatment as 'good' or 'excellent'. There were no statistically significant differences between the zolmitriptan and sumatriptan groups in this regard (Table 3).

### Headache recurrence

In each of the three groups, headache recurrence was reported in approximately 30% of those attacks with an initial 2-h headache response (zolmitriptan 2.5 mg (30.3% [494/1632]), zolmitriptan 5 mg (29.9% [530/1771]) and sumatriptan 50 mg (30.6% [539/1760]). Likewise, escape medication (most commonly non-combination paracetamol) was used in a similar proportion of attacks in the three groups: 23.6% (631/2671), 22.2% (608/2744) and 23.0% (620/2693) in the zolmitriptan 2.5 mg, zolmitriptan 5 mg and sumatriptan 50 mg groups, respectively.

### Migraine-associated symptoms

Photophobia, phonophobia and/or nausea were present with most headaches immediately before study treatment. The three treatments were similarly efficacious in reducing these migraine-associated symptoms at 1, 2 and 4 h post-dose (Table 4).

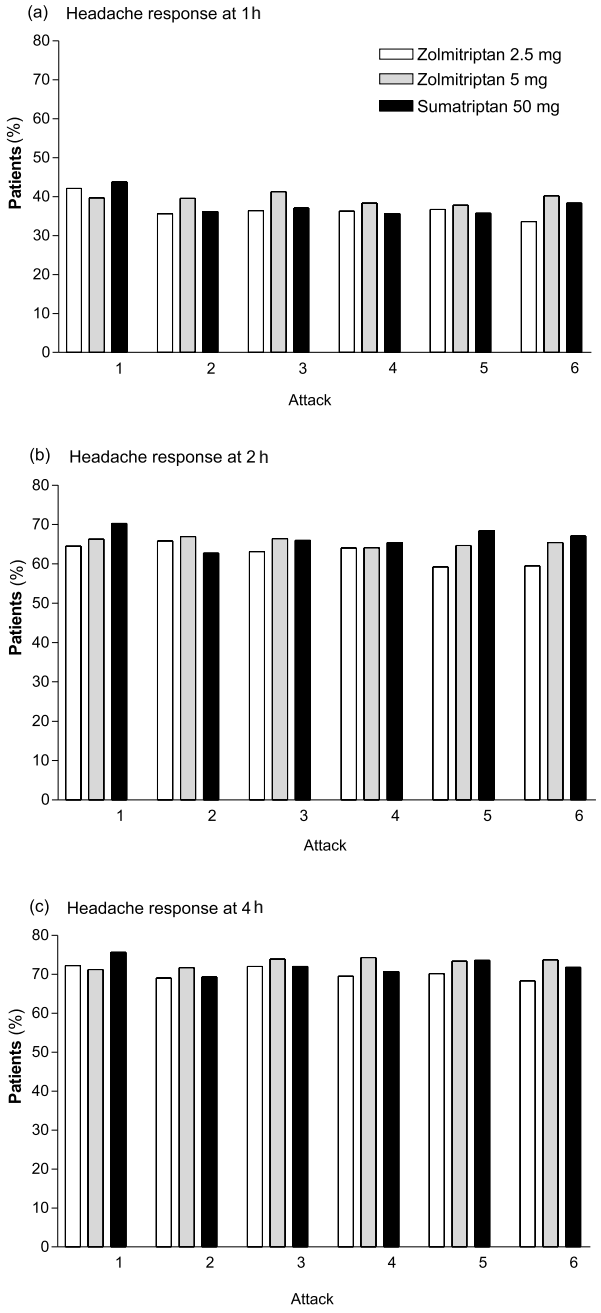


**Figure 1** Rates of headache response at 1, 2 and 4 h for each of the six attacks following acute oral migraine treatment with zolmitriptan 2.5 ($n = 500$) or 5 mg ($n = 514$) or sumatriptan 50 mg ($n = 508$).

### Tolerability

The number of doses of medication taken was similar across the three treatment groups. The proportion of patients who reported at least one adverse event was similar in the three groups: 34.8% (192/551) with zolmitriptan 2.5 mg, 37.7% (211/560) with zolmitriptan 5 mg and 34.4% (191/555) with sumatriptan 50 mg. The spectrum of adverse events reported was similar in the three groups, with asthenia, paraesthesia and dizziness being among the most common (Table 5).

