Drug Class Review

Triptans

Final Report
Update 4
Evidence Tables

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The literature on this topic is scanned periodically.

The purpose of this report is to make available information regarding the comparative effectiveness and safety profiles of different drugs within pharmaceutical classes. Reports are not usage guidelines, nor should they be read as an endorsement of, or recommendation for, any particular drug, use, or approach. Oregon Health & Science University does not recommend or endorse any guideline or recommendation developed by users of these reports.

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TABLE OF CONTENTS

The medical literature relating to this topic is scanned periodically. (See http://www.ohsu.edu/ohsuedu/research/policycenter/DERP/about/methods.cfm for description of scanning process). Prior versions of this report can be accessed at the DERP website.

Evidence Table 1. Characteristics of head-to-head trials

Author Year	Design	Setting	Number randomized	Age Gender Ethnicity	Patients	Inclusion criteria
Bomhof 1999	Multicenter single-dose RCT conducted in Europe of naratriptan vs. rizatriptan	Not stated	618	39 years 84% female 82% white 17% Hispanic	I H S criteria 18-65 men and women	6-month history of migraine; 1-8 reports per month; no evidence of CVD or of drug or alcohol abuse; pregnant or nursing
Carpay 1997	Open, randomized, cross-over	Patients treated themselves at home	124	Mean age=38.9 81% female	Male or female adults, aged 18-65 years that met IHS criteria for migraine	At least 1 year with 1-6 attacks/month adequate contraception

Evidence Table 1. Characteristics of head-to-head trials

Author Year	Exclusion criteria	Funding sources and role of funder	Other medications	Number screened/ eligible/ enrolled
Bomhof 1999	H.O cva, cardiovascular disease, significant ecg abnormality, history or drug or alcohol use, past use of study drugs	Merck, co-investigator (maker of rizatriptan)	Permitted	NR
Carpay 1997	Known narcotic/alcohol abuse ergotamine abuse pregnancy, breast-feeding history of ECG evidence of ischaemic heart disease significant concomitant disease significant psychiatric illness known hypersensitivity to/intolerance of sumatriptan current use of fluarizine	Glaxo	NR	142/124/124

Evidence Table 1. Characteristics of head-to-head trials

Author Year	Number withdrawn/ lost to follow-up
Bomhof 1999	96 (did not take study medication)
Carpay 1997	NR/NR

Evidence Table 1. Characteristics of head-to-head trials

Author Year	Design	Setting	Number randomized	Age Gender Ethnicity	Patients	Inclusion criteria
Charlesworth 2003	Multicentre, DB, Double-dummy, parallel, placebo	42 centers in 11 countries	1547	Mean age=19.2 74% female	Male or female adults, aged 18-65 years that met IHS criteria for migraine with or without aura,	1 year history of migraine, age <50 onset able to distinguish migraine vs non-migraine 1-6 migraines per month
Colman, 2001 Spierings, 2001	Multicenter, single-dose RCT conducted in the US of almotriptan vs sumatriptan	NR	1255	40.7 years 89% female Race NR	Men and women between 18 and 65 years; at least a 6-month migraine history (IHS criteria)	An average of at least 2 moderate or severe migraine headaches per month during the preceding 3 months, with an interval of at least 24 hours between consecutive attacks

Evidence Table 1. Characteristics of head-to-head trials

Author Year	Exclusion criteria	Funding sources and role of funder	Other medications	Number screened/ eligible/ enrolled
Charlesworth 2003	History of basilar, ophthalmoplegic migraine reported non-migraine > 10 days/month 6 months before study pregnancy, lactation, inadequate conception in women ischaemic heart disease, arrhythmias/cardiac accessory uncontrolled hypertension, use of monoamine oxidase-A inhibitors, methylergometrine within 2 weeks of study clinically significant abnormal laboratory result recent history of drug/alcohol abuse known hypersensitivity/adverse reaction to study treatments/triptans existing serious medical condition participation in another clinical study at same time of this study risk of transmitting Hep B/HIV	AstraZeneca	NR	1547/1383/1372
Colman, 2001 Spierings, 2001	Subjects could not have uncontrolled hypertension, defined as a diastolic blood pressure higher than 95 mm Hg or a systolic blood pressure higher than 160 mm Hg, or clinically significant disease affecting any system but especially the cardiovascular or gastrointestinal tract	Pharmacia	Rescue medications allowed at 2 hours	NR/NR/1255

Evidence Table 1. Characteristics of head-to-head trials

Author Year	Number withdrawn/ lost to follow-up
Charlesworth 2003	66/8
Colman, 2001	NR/NR
Spierings, 2001	

Evidence Table 1. Characteristics of head-to-head trials

Author Year	Design	Setting	Number randomized	Age Gender Ethnicity	Patients	Inclusion criteria
Diez 2007	Multicenter, randomized, open, crossover	NR	436	Mean age: 36.3 years 85.8% Female 99.7% White	Male or female adults, aged 18-65 years who met IHS criteria for migraine	At lest 6 month history of migraine, migrain onset prior to age 50, triptan naïve, average frequency of 2 to 6 migraine attacks per month
Dowson 2007	Randomized, open, crossover	NR	48	Mean age: 44.7 years White: 100% Female: 85.4%	Male or female adults, aged 18 to 65 years who met IHS criteria for migraine	History of 1 to 4 migraine attacks/month, minimum of 24 hours between each attack, able to distinguish migraine from other types of headaches
Dowson, 2002 Cabarrocas, 1998	Multicenter, single-dose RCT conducted in Europe of almotriptan vs sumatriptan	Primary care	668	41.8 years 84.9% female Race NR	IHS criteria; 18-65 men and women; 1 year history	1-6 attacks/month; age of onset of less than 50 years and at least 24 h free from headache between attacks

