SUMMARY

ASTRAZENECA

FINISHED PRODUCT: Zomig 2.5 mg orally dispersible tablet

ACTIVE INGREDIENT: Zolmitriptan

Study title (number): A Multicentre, Open, Crossover Study to Evaluate Preference for either Zolmitriptan (2.5 mg) Orally Dispersible Tablet or Sumatriptan (50 mg) Tablet for the Acute Treatment of Migraine in Adult Patients (311CIL/0114)

Clinical phase: IIIB

First subject recruited: 20 February 2001
Last subject completed: 4 October 2001
AstraZeneca approval date: 23 December 2004

Principal investigator(s) and location (centre number): None assigned in this study.

Publications: Dowson AJ, Charlesworth B. Patients with migraine prefer zolmitriptan orally disintegrating tablet to sumatriptan conventional oral tablet. Int. J. Clin. Pract. 2003;57(7):1-4.

OBJECTIVES

Primary: To evaluate patient preference for either zolmitriptan 2.5 mg orally dispersible tablet or sumatriptan 50 mg tablet for the treatment of acute migraine, by asking the question "Which of the two treatments you received did you prefer?" Patients were asked to state a preference for one of the two treatments.

Secondary: To assess the treatment method as excellent, good, fair or poor; to assess the preference of treatments on the basis of convenience of use, least disruptive to take, future use compared with any previous migraine therapy; to assess the preference of treatments in patients who experience nausea, vomiting and difficulty in swallowing tablets. The incidence and nature of adverse events occurring within 24 hours of treatment with the study medication were also evaluated.

METHODS

Design: Open, randomised, crossover study conducted on a multicentre basis in the UK. Patients treated 1 migraine attack of any intensity with each study medication. Visits took place at screening and within 1 week of treatment of each migraine attack.

Population: Adult patients with an established diagnosis of migraine, who experienced moderate or severe migraine-related disability as assessed by the Migraine Disability Assessment (MIDAS) questionnaire.

Key inclusion criteria: Male and female patients aged 18 to 65 years; an established diagnosis of migraine as defined by the International Headache Society (IHS) criteria; at least 1 migraine headache per month in the previous 3 months.

Key exclusion criteria: History of basilar, opthalmoplegic or hemiplegic migraine; history of or symptoms of ischaemic heart disease or other vascular disease; systolic blood pressure ≥ 150 mmHg or diastolic blood pressure ≥ 95 mmHg; risk factors for ischaemic heart disease, pregnancy; frequent non-migraine headaches; use of zolmitriptan or sumatriptan in the previous 3 months, or previous use of rizatriptan wafer.

Dosage: A single dose of zolmitriptan 2.5 mg orally dispersible tablet (ODT) (Zomig Rapimelt™) or sumatriptan 50 mg oral tablet (OT) (Imigran™) to treat a single migraine headache. A second tablet of study medication (or an approved escape medication) could be taken ≥ 2 hours after the first dose for treatment of persistent or recurrent headache. Patients placed the zolmitriptan 2.5 mg orally dispersible tablet on the tongue and allowed it to dissolve. The sumatriptan tablet was swallowed with water.

Key assessments:

Efficacy: Diary cards were used by patients to record the intensity of headache pain before taking study medication, date and time of intake of study drug and escape medication, and the assessment of each treatment. At the end of the study, patients who had been taking both treatments were asked by the investigator about their preference for treatment with respect to various attributes.

Primary endpoint: Patient preference for either zolmitriptan 2.5 mg ODT or sumatriptan 50 mg OT for the treatment of acute migraine. Preference was assessed by asking the question "Which of the two treatments you received did you prefer?"

Secondary endpoints: The secondary endpoints for this study assessed the basis for treatment preference, the patient's overall judgement of each treatment and the preference of treatment in patients in certain subgroups. These subgroups comprised patients who sometimes experienced nausea and/or vomiting during the attack and patients who in the past had experienced difficulties in swallowing tablets. The endpoints are listed below:

- Overall assessment of treatment method as excellent, good, fair or poor
- Assessment of each treatment with respect to: Convenient to use, pleasant taste, effective migraine treatment, easy to remove from its packaging, easy to take, and discreet
- Preference of study treatments for future use compared with any previous migraine therapy
- Satisfaction with zolmitriptan 2.5 mg ODT regarding treating a migraine attack anywhere and at any time

- Preference for treatment with respect to: disruptive to take, ease and convenience of taking, ability to maintain an active lifestyle
- Ease of taking in patients who had ever at any time had difficulty in swallowing tablets
- Overall preference for treatment in patients who in the past experienced nausea and/or vomiting during the attack

Other assessments: Use of further medication within 24 hours and time to use of further medication.

