A Comparison of the Cost-Effectiveness of Almotriptan and Sumatriptan in the Treatment of Acute Migraine Using a Composite Efficacy/Tolerability End Point

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ABSTRACT

OBJECTIVE: To use a composite efficacy/tolerability end point to compare the cost-effectiveness, from the perspective of a U.S. health care payer, of almotriptan and sumatriptan in the treatment of an acute migraine attack.

METHODS: The composite end point "**S**ustained pain free and **N**o **A**dverse **E**vents" (SNAE) was created from the sustained pain free and adverse event rates obtained in a meta-analysis of 53 placebo-controlled trials of oral triptans. The total direct cost of treating a single migraine attack was calculated from published sources.

RESULTS: In the base-case analysis, the average cost-effectiveness ratios (CERs) were $82, $133, and $138 (per attack at which SNAE is achieved, 2004 prices) for almotriptan 12.5 mg, sumatriptan 50 mg, and sumatriptan 100 mg, respectively; the incremental CERs for almotriptan 12.5 mg were $12 and $16 (compared with sumatriptan 50 mg and sumatriptan 100 mg, respectively) per incremental attack at which SNAE is achieved. Sensitivity analyses were conducted to explore the impact of (1) relaxing the base-case assumptions (independence of efficacy and tolerability, uniform apportionment of health service use costs across attacks, number of tablets used to treat 1 attack); (2) varying input costs; and (3) uncertainty in the efficacy and tolerability estimates from the meta-analysis. In all of these sensitivity analyses, almotriptan 12.5 mg remained cost effective compared with sumatriptan 50 mg and 100 mg.

CONCLUSION: Almotriptan was economically superior to sumatriptan in the treatment of a migraine attack.

KEYWORDS: Migraine, Triptans, Almotriptan, Cost effective, Sumatriptan

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Migraine causes substantial patient suffering and high costs to managed care organizations and employers.[1] Triptans (5-$HT_{1B/1D}$ receptor agonists) are effective and relatively safe for the acute treatment of migraine. Initial treatment with a triptan is recommended when the migraine is judged moderate to severe or in migraine of any severity when nonsteroidal anti-inflammatory drugs and combination analgesics have failed to relieve symptoms.[2]

Acute treatment of migraine with sumatriptan, the first available triptan,[3] has been shown to reduce migraine-related health care utilization.[4-6] For example, Lofland et al. showed significant reductions in the mean number of migraine-related physician office visits, emergency department visits, and medical procedures in the 6 months after sumatriptan therapy compared with the 6 months before sumatriptan was used.[6] They also showed that initiation of sumatriptan in patients previously treated with nontriptan therapy was cost effective and had an economic benefit for patients, employers, and society.[7]

Almotriptan was introduced in the United States in 2001 and has been shown to be efficacious and well tolerated in placebo-controlled clinical trials.[8-10] Direct comparative trials of sumatriptan and almotriptan have shown that these agents have similar efficacy for relieving migraine pain but that almotriptan 12.5 mg was associated with a significantly lower rate of adverse events compared with sumatriptan 50 mg (including a specific comparison for chest pain) and 100 mg.[11,12] A meta-analysis of data from 53 placebo-controlled trials of oral triptans found that a significantly greater proportion of patients achieved a sustained pain-free state with almotriptan 12.5 mg compared with sumatriptan 100 mg.[13,14] Almotriptan 12.5 mg also had a significantly lower rate of all adverse events, chest adverse events, and central nervous system adverse events than sumatriptan 100 mg.[13,14] Key results from this meta-analysis, for almotriptan and sumatriptan, are shown in Table 1.

In the present study, we use results from this meta-analysis to compare the cost-effectiveness of almotriptan with that of sumatriptan from a U.S. health care payer perspective.