Evidence Table 1. Characteristics of head-to-head trials

Author Year	Exclusion criteria	Funding sources and role of funder	Other medications	Number screened/ eligible/ enrolled
Diez 2007	Complex forms of migraine, pregnancy, lactation, hypersensitivity to any component of the study medications, history signs or symptoms of ischemic heart disease, cerebrovascular accidents, transient ischemic attack or peripheral vascular disease.	Almirall Prodesfarma	Rescue medication permitted (NSAIDs)	NR/436/372
Dowson 2007	Pregnant or breastfeeding women, contraindications to receiving zolmitriptan, history of significant psychiatric or other significiant illness, previous abuse of ergotamine, triptans, alcohol, or other recreational drugs	AstraZeneca	NR	NR/NR/48
Dowson, 2002 Cabarrocas, 1998	Migraine with prolonged aura; familial hemiplegic migraine; migrainous infarction; vertebrobasilar migraine or Raynaud's phenomenon associated with migraine; any other significant medical condition; cardiovascular disease (cardiac ischaemia, atherosclerosis, cardiac arrhythmia or hypertension); alcoholism; drug abuse or mental retardation	Laboratorios Almirall SA	Prophylactic medication as chosen by investigator (valproic acid, beta blockers, calcium antagonists) allowed if migraine pain did not disappear or become mild within 2 hours of treatment	NR/NR/668

Evidence Table 1. Characteristics of head-to-head trials

Author Year	Number withdrawn/ lost to follow-up
Diez 2007	54/10
Dowson 2007	20/0
Dowson, 2002	8(1.2%)
Cabarrocas, 1998	withdrawals/lost to fu NR

Evidence Table 1. Characteristics of head-to-head trials

Author Year	Design	Setting	Number randomized	Age Gender Ethnicity	Patients	Inclusion criteria
Gallagher 1999, 2000	Multicenter, multiple-dose analysis of DB RCT, 6 month study; conducted in Europe of zolmitriptan vs. sumatriptan.	Not stated	1212	39 years 85% female race/ethnicity not reported	IHS criteria; 1 year history of migraine	For women, use of reliable contraception. Patients who had 2 or more migraines included in the analysis.
Garcia-Ramos 2003 UK/Latin America Fair quality	Multicenter, single-attack, DB RCT conducted in the UK and Latin America Eletriptan vs encapsulated naratriptan	Not stated	548	Mean age=36.8 81% female Ethnicity NR	Male or female adults, aged 18-80 years that met IHS criteria for migraine with or without aura	A minimum of 1 acute migraine attack every 6 weeks

Evidence Table 1. Characteristics of head-to-head trials

Author Year	Exclusion criteria	Funding sources and role of funder	Other medications	Number screened/ eligible/ enrolled
Gallagher 1999, 2000	H/o ischemic heart disease, arrhythmia, hypertension, some types of migraine; drug or alcohol abuse, abnormal lab tests	Zeneca, co-investigator	Some permitted	NR
Garcia-Ramos 2003 UK/Latin America Fair quality	1) Coronary artery disease, heart failure, uncontrolled hypertension or abnormal ECG; 2) frequent migraine or concommitant nonmigrainous headache (<6 per month), migraine variants (e.g. familial hemiplegic or basilar migraine), and/or migraines which, in the clinical judgement of the investigator, had consistently failed to respond to adequate medical therapy; 3) hypersensitivity or known contra-indication to treatment with elatriptan or naratriptan; 4) concommitant use of potent CYP3A4 inhibitors or use of MAO inhibitors in the 2 weeks prior to study entry; 5) any clinically significant medical illness or laboratory abnormalities; 6) severe reduction in gastrointestinal absorption; 7) misuse or abuse of alcohol or other substances, including analgesics or egotamine; 8) use of any experimental drug within the past month; 9) (if female) current pregnancy, breast-feeding, or not using a medically accepted form of contraception	Pfizer	Rescue medication allowed by 4 hours post-dose (excluding any other triptan, ergotamine, or ergotamine-like substance)	563 screened/548 randomized/483 treated an attack

Evidence Table 1. Characteristics of head-to-head trials

Author Year	Number withdrawn/ lost to follow-up
Gallagher 1999, 2000	233 who had only 1 headache
Garcia-Ramos 2003 UK/Latin America Fair quality	65 not treated/4 withdrawn/1 (0.2%) lost to fu/459 (95%) analyzed at 1 hr; 464 (96%) analyzed at 2 hr

Evidence Table 1. Characteristics of head-to-head trials

Author Year	Design	Setting	Number randomized	Age Gender Ethnicity	Patients	Inclusion criteria
Geraud 2000	Multicenter, single-dose DB RCT conducted in Europe and Australia of zolmitriptan vs. sumatriptan vs. placebo in 8:8:1 ratio	Outpatient	1311	38 years 85% female race/ethnicity not reported	IHS criteria; 1 year history of migraine	Average of 1-6 attacks per month for the 6 months preceding the study.
Goadsby 2007	Multicenter, randomized, DB, parallel	NR	1061	Mean age: 39.5 years 85% Female 99% White	Male or female adults aged 18 to 65 years who met IHS criteria for migraine	1 year history of migraine, age <50 onset, 2 to 6 migraine attacks/month
Goadsby, 2000 Jackson, 1998	Multicenter, single-attack, DB RCT conducted in Europe and Australia Eletriptan vs encapsulated sumatriptan	NR	849	40.4 years 82.1% female Race NR	IHS criteria; 18 years of age or older	At least one acute attack every 6 weeks

Evidence Table 1. Characteristics of head-to-head trials

Author Year	Exclusion criteria	Funding sources and role of funder	Other medications	Number screened/ eligible/ enrolled
Geraud 2000	H/o ischemic heart disease, arrhythmias, uncontrolled hypertension, use of psychoactive drugs, history of drug or alcohol abuse; certain types of migraine; any condition that could interfere with efficacy assessments, pregnant or breastfeeding	Maker of zolmitriptan, co-investigator	Permitted	NR
Goadsby 2007	Hemiplegic or basilar migraine, tension-type headache >4 days/month, inability to distinguish between tension-type and migraine headache, history of ischaemic heart disease, severe or uncontrolled hypertension, cerebrovascular disease, peripheral artery disease, moderate to severe renal or hepatic disease, pregnancy, lactation, history of abuse of analgesics or ergot derivatives or triptans, allergy or sensitivity to sulfonamides or triptans	Almirall Prodesfarma	Rescue medication (other than triptans) was permitted	NR/NR/1298
Goadsby, 2000 Jackson, 1998	>6 migraine attacks per month, frequent tension-type headaches, recent history of alcohol or other substance misuse, serious allergic reactions to drugs, use of any experimental drug within the past month, pregnant or breastfeeding women, severely limited gastrointestinal absorption, any medical condition that might interfere with the interpretations of the study results, coronary artery disease, heart failure, uncontrolled hypertension, and receiving medication specifically contraindicated with sumatriptan	Pfizer, Ltd.	Rescue medication allowed after 2 hours	NR/NR/857