A similar proportion of patients in the three groups (2.7, 3.4 and 2.7%, respectively) were withdrawn from the trial because of adverse events. The most common adverse events leading to withdrawal were unintended pregnancy (six events), vomiting (six events) and dizziness (five events). No patients experienced serious adverse events within 24 h of taking study medication and there were no deaths during the study.

## Discussion

In this study no difference was observed between zolmitriptan and sumatriptan in terms of efficacy for the acute treatment of migraine. This is in contrast to that reported elsewhere for comparisons between zolmitriptan 2.5 mg, 5 mg and sumatriptan 50 mg (Gallagher *et al.*, 2000). The headache response rate obtained with sumatriptan in the present study (66.6%) was higher than that reported in single attack placebo-controlled studies (50–55%) (Cutler *et al.*, 1995; Sargent *et al.*, 1995).

The response rates for zolmitriptan and sumatriptan obtained in the present study are in a similar clinical range to those obtained in the recent six attack US study comparing zolmitriptan (2.5 or 5 mg) and sumatriptan (25 or 50 mg) (Gallagher *et al.*, 2000). However, in the latter study, zolmitriptan was shown to be significantly superior to sumatriptan according to the rates of headache response, MMR and pain-relief over 24 h. For example, the 2-h headache response rate with zolmitriptan 2.5 mg was 67.1%, compared with 63.8% with sumatriptan 50 mg ($P < 0.01$). Together, the data from these two studies indicate that zolmitriptan is at least as effective as sumatriptan both in terms of response rates and in patients' global impression of treatment, and can provide additional efficacy over sumatriptan in terms of 2 and 4 h response rates and pain relief over 24 h.

In the present study, both treatments were consistently effective across attacks. Approximately 40% of patients in each group reported a 2-h headache response in at least 80% of attacks treated. Moreover, zolmitriptan and sumatriptan each provided a sustained (24-h) headache response across the six attacks treated (i.e. a 2-h headache response without headache recurrence or use of escape medication or additional study medication within 24 h) in 37–48% of patients. These rates of sustained pain relief are similar to those observed in the recent US study (Gallagher *et al.*, 2000), although in that study zolmitriptan 5 mg was significantly more effective than sumatriptan 50 mg in providing sustained 24-h relief (42.5 vs. 38.1%;