Methods

Approach

We developed a model to compare the cost-effectiveness of almotriptan 12.5 mg and 2 dose levels of sumatriptan (50 mg and 100 mg) in the treatment of a single migraine attack from a U.S. health care payer perspective. Cost-effectiveness ratios

TABLE 1 Summary of Relevant Results From Ferrari et al.'s Meta-analysis[13]

	Almotriptan 12.5 mg	Sumatriptan 50 mg	Sumatriptan 100 mg
Number of patients	719	1,661	3,054
Absolute 2 hour headache response rate	61% (95%CI 58%-65%)	63% (95%CI 60%-65%)	59% (95%CI 57%-61%)
Absolute 2 hour pain-free rate	36% (95%CI 32%-39%)	29% (95%CI 27%-31%)	29% (95%CI 27%-31%)
Absolute sustained pain-free rate	26% (95%CI 23%-29%)	20% (95%CI 18%-22%)	20% (95%CI 18%-21%)
Absolute recurrence rate	26% (95%CI 22%-30%)	28% (95%CI 25%-31%)	30% (95%CI 27%-33%)
Placebo-corrected adverse event rate—CNS events	-1.5% (95%CI –3.9%-1.0%)	3.7% (95%CI 1.0%-6.4%)	6.3% (95%CI 3.2%-9.5%)
Placebo-corrected adverse event rate—chest events	-0.4% (95%CI –1.6%-0.8%)	1.9% (95%CI 0.4%-3.3%)	1.7% (95%CI 0.8%-2.5%)
Placebo-corrected adverse event rate—all events	1.8% (95%CI –2.7%-6.2%)	7.8% (95%CI (2.6%-13.1%)	13.2% (95%CI 8.6%-17.8%)

CNS = central nervous system.

FIGURE 1 Relationship Between Efficacy and Tolerability

Tolerability \ Efficacy	Sustained Pain Free YES (spf)	Sustained Pain Free NO (1-spf)	
Adverse Events YES (ae)	a (spf-SNAE)	b (ae-[spf-SNAE])	
Adverse Events NO (1-ae)	c (SNAE)	d (1-ae-SNAE)	

(CERs) were calculated as appropriate, and the robustness of the cost-effectiveness comparisons was tested in a range of sensitivity analyses.

Effectiveness

We used a composite "unqualified success" measure[15] as the primary index of effectiveness in this study, i.e., the proportion of patients who achieved sustained freedom from pain (defined as pain free at 2 hours after taking medication with no recurrence of moderate or severe headache and no rescue medication 2 to 24 hours postdose) without experiencing adverse events. We called this end point SNAE (**S**ustained pain free and **N**o **A**dverse **E**vents).

Data on sustained pain-free and adverse event rates were obtained from Ferrari et al.'s meta-analysis of 53 double-blind, randomized, controlled, clinical trials of oral triptans.[13,14] These included data on 719 patients treated with almotriptan and 4,715 patients treated with sumatriptan in placebo-controlled trials. Sustained pain-free and adverse event rates are the marginal totals in Figure 1, so the value of SNAE can be calculated only if the relationship between efficacy and tolerability is known or can be assumed. For the base case, efficacy and tolerability were assumed to be independent so that:

$$SNAE = (\text{sustained pain-free rate})(1-[\text{adverse event rate}])$$

The impact of relaxing this independence assumption was explored in the sensitivity analysis, as the true nature of the relationship between efficacy and tolerability of triptan treatment is not known.

Absolute rates are more appropriate than placebo-corrected rates for cost-effectiveness analysis, as the placebo effect is a component of real-world effectiveness. Ferrari et al. published absolute sustained pain-free rates but only placebo-corrected, and not absolute, adverse event rates.[13,14] The placebo adverse event rates from the same meta-analysis, published elsewhere,[16] were therefore added to the placebo-corrected rates to result in estimated absolute adverse event rates for almotriptan and sumatriptan.

Costs

The perspective taken for this analysis was that of a U.S. health care payer, so only direct medical care costs were included. Migraine-related health service use costs were obtained from Hu et al.'s study of the economic burden of migraine in the United States.[1] It was assumed in the base case that these costs could be apportioned uniformly across attacks, so the estimated cost per attack was obtained by dividing the annual per-migraineur health service use costs (physician visits, emergency room attendance, hospitalization) by the annual attack frequency from Hu et al.[1] In the base case, these costs were assumed to be uninfluenced by choice of triptan (an assumption that acts in favor of sumatriptan [which has higher adverse event rates than almotriptan; see Table 1], and is therefore conservative with respect to the cost-effectiveness comparison). This study was conducted in 1999, so their costs have been inflated by 3%[17] for each of the 5 intervening years.