Evidence Table 1. Characteristics of head-to-head trials

Author Year	Number withdrawn/ lost to follow-up
Geraud 2000	253; 225 did not take medication, 28 were lost to follow-up
Goadsby 2007	122/NR
Goadsby, 2000	157/849 (18.5%) not treated; 17/692(2.4%) withdrawn; lost to fu
Jackson, 1998	NR

Evidence Table 1. Characteristics of head-to-head trials

Author Year	Design	Setting	Number randomized	Age Gender Ethnicity	Patients	Inclusion criteria
Gruffyd-Jones 2001	Multicenter, double-dummy RCT conducted in 21 countries of zolmitriptan vs. sumatriptan.	Not stated	1787	42 years 86% female 96% white	IHS criteria 18-65 men and women; 1 year history of migraine with age of onset < 50	Average of 1-6 attacks per month for 2 months preceding the study.
Havanka 2000	Multicenter single-dose DB RCT conducted in Europe of naratriptan vs. sumatriptan vs. placebo	Patients were treated in clinic	643	Age NR 88% women 99% white	I H S criteria 18-55 men and women.	1-year history of migraine, 1 to 6 moderate to severe attacks per month during the past 2 months

Evidence Table 1. Characteristics of head-to-head trials

Author Year	Exclusion criteria	Funding sources and role of funder	Other medications	Number screened/ eligible/ enrolled
Gruffyd-Jones 2001	Pregnancy, lactating, inadequate contraception in females, ischemic heart disease, arrhythmias, cardiac accessory pathway disorders, hypertension, use of MAO inhibitors, recent history of alcohol or drug abuse, abnormal clinical lab result, STDs, hepatitis B.	Astra-Zeneca, funder	Most prohibited	NR
Havanka 2000	History suggestive of cardiovascular or cerebrovascular disease; hypertension; pregnant or lactating; history of drug or alcohol or ergotamine abuse; use of MAO inhibitors, SSRIs, lithium, or flunarizine.	Glaxo, co-investigator	Prophylactic medications stopped 1 week before the study; rescue drugs not permitted	NR

Evidence Table 1. Characteristics of head-to-head trials

Author Year	Number withdrawn/ lost to follow-up
Gruffyd-Jones 2001	620, many because they did not have 6 attacks
Havanka 2000	NR

Evidence Table 1. Characteristics of head-to-head trials

Author Year	Design	Setting	Number randomized	Age Gender Ethnicity	Patients	Inclusion criteria
Kolodny 2004 (b)	Multicenter, randomized, placebo, crossover, DB	NR	1288	mean age: 40 years, White: 87% Female: 86%	Male or female adults, aged over 18 years that met IHS criteria for migraine	At least 6 month history of migraine good health standing
Kolodny 2004(a)	Multicenter, randomized, placebo, crossover, DB	NR	1447	Mean age: 40 years, White: 87% Female: 86%	Male or female adults, aged over 18 years that met IHS criteria for migraine	At least 6 month history of migraine good health standing
Lainez 2006	Randomized, open, crossover	NR	439		Adults aged 18 to 65 years who met IHS criteria for migraine	Be in good health, 1 to 8 migraines/month
Lines 1997 Lines 2001	Multicenter single-dose DB RCT conducted in Sweden, Norway, the United Kingdom and Switzerland of rizatriptan vs. sumatriptan vs. placebo	Not stated	792	40 years 80% women ethnicity NR	I H S criteria 18-65 men and women.	6-month history of migraine; 1-8 attacks per month

Evidence Table 1. Characteristics of head-to-head trials

Author Year	Exclusion criteria	Funding sources and role of funder	Other medications	Number screened/ eligible/ enrolled
Kolodny 2004 (b)	Use of monoamine oxidase inhibitors, methysergide/propranolol, participation in study 1	Merck	Standard antimigraine prophylactic (with exception of non-steroidal anti-inflammatory drugs, daily analgesics, or propranolol)	1287/1287/1287
Kolodny 2004(a)	Use of monoamine oxidase inhibitors, methysergide/propranolol	Merck	Standard antimigraine prophylactic (with exception of non-steroidal anti-inflammatory drugs, daily analgesics, or propranolol)	1447/1447/1447
Lainez 2006	Preponderance of mild attacks, baslar or hemiplegic migraines, difficutly distinguishing migraine from tension or other interval headache, cardiovascular disease, ECG abnormality, uncontrolled hypertension, renal, hepati or other systemic disease	NR	Rescue medication permitted (NSAIDs)	509/506/439
Lines 1997 Lines 2001	NR	Merck, co-investigator	Escape medications, consisting of standard analgesics or anti-emetics, were allowed from 2 hours onwards.	NR

Evidence Table 1. Characteristics of head-to-head trials

Author Year	Number withdrawn/ lost to follow-up
Kolodny 2004 (b)	NR/NR
Kolodny 2004(a)	13/18
Lainez 2006	67/0
Lines 1997 Lines 2001	141 (did not take study medication)

Evidence Table 1. Characteristics of head-to-head trials

Author Year	Design	Setting	Number randomized	Age Gender Ethnicity	Patients	Inclusion criteria
Loder 2001	Multicenter, randomized, open, crossover	NR	384	Mean age=37.3 years 82% female Ethnicity: White: 78% Asian: 2% Black: 14% Hispanic: 22% Other: 1%	Male or female adults who met IHS criteria for migraine	At least 6 month history of migraine over 18 years of age good health standing
Mathew	Multicenter, international, single-dose RCT of eletriptan vs sumatriptan (encapsulated) using a double-dummy design.	NR	2421	41.5 years 86.6% female Race NR	IHS criteria; 18-65 men and women; 1-6 attacks/month	IHS criteria for migraine with or without aura; monthly frequency of 1-6 attacks
Pascual 2000	Multicenter single-dose stratified DB RCT conducted at 66 international sites of rizatriptan vs. zolmitriptan, 9 month study period.	Not stated	882	38.8 years 83% female 77% white 19% Hispanic	I H S criteria 18-65 men and women.	6-month history of migraine; 1-8 reports per month.