RESULTS

Demography: A total of 218 migraine patients were recruited from 20 centres in the UK and were randomised to either treatment sequence, i.e. zolmitriptan-sumatriptan (106) or sumatriptan-zolmitriptan (112). Of all patients enrolled, 186 patients treated at least one attack and were assessed for safety. No patient was excluded from the ITT population, so 186 patients were assessed for efficacy in the ITT analysis, i.e. the safety and the ITT populations were identical. Eighteen patients took only one treatment and in consequence 168 patients were included in the analyses of primary and secondary preference endpoints. All patients but one were Caucasian and the majority were females (86.0%). The mean age was 43.5 years (range 21-69 years) and the mean weight was 71.7 kg (range 44-139 kg).

Dosing: A large proportion of patients took the study medication shortly after the migraine headache started, about 38% within 15 minutes and more than 50% within 30 minutes. There was only a slight difference in time of dosing for zolmitriptan and sumatriptan.

Primary endpoint: Based on assessment of all treatment attributes during the treatment of 2 attacks, significantly more patients preferred zolmitriptan 50 mg ODT (60.1%) to sumatriptan 50 mg OT (39.9%), p=0.0130.

Secondary endpoints:

Assessment of each treatment: After treatment of the first migraine attack with each treatment, 69.5% of the patients rated zolmitriptan 2.5 mg OT as excellent or good, compared to 52.0% of the patients following sumatriptan 50 mg OT treatment. The treatment was considered an effective migraine therapy by 76.7% of the patients on zolmitriptan and 63.4% on sumatriptan. More than 90% of patients treated with zolmitriptan stated that the orally dispersible tablet would allow them to treat a migraine attack at any time (90.2%) and anywhere (91.4%).

Assessment of treatment attributes: The treatment attributes assessed were well perceived for both treatments. More than 95% of the patients found zolmitriptan 2.5 mg ODT and sumatriptan 50 mg OT both convenient to use and easy to take. Zolmitriptan 2.5 mg ODT was favoured by more patients in terms of being discreet (96% versus 86%). More patients found sumatriptan 50 mg OT easy to remove from the blister pack than the zolmitriptan 2.5 mg ODT, 98.9% and 81.4% respectively. A greater proportion of patients expressed preference for zolmitriptan 2.5 mg ODT in the future than for sumatriptan 50 mg OT, compared with any previous migraine therapy. (64.4% versus 45.5%).

Preference assessments: Zolmitriptan 2.5 mg ODT was preferred to sumatriptan 50 mg OT by significantly more patients in all aspects assessed (Table I).

Table I Preference for treatment with respect to formulation attributes

		All patients (N=168)		
		N	(%) [a]	p-value [b]
Least disruptive treatment	Zolmitriptan 2.5 mg ODT	138	(83.6)	<0.0001
	Sumatriptan 50 mg OT	27	(16.4)	
Treatment which was easier to take	Zolmitriptan 2.5 mg ODT	141	(85.5)	<0.0001
	Sumatriptan 50 mg OT	24	(14.5)	
More convenient to take	Zolmitriptan 2.5 mg ODT	142	(86.1)	<0.0001
	Sumatriptan 50 mg OT	23	(13.9)	
Treatment best enabling maintenance of an active lifestyle	Zolmitriptan 2.5 mg ODT	110	(65.5)	<0.0001
	Sumatriptan 50 mg OT	58	(34.5)	

[a] Percentages were calculated using the number of patients with available data as the denominator.
[b] Mainland-Gart test.
Data derived from Tables T18.1.1 and T18.1.12.

When compared with sumatriptan, zolmitriptan was judged to be the least disruptive treatment to take (83.6% versus 16.4%, p<0.0001) and to be the treatment best enabling maintenance of an active lifestyle (65.5% versus 34.5%, p<0.0001). Significantly more patients found zolmitriptan both easier and more convenient to take than sumatriptan, approximately 85% versus 15%. The preference for zolmitriptan regarding ease of taking was higher in patients who in the past had experienced difficulties swallowing tablets than in patients who had not (95.5% versus 81.8%). Overall, zolmitriptan was preferred to sumatriptan in patients who reported a history of nausea and/or vomiting associated with their migraine attack (59.6% versus 40.4%).
Further medication: The proportion of patients who used further medication (second dose of study medication or escape medication) within 24 hours was similar following the first dose of zolmitriptan and sumatriptan, respectively, 58.8% compared to 61%. Most patients taking further medication took a second dose of study medication, regardless of treatment.
Safety: Table II shows the number of patients with various categories of adverse events.