Another base-case assumption was that a migraine attack was treated with 1 tablet, which is consistent with the conditions under which the efficacy and adverse event data were collected (the impact of relaxing the "1 tablet per attack" assumption was explored in the sensitivity analysis). On this basis, estimates for the total direct cost per attack were obtained by adding the drug acquisition cost ($ per tablet) to the estimated health service use cost per attack. The cost per tablet of each

triptan was obtained from http://www.drugstore.com,[18] (whose prices more closely approximate to actual managed care pharmacy prices than average wholesale prices), and take into account the January 2004 price rise for almotriptan.

Sensitivity Analyses

Relationship Between Efficacy and Tolerability

The calculation of SNAE in the base-case analysis assumed efficacy and tolerability to be independent. In sensitivity analyses, odds ratios (OR) were specified for the relationship between efficacy and tolerability (ranging from OR = 0.1 [strongly negative relationship] to OR = 10 [strongly positive relationship]), SNAE was calculated by the method described in Figure 2, and CERs were calculated across this 100-fold range for the strength and direction of the efficacy/tolerability relationship.

Health Service Use Costs

In the base case, health service use costs were apportioned uniformly across attacks. Patients responding to treatment with an oral triptan, however, are unlikely to incur emergency room attendance and hospitalization costs. Therefore, the analyses were repeated assuming that these costs would be incurred only by patients not achieving sustained freedom from pain. Sustained pain-free rates were different for almotriptan and sumatriptan and, consequently, health service use costs were different. Thus, this analysis tested the effect of relaxing the assumption that health service use costs were the same irrespective of triptan choice.

Tablets per Attack

As the analysis was based on clinical trials data, it was assumed that an attack was treated with 1 tablet (of almotriptan or sumatriptan) in the base case. The impact of relaxing this assumption was explored separately for positive, negative, and independent relationships between efficacy and tolerability.

Impact of Uncertainty in the Efficacy and Tolerability Estimates From the Meta-analysis

An OR for the efficacy/tolerability relationship was first specified. Then the values and confidence intervals from the meta-analysis were used to calculate standard deviations for SNAE. The variance of SNAE was estimated using Haugen's approximation for the variance of a product of 2 variables (cited by Luttinen).[19] Next, these standard deviations were used in a Monte Carlo model to define distributions from which 10,000 triplets of values for SNAE (for almotriptan and sumatriptan 50 mg and 100 mg) were drawn and then used to calculate CERs. Finally, the exact probability that almotriptan was cost effective (compared with the 2 dose levels of sumatriptan) was assessed across the 10,000 iterations. This was done 7 times, for different values of the OR for the relationship between efficacy and tolerability (ranging from strongly negative, OR = 0.1, to strongly positive, OR = 10).

FIGURE 2 *Calculating the Value of SNAE When Efficacy and Tolerability Are Not Independent*

In the notation of Figure 1, the odds ratio (OR) that defines the relationship between efficacy and tolerability is

$$OR = (a/c)/(b/d) = ad/bc \quad [1]$$

Cells a, b, c, and d in Figure 1 can be expressed in terms of the adverse event rate (ae), the sustained pain-free rate (spf), and SNAE, i.e.,

$a = spf\text{-}SNAE$

$b = ae\text{-}(spf\text{-}SNAE) = ae\text{-}spf+SNAE$

$c = SNAE$

$d = 1\text{-}ae\text{-}SNAE$

Substituting these into equation [1] gives

$$OR = (spf\text{-}SNAE)(1\text{-}ae\text{-}SNAE)/([ae\text{-}spf+SNAE]SNAE) \quad [2]$$