Evidence Table 1. Characteristics of head-to-head trials

Author Year	Exclusion criteria	Funding sources and role of funder	Other medications	Number screened/ eligible/ enrolled
Loder 2001	History or clinical evidence of cardiovascular disease, clinically significant electrocardiogram abnormality, resting systolic blood pressure of more than 160mm Hg evidence of significant systemic disease previously exposed to rizatriptan or sumatriptan hypersensitivity to other 5-HT receptor agonists currently taking methysergide or propranolol history of drug alcohol abuse within 1 year, pregnancy/lactation, unable to distinguish migraine vs non-migraine exposure to investigational compound	Merck	NR	524/524/384
Mathew	Concurrent nonmigrainous headache or treatment-resistant migraine; migraine variants; coronary artery disease; heart failure; uncontrolled hypertension; abnormal ECG; clinically significant medical illness or laboratory abnormality; severe reduction in gastrointestinal absorption;	Pfizer, Ltd.	Rescue medication allowed after 2 hours	NR/NR/2421
Pascual 2000	Cardiovascular disease, hypertension, EKG abnormality; drug or alcohol abuse; pregnant or breast-feeding	Merck, co-investigator (maker of rizatriptan)	Recent propranolol, ergot, MAO inhibitor, opiates prohibited; other prophylaxis permitted; NSAIDs and opiates permitted for rescue	NR

Evidence Table 1. Characteristics of head-to-head trials

Author Year	Number withdrawn/ lost to follow-up
Loder 2001	2/NR
Mathew	308(12.7%) not treated; 4(0.2%) discontinued; 2072; 349(14.4%) not included in ITT population
Pascual 2000	116 (did not take study medication)

Evidence Table 1. Characteristics of head-to-head trials

Author Year	Design	Setting	Number randomized	Age Gender Ethnicity	Patients	Inclusion criteria
Sandrini, 2002 Pryse-Phillips, 1999	Multicenter, three-attack, DB RCT conducted in Europe, Canada and South Africa Eletriptan vs encapsulated sumatriptan	NR	1008	38.2 years 88% female Race NR	IHS criteria; 18 years of age or older (age limit of 65 in Canada)	At least one acute attack every 6 weeks
Schoenen 2005	Multicenter, randomized, open, crossover	NR	311	Mean age: 41.65 82% Female Ethnicity NR	Male or female adults, aged 18-65 years that met IHS criteria for migraine	Suffering at least 1 attack every 6 weeks, previous treated (and well-tolerated) with sumatriptan

Evidence Table 1. Characteristics of head-to-head trials

Author Year	Exclusion criteria	Funding sources and role of funder	Other medications	Number screened/ eligible/ enrolled
Sandrini, 2002 Pryse-Phillips, 1999	Patients who had previously taken oral eletriptan or any formulation of sumatriptan were excluded from the trial, as were patients who had taken any experimental drug within the previous month; patients with frequent nonmigrainous headache, atypical migraine that had not previously responded to therapy, migraine with prolonged aura, familial hemiplegic migraine, basilar migraine, or migrainous infarction were excluded from the trial; patients with a history of heart disease, uncontrolled hypertension, cardiac arrhythmias, abnormalities on laboratory tests or EKGs, documented allergic reactions to drugs or any other clinically significant disease	Pfizer, Ltd.	Rescue medication allowed two hours after optional second dose of study medication	1013/NR/1008
Schoenen 2005	Presence of frequent concurrent non-migraine and/or treatment-resistant migraine known history of coronary artery disease clinically significant arrhythmia, heart failure or uncontrolled hypertension, poor tolerance to sumatriptan, clinically significant	Pfizer	Rescue medication permitted- list NR	323/NR/311

Evidence Table 1. Characteristics of head-to-head trials

Author Year	Number withdrawn/ lost to follow-up
Sandrini, 2002	234/1008 (23%) not
Pryse-Phillips,	treated/386/774(49.9%
1999	) withdrawn/lost to fu
	NR
Schoenen 2005	0/0

Evidence Table 1. Characteristics of head-to-head trials

Author Year	Design	Setting	Number randomized	Age Gender Ethnicity	Patients	Inclusion criteria
Steiner 2003 Europe	Multicenter, single-attack, DB RCT conducted in Europe Eletriptan vs encapsulated zolmitriptan	Not stated	1587	Mean age=40.2 85% female Ethnicity NR	Male or female adults, aged 18-65 years that met IHS criteria for migraine with or without aura	Attacks at least once every 6 weeks.
Tfelt-Hansen 1998	Multicenter single-dose DB RCT conducted in Europe of rizatriptan vs. sumatriptan	Not stated	1268	38 years 81% female race/ethnicity not stated	I H S criteria 18-65 men and women.	6-month history of migraine; 1-8 attacks per month; good general health

Evidence Table 1. Characteristics of head-to-head trials

Author Year	Exclusion criteria	Funding sources and role of funder	Other medications	Number screened/ eligible/ enrolled
Steiner 2003 Europe	1) Migraine that had been consistently resistant to all treatments 2) basilar migraine; 3) hemiplegic migraine 4) frequent nonmigrainous headaches 5) any clinically significant medical illness or laboratory abnormalities, especially those indicative of coronary artery disease, heart failure or uncontrolled hypertension; 6) other contraindications to treatment with eletriptan or zolmitriptan including use of potent CYP3A4 inhibitors concomitantly or of MAO inhibitors within 2 weeks of entry; 7) severe reduction in gastrointestinal absorption; 8) misuse of alcohol or other substances including analgesics, ergotamine or triptans; 9) pregnancy or breast-feeding 10) Women who might become pregnant were required to use effective contraception	Pfizer	Rescue medication permitted by 2 hours post-dose, but not any triptan or ergot	1592 screened/1587 randomized/1337 treated
Tfelt-Hansen 1998	CVD, hypertension, drug or alcohol abuse; pregnant or nursing.	Merck, co-investigator	Escape medication permitted; NSAIDs not permitted	NR

Evidence Table 1. Characteristics of head-to-head trials

Author Year	Number withdrawn/ lost to follow-up
Steiner 2003 Europe	250 (16%) not treated/7 (0.5%) withdrawn/lost to fu NR/1337 analyzed at 1 hr (92% of treated population); 1235 analyzed at 2 hr (92% of treated population)
Tfelt-Hansen 1998	169 (did not take study medication)/2 lost to fu

Evidence Table 1. Characteristics of head-to-head trials

Author Year	Design	Setting	Number randomized	Age Gender Ethnicity	Patients	Inclusion criteria
Visser, 1996	Multicenter, single-attack, DB RCT conducted in the US and Dutch outpatient facilities Rizatriptan vs encapsulated sumatriptan	Outpatient	581	40.2 years 89.5% female Race NR	Men and women between 18 and 55 years of age with a six-month history of migraine with or without aura	8 or fewer migraine attacks per month
Vollono 2005	Randomized, single-blinded, crossover	Headache center of the A. Gemelli Hospital in Rome	42			Age between 18 and 65 years, migraine diagnosis in accordance with the IHS criteria, migraine history of $\geq$ 1 year, no prior use of triptans.