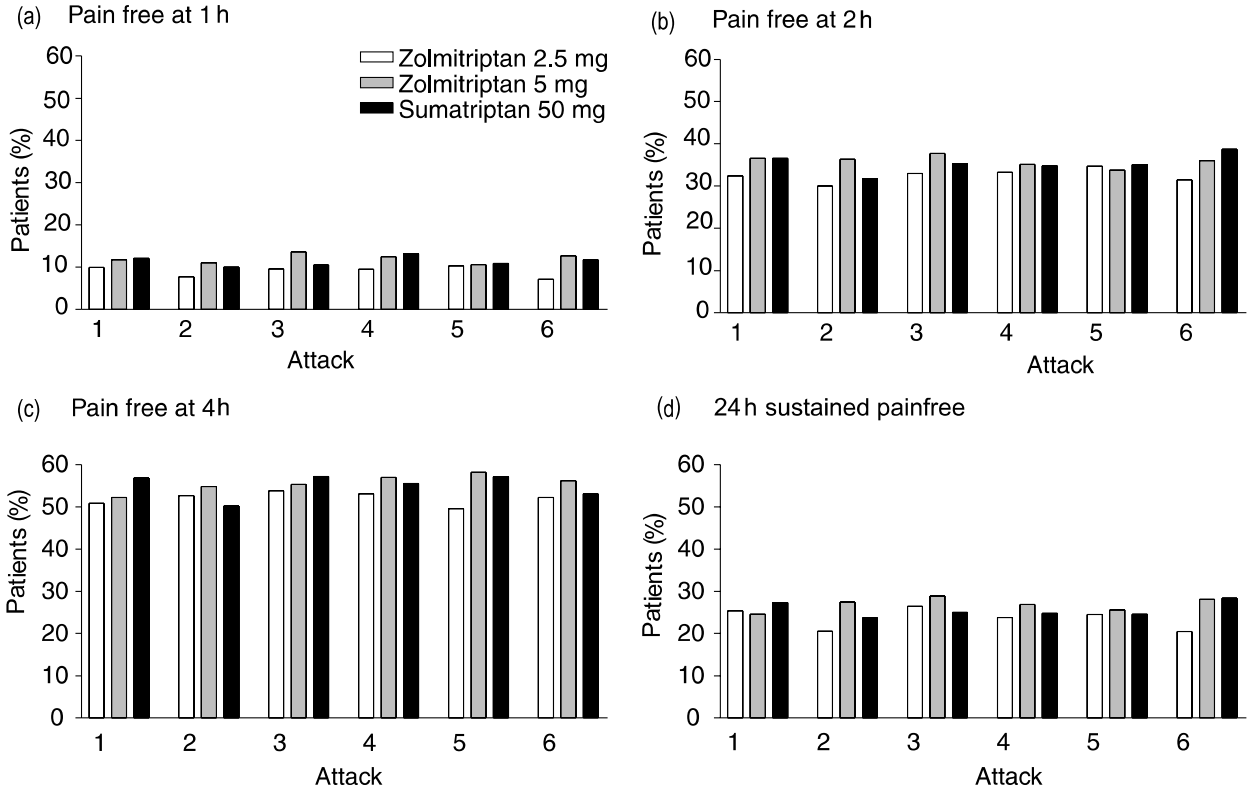


**Figure 2** Rates of pain free response at 1, 2 and 4 h, and sustained pain-free response over 24 h for each of the six attacks following acute oral migraine treatment with zolmitriptan 2.5 ($n = 500$) or 5 mg ($n = 514$) or sumatriptan 50 mg ($n = 508$).

**Table 4** Rates of photophobia, phonophobia and nausea following acute oral migraine treatment with zolmitriptan (2.5 or 5 mg) or sumatriptan (50 mg) in those patients with baseline symptoms

| Migraine-associated symptom | Overall number of attacks where symptom was present (%) | | |
|---|---|---|---|
| | Zolmitriptan (mg) | | Sumatriptan (mg) |
| | 5 | 2.5 | 50 |
| Photophobia | ($n = 2298$) | ($n = 2245$) | ($n = 2229$) |
| 1 h | 79 | 77 | 78 |
| 2 h | 54 | 54 | 52 |
| 4 h | 38 | 40 | 39 |
| Phonophobia | ($n = 2108$) | ($n = 1994$) | ($n = 1996$) |
| 1 h | 80 | 80 | 79 |
| 2 h | 54 | 57 | 53 |
| 4 h | 37 | 41 | 38 |
| Nausea | ($n = 1959$) | ($n = 1882$) | ($n = 1852$) |
| 1 h | 79 | 77 | 78 |
| 2 h | 54 | 54 | 52 |
| 4 h | 38 | 40 | 39 |

$P < 0.001$). The two agents were similarly effective according to the end-points of MMR, the patients' global impression, headache recurrence and the relief of migraine-associated symptoms.

**Table 5** Adverse events occurring in ≥ 4% of patients in any treatment group during treatment with zolmitriptan (2.5 or 5 mg) or sumatriptan (50 mg)

| Adverse events | Number of patients (%) | | |
|---|---|---|---|
| | Zolmitriptan (mg) | | Sumatriptan 50 mg ($n = 560$) |
| | 5 ($n = 551$) | 2.5 ($n = 555$) | |
| Asthenia | 37 (6.6) | 29 (5.3) | 25 (4.5) |
| Paraesthesia | 29 (5.2) | 29 (5.3) | 30 (5.4) |
| Tightness | 28 (5.0) | 19 (3.4) | 17 (3.1) |
| Dizziness | 32 (5.7) | 19 (3.4) | 28 (5.0) |
| Somnolence | 28 (5.0) | 17 (3.1) | 25 (4.5) |
| Aggravation reaction[a] | 24 (4.3) | 14 (2.5) | 16 (2.9) |

[a] Included aggravation of any pre-existing illness.

The tolerability profiles of zolmitriptan and sumatriptan in the present study were consistent with previous reports (Simmons and Blakeborough, 1994; Edmeads and Millson, 1997). Both agents were generally well tolerated and few patients were withdrawn because of adverse events. The slightly higher incidence of some adverse events in the higher zolmitriptan dose group, coupled with the similar efficacy of the two doses, confirms zolmitriptan 2.5 mg as the optimal dose.

In conclusion, zolmitriptan (2.5 or 5 mg) proved similarly efficacious compared with sumatriptan (50 mg) in the treatment of up to six migraine attacks, both in terms of response rates and consistency across attacks.

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