Equation [2] can be manipulated to give a quadratic equation, as follows:

$$OR = (spf\text{-}SNAE)(1\text{-}ae\text{-}SNAE)/(ae*SNAE\text{-}spf*SNAE+SNAE^2)$$

$$OR = (spf\text{-}spf*ae\text{-}spf*SNAE\text{-}SNAE+SNAE*ae+SNAE^2)/(ae*SNAE\text{-}spf*SNAE+SNAE^2)$$

$$OR(ae*SNAE\text{-}spf*SNAE+SNAE^2) = spf\text{-}spf*ae\text{-}spf*SNAE\text{-}SNAE+SNAE*ae+SNAE^2$$

$$OR*ae*SNAE\text{-}OR*spf*SNAE+OR*SNAE^2 = spf\text{-}spf*ae\text{-}spf*SNAE\text{-}SNAE+SNAE*ae+SNAE^2$$

$$0 = OR*ae*SNAE\text{-}OR*spf*SNAE+OR*SNAE^2\text{-}spf+spf*ae+spf*SNAE+SNAE\text{-}SNAE*ae\text{-}SNAE^2$$

$$0 = (OR-1)SNAE^2+(OR*ae\text{-}OR*spf+spf+1\text{-}ae)SNAE - spf(1\text{-}ae) \quad [3]$$

Equation [3] can be rewritten as

$$0 = x*SNAE^2+y*SNAE+z, \text{ where} \quad [4]$$

$x = OR-1$

$y = OR*ae\text{-}OR*spf+spf+1\text{-}ae$

$z = -spf(1\text{-}ae)$

Using the standard approach to solving a quadratic equation, SNAE can be found by solving equation [4] with any value for OR and with known values of spf and ae, as follows

$$SNAE = (-y \pm \sqrt{[y^2-4xz]})/2x \quad [5]$$

Equation [5] has 2 solutions, $(-y-\sqrt{[y^2-4xz]})/2x$ and $(-y\sqrt{[y^2-4xz]})/2x$. The solution that conforms to the condition $0 < \text{solution} < \min(spf,ae)$ is the value of SNAE.

Results

Effectiveness

Sustained pain-free rates and adverse event rates for almotriptan 12.5 mg, sumatriptan 50 mg, and sumatriptan 100 mg obtained from the meta-analysis[13,14] are shown in Table 2. The table also shows the values for SNAE calculated under the base-case assumption that efficacy and tolerability are independent.

Costs

Table 3a shows health service use costs ($ per migraineur per year) taken from Hu et al.'s analysis of the burden of migraine

TABLE 2 Calculation of SNAE

	Almotriptan 12.5 mg	Sumatriptan 50 mg	Sumatriptan 100 mg
[a] Absolute sustained pain-free rate[14]	25.9%	19.8%	20.0%
[b] Placebo-corrected adverse event rate—all events[14]	1.8%	7.8%	13.2%
[c] Placebo adverse event rate—all events[15]	12%	27%	27%
[d]=[b]+[c] Calculated absolute adverse event rate—all events	13.8%	34.8%	40.2%
[a]*(1-[d]) Base-case SNAE	22.3%	12.9%	12.0%

TABLE 3A Health Service Use Costs ($per Migraineur per Year, 1999)[1]

	Men	Women
Physician visits	$59.34	$53.90
Emergency room attendance	$0.13	$0.34
Hospitalization	$5.94	$15.75
Total health service use costs/migraineur/year	$65.41	$69.99
Annual frequency of migraine attacks	34.0	37.4
Health service use costs/attack	$1.92	$1.87
Gender-weighted average cost per attack	$1.88	

TABLE 3B Total Direct Costs per Attack ($ per Attack, 2004 Prices)

	Almotriptan 12.5 mg	Sumatriptan 50 mg	Sumatriptan 100 mg
Health service use costs/attack	$ 2.18	$ 2.18	$ 2.18
Drug acquisition cost ($/tablet)[18]	$16.05	$14.96	$14.41
Total direct costs/attack	$18.23	$17.14	$16.59

TABLE 4 Base Case Cost-Effectiveness

	Almotriptan 12.5 mg	Sumatriptan 50 mg	Sumatriptan 100 mg
Total direct costs/attack (from Table 2)	$18.23	$17.14	$16.59
Base-case SNAE (from Table 1)	22.3%	12.9%	12.0%
Average CER ($ per SNAE)	$18.23/22.3% = $81.75	$17.14/12.9% = $132.87	$16.59/12.0% = $138.25
Incremental CER ($ per additional SNAE)	cf. sumatriptan 50 mg: $11.60 cf. sumatriptan 100 mg: $15.92	–	–

in the United States.[1] In their analyses, Hu et al. used average annual attack frequencies of 34.0 for men and 37.4 for women obtained from Stewart et al.[1,20] Applying these frequencies to the data in Table 3a gives $1.92 as the average health service use cost per attack for men and $1.87 for women. The weighted average of these gender-specific costs (weighted for the relative frequency of treated migraine attacks, based on data in Hu et al.)[1] was $1.88: inflating this figure by 3% per year for 5 years gives $2.18, the figure used in the cost-effectiveness analysis.