Evidence Table 1. Characteristics of head-to-head trials

Author Year	Exclusion criteria	Funding sources and role of funder	Other medications	Number screened/ eligible/ enrolled
Visser, 1996	History, clinical evidence, or an electrocardiogram that was suggestive of a significant cardiovascular disease; hypertension (at screening; resting SBP > 160 mm Hg or DBP > 95 mm Hg); or renal, gastrointestinal, pulmonary, hepatic, endocrine, neurological (other than migraine), or other systemic disease	Merck	Rescue medication allowed after 4 hours	NR/NR/581
Vollono 2005	Patients with basilar, ophthalmoplegic and hemiplegic migraine, pregnancy and nursing, patients with > 10 days of monthly headache in the 6 months preceding the study, history of ischaemic heart disease, printzmetal angina, dysrhythmias, HTN, the use of MAOI, alcohol or drug abuse.	NR	Previously agreed upon rescue medication was permitted (non-steroidal analgesics and antiemetics)	NR/42/42

Evidence Table 1. Characteristics of head-to-head trials

Author Year	Number withdrawn/ lost to follow-up
Visser, 1996	132/581 (22.7%) withdrawn/6 (4%) lost to fu
Vollono 2005	12/NR

Evidence Table 2. Results of triptan head-to-head trials

0.5-Hour Pain Relief		% of patients									
Ref.	p value	A12.5	E40	E80	N2.5	R5	R10	S25	S50	S100	Z2.5
Bomhof	NS	-	-	-	11	-	14	-	-	-	-
Pascual	NS	-	-	-	-	-	14	-	-	-	14.9
Tfelt-Hansen	NS	-	-	-	-	12	13	-	-	11	-
Goadsby	NS	-	5	12	-	-	-	-	-	10	-
Sandrini	n/a	-	nr	nr	-	-	-	-	nr	nr	-
Garcia-Ramos, 2003	NS	-	12	-	5	-	-	-	-	-	-
Steiner, 2003	NS	-	-	12	-	-	-	-	-	-	7
Kolodny (a)	0.049	-	-	-		15		11.6			-
Kolodny (b)	0.118	-	-	-			15.5		12.2		-
Spierings, 2001	NS	12.9							12.4		

0.5-Hour Pain Free		% of patients								
Ref.	p value	A12.5	E40	E80	N2.5	R5	R10	S50	S100	Z2.5
Bomhof	NS	-	-	-	1	-	1.5	-	-	-
Pascual	NS	-	-	-	-	-	2.7	-	-	0.7
Tfelt-Hansen	NS	-	-	-	-	1	2	-	1	-
Goadsby	NS	-	nr	nr	-	-	-	-	nr	-
Sandrini	n/a	-	nr	nr	-	-	-	nr	nr	-
Spierings, 2001	NS	1.2							0.9	

1 Hour Pain Relief		% of patients										
Ref.	p value	A12.5	E40	E80	N2.5	R5	R10	S25	S50	S100	Z2.5	Z5
Havanka	NS	-	-	-	30	-	-	-	-	35	-	-
Bomhof	p<0.029	-	-	-	27.8	-	38	-	-	-	-	-
Pascual	p<0.05	-	-	-	-	-	42.5	-	-	-	35.3	-
Tfelt-Hansen	p<0.05	-	-	-	-	30	37	-	-	28	-	-
Geraud	NS	-	-	-	-	-	-	-	-	35	-	34
Gallagher	p=0.014	-	-	-	-	-	-	39.2	47.1	-	43.4	45.5
Gruffyd-Jones	NS	-	-	-	-	-	-	-	38	-	36.9	35.9
Goadsby	<0.01	-	38	41	-	-	-	-	-	20	-	-
Sandrini	<0.05	-	30	37	-	-	-	-	24	27	-	-
Mathew, 2003	<0.01	-	34	-	-	-	-	-	-	27	-	-
Garcia-Ramos, 2003	<0.05	-	34	-	25	-	-	-	-	-	-	-
Steiner, 2003	<0.0001	-	-	40	-	-	-	-	-	-	25	-
Dowson, 2002	NR	35.3								37.6		
Spierings, 2001	NS	34.2							35.5			
Kolodny (a)	0.097	-	-	-	-	36.4	-	37.2	-	-	-	-
Kolodny (b)	0.041	-	-	-	-	-	40.5	-	34.8	-	-	-

Evidence Table 2. Results of triptan head-to-head trials

1 Hour Pain Free		% of patients									
Ref.	p value	A12.5	E40	E80	N2.5	R5	R10	S50	S100	Z2.5	Z5
Bomhof	<0.05	-	-	-	3.3	-	9.5	-	-	-	-
Pascual	NS	-	-	-	-	-	12.7	-	-	10.4	-
Tfelt-Hansen	NS	-	-	-	-	7	10	-	8	-	-
Geraud	NS	-	-	-	-	-	-	-	11	-	8
Gruffyd-Jones	NS	-	-	-	-	-	-	11.4	-	9.1	12
Goadsby	NS	-	8	17	-	-	-	-	6	-	-
Sandrini	<0.05	-	6	13	-	-	-	5	7	-	-
Mathew, 2003	NS	-	7	-	-	-	-	-	5	-	-
Garcia-Ramos, 2003	0.05	-	12	-	6	-	-	-	-	-	-
Dowson, 2002	NR	4.8							7.7		
Speirings, 2001	NS	5.4						0.9			
Steiner, 2003	<0.01	-	-	12	-	-	-	-	-	6	-