Table II Overview of patients with adverse events (safety population)

Category	Zolmitriptan 2.5 mg (N=177)		Sumatriptan 50 mg (N=177)	
	n	(%)[a]	n	(%)[a]
All adverse events[b]	74	(41.8)	59	(33.3)
Adverse events within 24 hours after treatment	74	(41.8)	58	(32.8)
All serious adverse events	0	(0)	1	(0.6)
Before treatment	0	(0)	0	(0)
Within 24 hours after treatment	0	(0)	0	(0)
More than 24 hours after treatment	0	(0)	1	(0.6)
All drug-related adverse events	62	(35.0)	47	(26.6)
Adverse events leading to death	0	(0)	0	(0)
Adverse events leading to withdrawal	0	(0)	2	(1.1)
Pregnancies	0	(0)	0	(0)

[a] Percentages were calculated using N as the denominator.
[b] Non-serious adverse events within 24 hours and all serious adverse events.
Data derived from Table T23.1.1.

Adverse events were reported by 74 (41.8%) patients after zolmitriptan 2.5 mg ODT treatment and by 59 (33.3%) patients after sumatriptan 50 mg OT treatment. The number of attacks associated with adverse events was 83 (31.6%) after zolmitriptan 2.5 mg ODT treatment and 64 (25.0%) after sumatriptan 50 mg OT treatment. The majority of adverse events in both treatment groups were transient, self-limiting and mild to moderate in intensity. Adverse events were those frequently seen with the triptan class of drugs (paraesthesia, dry mouth, dizziness, asthenia, somnolence, pain throat, hyperaesthesia, nausea and sensation of warmth). The incidence of adverse events was similar with both treatments. Any apparent difference was based on small absolute numbers.

Only one serious adverse event was reported, but was not classified as a valid case, since the event was unknown. The patient was on sumatriptan 50 mg OT. Two patients were withdrawn from the study due to adverse events, both after treatment with sumatriptan 50 mg OT. One of these patients experienced a serious adverse event.

OVERALL CONCLUSIONS

The objective of this open-label, randomised, crossover study was to compare treatment attributes of zolmitriptan 2.5 mg ODT and sumatriptan 50 mg OT through patient perception and preference assessments. The conclusions are as follows:

- Overall, zolmitriptan 2.5 mg ODT was preferred to sumatriptan 50 mg OT by significantly more patients (60.1% versus 39.9%).
- The majority of patients (76.7%) considered zolmitriptan 2.5 mg ODT to be an effective treatment.
- 69.5% of patients rated zolmitriptan 2.5 mg ODT as good or excellent, compared to only 52.0% for sumatriptan 50 mg OT.
- Significantly more patients found zolmitriptan 2.5 mg ODT to be the least disruptive treatment to take compared to sumatriptan 50 mg OT (83.6% versus 16.4%).
- When asked about future use, a greater proportion of patients expressed a preference for zolmitriptan 2.5 mg ODT (64.4%) than for sumatriptan 50 mg OT (45.5%) compared with any previous migraine therapy.
- Significantly more patients found zolmitriptan 2.5 mg ODT both easier to take and more convenient to take than sumatriptan 50 mg OT (approximately 86% versus 14% on both).
- More than 90% of patients considered that zolmitriptan 2.5 mg ODT would allow them to treat the migraine at any time and anywhere an attack struck.
- Zolmitriptan 2.5 mg ODT was favoured over sumatriptan 50 mg OT by patients in terms of being discreet (96.0% versus 86.9%).
- Significantly more patients preferred zolmitriptan 2.5 mg ODT to sumatriptan 50 mg OT as the treatment that would best enable maintenance of an active lifestyle (65.5% versus 34.5%).
- More than 95% of patients with difficulties swallowing conventional tablets perceived zolmitriptan 2.5 mg ODT as easier to take than sumatriptan 50 mg OT.
- Overall, zolmitriptan 2.5 mg ODT was preferred to sumatriptan 50 mg OT in patients who reported a history of nausea and/or vomiting associated with their migraine attack, 59.6% versus 40.4%.
- Zolmitriptan 2.5 mg ODT was well tolerated. Adverse events were of the kind frequently seen with the triptan class of drugs and the incidence was similar for zolmitriptan 2.5 mg ODT and sumatriptan 50 mg OT. The majority of adverse events with both treatments were transient, self-limiting and of mild to moderate in intensity, with none meeting the criteria for a serious adverse event.