Table 3b shows the www.drugstore.com price of the triptans[18] and the total direct costs incurred in treating an attack (under the base-case assumption of 1 tablet per attack).

Base Case Cost-Effectiveness

The unit of measurement for the CERs in this analysis (Table 4) is cost in 2004 dollars per attack at which SNAE is achieved following triptan treatment. For convenience, this will be referred to as $ per SNAE.

Average CERs

Table 4 shows that the average CER for almotriptan 12.5 mg was $81.75 per SNAE ($18.23 [from Table 3b] divided by 22.3% [from Table 2]). Corresponding calculations for sumatriptan 50 mg and sumatriptan 100 mg yield average CERs of $132.87 and $138.25 per SNAE, respectively.

Consider that $10,000 is available to be spent on treating migraine with either almotriptan or sumatriptan. With almotriptan, approximately 548 attacks ($10,000/$18.23 [Table 3b]) could be treated. SNAE would be achieved in 22.3% of these attacks (Table 2). Therefore, spending $10,000 on treating migraine with almotriptan 12.5 mg would result in approximately 122 successfully treated attacks ($10,000/$18.23*22.3%), at a cost of $81.75 per success (the average CER set out above). With sumatriptan 50 mg, approximately 583 attacks ($10,000/$17.14) would be treated. SNAE would occur in 12.9%, so spending $10,000 on this treatment would result in approximately 75 successes ($10,000/$17.14*12.9%) at a cost of $132.87 each. Spending the equivalent resource on treating migraine with sumatriptan 100 mg would result in approximately 72 ($10,000/$16.59*12.0%) successes at a cost of $138.25 each.

While the focus of our analysis was on SNAE, we recognize that this composite efficacy-tolerability end point is the most stringent of a hierarchy of efficacy end points, and will therefore be achieved in only a minority of patients. For completeness, therefore, Table 5 shows the hierarchy of end points and for each endpoint, the number of successes that can be purchased for $10,000 (calculated as described above, using rates from Table 1).

Incremental CER for Almotriptan

Compared with sumatriptan 50 mg, the incremental cost-effectiveness ratio of almotriptan 12.5 mg was ($18.23-

17.14)/(22.3%-12.9%) = $11.60 per additional SNAE; the corresponding figure for the comparison with sumatriptan 100 mg was ($18.23-16.59)/(22.3%-12.0%) = $15.92 per additional SNAE. These incremental CERs are substantially smaller than the average CERs for sumatriptan, so in the base case, according to the principle of extended dominance, almotriptan 12.5 mg was economically superior to both strengths of sumatriptan.

Sensitivity Analyses

Relationship Between Efficacy and Tolerability

The calculation of SNAE in the base case assumed independence between efficacy and tolerability. Values for SNAE and for the CERs were recalculated assuming positive relationships between sustained pain-free and adverse events (responders more likely to experience adverse events) and then assuming negative relationships (responders less likely to experience adverse events).

Figure 3 shows average and incremental CERs calculated across the range of assumptions for the relationship between efficacy and tolerability (strongly negative, OR = 0.1, to strongly positive, OR = 10). The average cost per SNAE was always greater with sumatriptan (both dose levels) than with almotriptan. In incremental analyses, almotriptan remained cost effective (according to the principle of extended dominance) over both dose levels of sumatriptan across the entire range tested.

Health Service Use Costs

Health service use costs were apportioned equally across attacks in the base case. Treatment-responsive patients are unlikely to attend emergency rooms or be hospitalized. The analyses were repeated assuming health service use costs were incurred only by patients not achieving sustained freedom from pain. In this analysis, health service use costs and sustained pain-free rates were different for almotriptan and sumatriptan. The impact was trivial; in all cases (OR for the efficacy/tolerability relationship ranging from 0.1 to 10), the impact on the CERs was less than $1 per SNAE. We made no attempt to account for possible differences in health service use costs attributable to treatment of adverse events—not doing so favors sumatriptan (i.e., the cost-effectiveness comparison is conservative), as any such adjustment would favor almotriptan, due to its lower adverse event rate.