2 Hour Pain Relief		% of patients											
Ref.	p value	A12.5	E40	E80	N2.5	R5	R10	S25	S50	S100	Z2.5	Z5	Z2.5-nasal
Havanka (4-hr)	NS	-	-	-	52	-	-	-	-	60	-	-	-
Bomhof	<0.001	-	-	-	48.4	-	68.7	-	-	-	-	-	-
Pascual	NS	-	-	-	-	-	70.5	-	-	-	66.8	-	-
Tfelt-Hansen	NS	-	-	-	-	60	67	-	-	62	-	-	-
Lines	NS	-	-	-	-	63	-	-	67	-	-	-	-
Geraud	NS	-	-	-	-	-	-	-	-	61	-	59	-
Gallagher	<0.001	-	-	-	-	-	-	66.2	67.9	-	72.2	72.2	-
Gruffyd-Jones	NS	-	-	-	-	-	-	-	66.6	-	62.9	65.7	-
Goadsby	<0.01	-	65	77	-	-	-	-	-	55	-	-	-
Sandrini	<0.05	-	64	67	-	-	-	-	50	53	-	-	-
Mathew, 2003	<0.0001	-	67	-	-	-	-	-	-	59	-	-	-
Garcia-Ramos, 2003	<0.01	-	56	-	42	-	-	-	-	-	-	-	-
Steiner, 2003	<0.0001	-	-	74	-	-	-	-	-	-	60	-	-
Charlesworth 2003	NR	-	-	-	-	-	-	-	-	-	61.3	-	58.6
Loder 2001	<0.01	-	-	-	-	-	60	-	52	-	-	-	-
Kolodny (a)	0.004	-	-	-	-	65.7	-	57.8	-	-	-	-	-
Kolodny (b)	0.29	-	-	-	-	-	68	-	65.6	-	-	-	-
Diez, 2007	NS	75	-	-	-	-	-	-	-	-	-	-	-
Diez, 2007	NS	-	-	-	-	-	78	-	-	-	-	-	-
Dowson, 2002	NR	56.8								63.7			
Lainez, 2006	NS	-	77	-	-	-	-	-	-	-	-	-	-
Lainez, 2006	NS	-	-	-	-	-	77	-	-	-	-	-	-
Goadsby, 2007	0.094	65.4	-	-	-	-	-	-	-	-	-	-	-
Goadsby, 2007	0.094	-	-	-	-	-	-	-	-	-	70.2	-	-
Spierings, 2001	NS	58							57.3				

Evidence Table 2. Results of triptan head-to-head trials

2 Hour Pain Free		% of patients										
Ref.	p value	A12.5	E40	E80	N2.5	R5	R10	S6-inj	S50	S100	Z2.5	Z5
Bomhof	<0.001	-	-	-	20.7	-	44.8	-	-	-	-	-
Pascual	<0.05	-	-	-	-	-	43.2	-	-	-	35.6	-
Tfelt-Hansen	<0.05	-	-	-	-	25	40	-	-	33	-	-
Lines	NS	-	-	-	-	22	-	-	28	-	-	-
Geraud	NS	-	-	-	-	-	-	-	-	30	-	29
Gruffyd-Jones	NS	-	-	-	-	-	-	-	35.3	-	32.4	36
Goadsby	<0.05	-	29	37	-	-	-	-	-	23	-	-
Sandrini	<0.05	-	31	37	-	-	-	-	19	18	-	-
Sandrini	<0.0005	-	31	37	-	-	-	-	19	18		-
Mathew, 2003	<0.0001	-	36	-	-	-	-	-	-	27	-	-
Garcia-Ramos, 2003	<0.001	-	35	-	18	-	-	-	-	-	-	-
Steiner, 2003	<0.0001	-	-	44	-	-	-	-	-	-	26	-
Schoenen	<0.05	-	-	61	-	-	-	58	-	-	-	-
Diez, 2007	0.0301	52	-	-	-	-	58.5	-	-	-	-	-
Dowson, 2002	NS	27.7								33.5		
Lainez, 2006	NS	-	50	-	-	-	52	-	-	-	-	-
Goadsby, 2007	0.117	43.5	-	-	-	-	-	-	-	-	48.3	-
Spierings, 2001	0.005	17.9							24.6			
Vollono, 2005	<0.001	-	-	-	-	-	66	-	-	-	-	-
Vollono, 2005	<0.001	54	63.3	-	-	-	-	-	-	50	54.7	-

24-Hour Sustained Relief		% of patients									
Ref.	p value	A12.5	E40	E80	N2.5	R10	S25	S50	S100	Z2.5	Z5
Havanka	nr	-	-	-	48	-	-	-	44	-	-
Bomhof	nr	-	-	-	21	33	-	-	-	-	-
Pascual	nr	-	-	-	-	28	-	-	-	29	-
Gallagher	<0.001	-	-	-	-	-	33.1	-	-	40.7	42.5
Gruffyd-Jones	nr	-	-	-	-	-	-	30.6	-	30.3	29.9
Goadsby	NS	-	34	32	-	-	-	-	33	-	-
Sandrini	0.005	-	50	54	-	-	-	34	38	-	-
Mathew, 2003	<0.0003	-	34	-	-	-	-	-	43	-	-
Garcia-Ramos, 2003	<0.05	-	38	-	27	-	-	-	-	-	-
Steiner, 2003	<0.001	-	-	47	-	-	-	-	-	35	-
Steiner, 2003	<0.01	-	44	-	-	-	-	-	-	35	-
Lainez, 2006	NS	-	37	-	-	-	-	-	-	-	-
Lainez, 2006	NS	-	-	-	-	39	-	-	-	-	-
Spierings, 2001	NS	72.6						76			
Vollono, 2005	<0.001	-	-	-	-	56	-	-	-	-	-
Vollono, 2005	<0.001	-	56	-	-	-	-	-	-	-	-
Vollono, 2005	<0.001	-	-	-	-	-	-	-	40	-	-
Vollono, 2005	<0.001	51	-	-	-	-	-	-	-	-	-
Vollono, 2005	<0.001	-	-	-	-	-	-	-	-	50	-

Evidence Table 2. Results of triptan head-to-head trials

Satisfaction		% of patients								
Ref.	p value	A12.5	E40	E80	N2.5	R10	S50	S100	Z2.5	Z5
Pascual	0.045	-	-	-	-	62.7	-	-	54.6	-
Havanka	NS	-	-	-	49	-	-	51	-	-
Bomhof	<0.001	-	-	-	4.2	3.55	-	-	-	-
Gruffyd-Jones	NS	-	-	-	-	-	65.9	-	65.8	69.7
Steiner	<0.01	-	-	66	-	-	-	-	55	-
Steiner	<0.01	-	64	-	-	-	-	-	55	-