Tablets per Attack

The base-case assumption was that attacks were treated with a single tablet only, which is appropriate, given that effectiveness was based on clinical trials data. The economic advantage of almotriptan would be reduced if, in the real world, more almotriptan than sumatriptan tablets were used to treat a given attack. In this sensitivity analysis, we held the number of sumatriptan tablets constant (=1) and increased the number of almotriptan tablets (per attack) to identify the threshold at which the 2 treatments became equivalently cost effective.

TABLE 5 Successes Purchased for $10,000

Efficacy variable	Almotriptan 12.5 mg	Sumatriptan 50 mg	Sumatriptan 100 mg
SNAE	122	75	72
Sustained freedom from pain	142	116	120
Freedom from pain at 2 hours	197	169	174
Headache response at 2 hours	334	367	355

FIGURE 3 Sensitivity Analysis: Relationship Between Efficacy and Tolerability

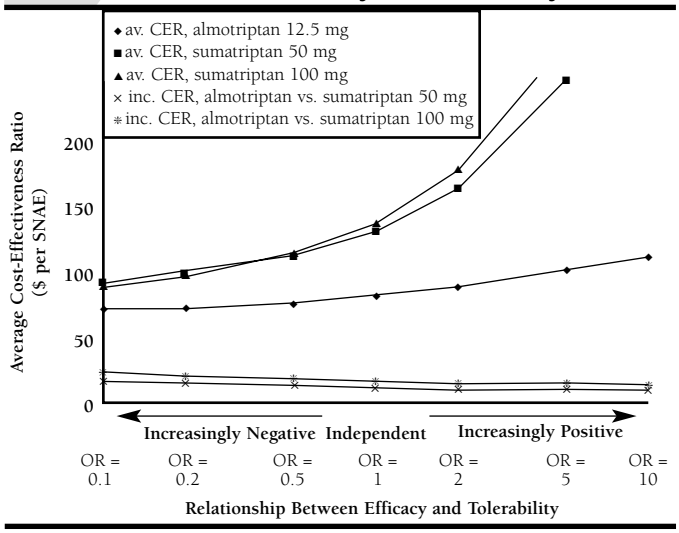

TABLE 6 Sensitivity Analysis: Number of Tablets Used to Treat an Attack

Efficacy/Tolerability Relationship	Threshold Number of Tablets of Almotriptan 12.5 mg at Which Almotriptan and Sumatriptan (1 tablet) Become Equivalently Cost Effective	
	cf. Sumatriptan 50 mg	cf. Sumatriptan 100 mg
Negative (OR = 0.1)	1.3	1.3
Independent (OR = 1)	1.7	1.8
Positive (OR = 10)	3.6	4.3

These thresholds are seen in Table 6.

Impact of Uncertainty in the Efficacy and Tolerability Estimates

As described earlier, the exact probability that almotriptan 12.5 mg was economically superior to sumatriptan was

estimated, taking uncertainty in the efficacy and tolerability estimates from the meta-analysis into account. These exact probabilities, which can be interpreted as levels of confidence in the result,[21] exceeded 99% across the entire range of efficacy/tolerability relationships tested (from strongly negative, OR = 0.1, to strongly positive OR = 10), for both strengths of sumatriptan.

Discussion

Of the few comparisons of the cost-effectiveness of triptans in the literature, most are based on drug acquisition costs rather than health care resource utilization. Gerth et al. compared the cost per successful treatment using data from 5 randomized controlled trials of rizatriptan 10 mg versus sumatriptan 50 mg or 100 mg, naratriptan 2.5 mg, or zolmitriptan 2.5 mg in acute migraine.[22] Rizatriptan had a lower cost per successful treatment, defined as pain free at 2 hours with no functional disability or associated symptoms. Another study used clinical data from a randomized, double-blind trial of eletriptan 40 mg or 80 mg and sumatriptan 50 mg or 100 mg to perform a cost-effectiveness analysis.[23] Based on drug acquisition costs in the United Kingdom, both strengths of eletriptan were associated with a lower cost than sumatriptan. Similar to our analysis, the efficacy measure was the sustained pain-free rate, but adverse events were not considered.