Return to Normal Function		% of patients										
Ref.	p value	A12.5	E40	E80	N2.5	R10	S6-inj	S20-nasal	S50	S100	Z2.5	
Pascual	0.025	-	-	-	-	45.4	-	-	-	-	37	2hr
Tfelt-Hansen	0.031	-	-	-	-	14	-	-	-	9	-	1hr
Tfelt-Hansen	0.017	-	-	-	-	27	-	-	-	19	-	1.5hr
Tfelt-Hansen	0.015	-	-	-	-	42	-	-	-	33	-	2hr
Bomhof	<0.001	-	-	-	22.6	39.3	-	-	-	-	-	2hr
Goadsby*	nr	-	32	23	-	-	-	-	-	42	-	2hr
Sandrini	<0.005	-	63	55	-	-	-	-	46	46	-	2hr
Mathew, 2003	<0.01	-	68	-	-	-	-	-	-	61	-	2hr
Hardebo, 1998	NR	-	-	-	-	-	94	48	-	-	-	2hr

*Reporting moderate to severe functional impairment at 2 hours

Relief of migraine-related symptoms

Nausea (%without symptoms at 2 hours)

Ref.	p value	A12.5	E40	E80	N2.5	R5	R10	S25	S50	S100	Z2.5	Z5
Havanka	stats ND	-	-	-	70	-	-	-	-	70	-	-
Bomhof	NS	-	-	-	59.4	-	68.5	-	-	-	-	-
Pascual	0.046	-	-	-	-	-	74.8	-	-	-	67.5	-
Tfelt-Hansen	<0.05	-	-	-	-	77	75	-	-	67	-	-
Geraud**	NS	-	-	-	-	-	-	-	-	35	-	33
Gallagher***	NS	-	-	-	-	-	-	% nr	% nr	-	% nr	% nr
Gruffyd-Jones**	NS	-	-	-	-	-	-	-	52	-	54	54
Goadsby**	NS	-	30	22	-	-	-	-	-	34	-	-
Sandrini**	<0.05	-	29	35	-	-	-	-	40	42	-	-
Mathew, 2003	<0.01	-	74	-	-	-	-	-	-	67	-	-
Garcia-Ramos, 2003	NS	-	73	-	68	-	-	-	-	-	-	-
Steiner, 2003	<0.05	-	-	72	-	-	-	-	-	-	64	-
Steiner, 2003	<0.05	-	72	-	-	-	-	-	-	-	64	-
Dowson, 2002	NS	68								69		
Lainez, 2006	nr	-	4.3	-	-	-	-	-	-	-	-	-
Lainez, 2006	nr	-	-	-	-	-	2.4	-	-	-	-	-
Spierings, 2001	NS	53.9							53			

Evidence Table 2. Results of triptan head-to-head trials

Vomiting (%without symptoms at 2 hours)											
Ref.	p value	A12.5	E40	E80	N2.5	R10	S25	S50	S100	Z2.5	Z5
Bomhof	NS	-	-	-	92.3	95.5	-	-	-	-	-
Pascual	NS	-	-	-	-	96.1	-	-	-	96.4	-
Gallagher**	NS	-	-	-	-	-	% nr	% nr	-	% nr	% nr
Goadsby	n/a	-	nr	nr	-	-	-	-	nr	-	-
Dowson, 2002	NS	96.7							92.3		
Sandrini	n/a	-	nr	nr	-	-	-	nr	nr	-	-
Spierings, 2001	NS	91.1						92.8			

Photophobia (%without symptoms at 2 hours)												
Ref.	p value	A12.5	E40	E80	N2.5	R5	R10	S25	S50	S100	Z2.5	Z5
Havanka	stats ND	-	-	-	56*	-	-	-	-	61*	-	-
Bomhof	<0.05	-	-	-	47.2	-	59.2	-	-	-	-	-
Pascual	0.029	-	-	-	-	-	64.4	-	-	-	56.5	-
Tfelt-Hansen	NS	-	-	-	-	57	61	-	-	58	-	-
Geraud**	NS	-	-	-	-	-	-	-	-	33	-	37
Gallagher***	NS	-	-	-	-	-	-	% nr	% nr	-	% nr	% nr
Gruffyd-Jones**	NS	-	-	-	-	-	-	-	52	-	54	54
Goadsby*	NS	-	37	29	-	-	-	-	-	43	-	-
Dowson, 2002	NS	73.4								75.3		
Spierings, 2001	NS	31.6							37.7			
Sandrini	<0.05	-	40	30	-	-	-	-	49	46	-	-
Mathew, 2003	<0.01	-	71	-	-	-	-	-	-	63	-	-
Steiner, 2003	NS	-	-	71	-	-	-	-	-	-	74	-

Evidence Table 2. Results of triptan head-to-head trials

Phonophobia (%without symptoms at 2 hours)

Ref.	p value	A12.5	E40	E80	N2.5	R5	R10	S25	S50	S100	Z2.5	Z5
Bomhof	<0.05	-	-	-	51.9	-	65	-	-	-	-	-
Pascual	NS	-	-	-	-	-	66.3	-	-	-	63.9	-
Tfelt-Hansen	NS	-	-	-	-	63	66	-	-	60	-	-
Geraud**	NS	-	-	-	-	-	-	-	-	36	-	39
Gallagher***	NS	-	-	-	-	-	-	% nr	% nr	-	% nr	% nr
Gruffyd-Jones**	NS	-	-	-	-	-	-	-	53	-	57	54
Goadsby	n/a	-	nr	nr	-	-	-	-	-	nr	-	-
Dowson, 2002	NS	79.9								82.5		
Spierings, 2001	NS	39.8								44.2		
Sandrini	<0.05	-	38	32	-	-	-	-	45	48	-	-
Sandrini	<0.01	-	38	32	-	-	-	-	45	48	-	-
Mathew, 2003	<0.01	-	74	-	-	-	-	-	-	67	-	-
Steiner, 2003	0.064	-	-	73	-	-	-	-	-	-	68	-

*combined photophobia/phonophobia; **percent with symptoms at 2 hours; ***time endpoint unclear; ¶ presence of symptoms

A=almotriptan, E=eletriptan, N=naratriptan, R=rizatriptan, S=sumatriptan, Z=zolmitriptan