Reeder et al.[24] combined data from the meta-analysis[13,14] and drug acquisition costs to determine the cost of attaining 100 sustained pain-free patients with and without adverse events. Almotriptan 12.5 mg was the most cost-effective triptan on both measures. Rothermich et al. performed a cost minimization analysis of almotriptan 12.5 mg and sumatriptan 50 mg.[25] Clinical and resource utilization data were collected from a randomized, double-blind trial of both drugs in acute migraine patients. Among 1,073 patients, health care system costs were significantly lower with almotriptan than with sumatriptan.

Adelman and Belsey[26] conducted their own meta-analysis of triptan treatment trials, focusing on the number needed to treat to achieve freedom from pain within 2 hours. They then used this as the basis for a cost-effectiveness comparison in which almotriptan 12.5 mg and rizatriptan 10 mg were found to be the most cost effective of the triptans.

In this present study, we compared the cost-effectiveness of almotriptan 12.5 mg and sumatriptan 50 mg and 100 mg using a composite measure of effectiveness—SNAE. Sumatriptan was selected for comparison because it is the most widely prescribed oral triptan in the United States and also was used as the standard for comparison in the meta-analysis of triptans.[13,14] We selected sustained pain free as the efficacy component because it has been described as the ideal measure for assessing response to acute migraine therapy.[27] It is also consistent with what patients desire from treatment because it incorporates features of rapid onset of action, freedom from pain, and absence of recurrence.[28] Freedom from adverse events is also important to patients,[29] hence the composite measure SNAE.

The average CERs for almotriptan 12.5 mg, sumatriptan 50 mg, and sumatriptan 100 mg were $82, $132, and $139 per SNAE, respectively. For decision makers in managed care who administer plans covering thousands of patients who suffer from acute migraine, $10,000 invested in treatment of migraine with a triptan would yield 122 successes (attacks at which SNAE is achieved following triptan treatment) with almotriptan, compared with 75 and 72 successes with the 2 strengths of sumatriptan (50 mg and 100 mg, respectively).

Studies such as this are, in general, constrained by 3 kinds of limitations—those imposed by the data, those imposed by the assumptions, and those inherent in the analytic methods. We have attempted to keep these limitations to a minimum. Our data have come only from published sources. Hu et al.'s study of migraine-related health care costs is comprehensive, population-based, and reasonably up-to-date.[1] Ferrari et al.'s meta-analysis of placebo-controlled triptan treatment trials is the most comprehensive synthesis of currently available knowledge in this area, and analyses of this kind are at the apex of the hierarchy of evidence.[30] However, by using data from published sources only, we were constrained by the analyses and interpretations provided in these publications. For this reason, we were constrained to using placebo-subtracted rates for adverse events from the meta-analysis and had to calculate absolute rates (we should emphasize, however, that all the rates used in this calculation came from the same meta-analysis). The difference in placebo adverse event rates between almotriptan and sumatriptan is perhaps worthy of comment, although the authors of the meta-analysis offer no explanation, except that "there were no differences in study design or population to explain these differences."[16]

Clearly, the key assumption is that concerning the relationship between efficacy and tolerability, an issue at the heart of the principal limitation inherent in the analytic method (the calculation of SNAE from sustained pain-free and adverse event rates). In the sensitivity analysis, the economic superiority of almotriptan increases as the efficacy/tolerability relationship tends to the positive and decreases as it tends to the negative (although almotriptan remained superior across the 100-fold range tested). Little is known, however, about the true nature of the efficacy/tolerability relationship, so the results of further research on this topic are awaited with interest.

Conclusion

Within the limitations discussed here, we conclude that almotriptan 12.5 mg is more cost effective than either sumatriptan 50 mg or 100 mg in the acute treatment of a migraine attack, a finding that is robust in a range of sensitivity analyses. These findings should help decision makers in managed care and those engaged in designing drug formularies, for whom balancing optimal care with value for money is an ongoing challenge.

DISCLOSURES

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