Evidence Table 3. Head-to-head trials: Internal validity

	Internal Validity				
Author, Year Country	**Randomization adequate?**	**Allocation concealment adequate?**	**Groups similar at baseline?**	**Eligibility criteria specified?**	**Outcome assessors masked?**
Bomhof 1999	Yes	Yes	Yes	Yes	Yes
Carpay, 1997	NR	NR	NR	Yes	N/A-Open
Charlesworth, 2003	Yes	Yes	Yes	Yes	Yes
Dahlof, 1998	NR	NR	Yes	Yes	Yes
Diez, 2007	NR	NR	Yes	Yes	N/A-Open
Dowson 2002	NR	NR	No; higher proportions of severe pain in almotriptan groups compared with placebo	Yes	Yes
Dowson 2003	NR	NR	Crossover study, comparison of baseline characteristics for first treatment sequence NR	Yes	N/A-Open
Dowson, 2007	NR	No	Yes	Yes	N/A-Open

Evidence Table 3. Head-to-head trials: Internal validity

Author, Year Country	Care provider masked?	Patient masked?	Reporting of attrition, crossovers, adherence, and contamination	Loss to follow-up: differential/high	Intention-to-treat (ITT) analysis
Bomhof 1999	Yes	Yes	Yes, Yes, N/A, Yes	No/No	< 1% were excluded from efficacy analyses
Carpay, 1997	N/A-Open	N/A-Open	Yes/NR/NR/NR	No/No	No-excluded 13/137 (95%)
Charlesworth, 2003	Yes	Yes	Yes/NR/NR/NR	No	Yes
Dahlof, 1998	Yes	Yes	NR/NR/NR/NR	NR	Yes
Diez, 2007	N/A-Open	N/A-Open	Yes/Yes/Yes/NR	NR/No	Analyzed 327/436 (75%) who treated 2 attacks
Dowson 2002	Yes	Yes	Yes/No/No/No	No/No	No; excluded 1/184 in almotriptan 12.5 mg and 1/194 in sumatriptan 100 mg groups that were "unevaluable"
Dowson 2003	N/A-Open	N/A-Open	Yes/No/No/No	NR/No	Analysis of patient preference excluded 18 (10%) of patients who only treated one of two attacks
Dowson, 2007	N/A-Open	N/A-Open	Yes/Yes/Yes/NR	Yes	No

Evidence Table 3. Head-to-head trials: Internal validity

Author, Year Country	Post-randomization exclusions	Quality Rating	Funding
Bomhof 1999	No	Good	Merck
Carpay, 1997	No	Poor	Glaxo-Wellcome
Charlesworth, 2003	No	Good	AstraZeneca
Dahlof, 1998	No	Fair	NR- authors w/Glaxo-Wellcome
Diez, 2007	No	Fair	Almirall Prodesfarma
Dowson 2002	No	Fair	Laboratorios Almirall
Dowson 2003	No	Fair	NR; second author affiliated with AstraZeneca
Dowson, 2007	Yes	Poor	AstraZeneca

Evidence Table 3. Head-to-head trials: Internal validity

Internal Validity

Author, Year Country	Randomization adequate?	Allocation concealment adequate?	Groups similar at baseline?	Eligibility criteria specified?	Outcome assessors masked?
Gallagher 2000	NR	NR	Yes	Yes	Yes
Garcia-Ramos 2003	NR	NR	Yes	Yes	Yes
Geraud 2000	NR	NR	Yes for subgroup of 1058 (81%) who took study medication	Yes	Yes
Goadsby 2000	Yes, computer generated	NR	Yes for subgroup of 692 (81%) who received study treatment	Yes	Yes
Goadsby, 2007	NR	NR	Yes	Yes	NR
Gobel 2000	NR	NR	Crossover study, comparison of baseline characteristics for first treatment sequence NR	Yes	Yes
Goldstein 1998	Yes	Yes	Yes for subgroup of 1329 (86%) who took study drug	Yes	Yes
Gruffyd-Jones 2001	Yes; computer-generated random numbers scheme	NR	Yes for subgroup of 1522 (85%) who treated at least 2 migraines	Yes	Yes
Hardebo, 1998	No	NR	NR	Yes	N/A
Havanka 2000	Yes	Yes	Yes	Yes	Yes
Kolodny, 2004	Yes	NR	Yes	Yes	Yes
Lainez, 2006	Yes	Yes	Yes	Yes	N/A-Open
Lines 2001	NR	NR	Yes for subgroup of 792 (85%) of those who "took treatment"	Yes	Yes
Loder, 2001	Yes; computer-generated	Yes	Yes for all randomized patients	Yes	N/A-Open
Mathew 2003	NR	NR	Yes, for subgroup of 2072 (98%) of 2113 patients who treated an attack	Yes	Yes

Evidence Table 3. Head-to-head trials: Internal validity

Author, Year Country	Care provider masked?	Patient masked?	Reporting of attrition, crossovers, adherence, and contamination	Loss to follow-up: differential/high	Intention-to-treat (ITT) analysis
Gallagher 2000	Yes	Yes	Yes/No/No/No	NR/No	Analyzed 233/1445 (16%) who treated at least 2 attacks
Garcia-Ramos 2003	Yes	Yes	Yes/No/No/No	No/No	Analyzed 483/563 (12%) who treated an attack
Geraud 2000	Yes	Yes	Yes/No/No/No	Unclear/No	Analyzed all 1058 (81%) who took study medication
Goadsby 2000	Yes	Yes	Yes/No/No/No	No/No	No; of the 692 who received study treatment, only 605 (87%) were "evaluable for efficacy"
Goadsby, 2007	Yes	Yes	Yes/NR/Yes/NR	No/No	Yes
Gobel 2000	Yes	Yes	Yes/No/No/No	No/No	No; excluded 10 (4%) of 225 patients that treated both attacks
Goldstein 1998	Yes	Yes	Yes/Yes/N/A/Yes	No/No	Analyzed 1265 (82%) who treated 2 attacks
Gruffyd-Jones 2001	Yes	Yes	Yes/No/No/No	No/No	Analyzed all 1522 who treated 2 attacks
Hardebo, 1998	N/A	N/A	Yes/NR/NR/NR	Yes	No
Havanka 2000	Yes	Yes	Yes/No/No/No	No/No	Yes
Kolodny, 2004	Yes	Yes	Yes/NR/NR/NR	NR/No	No
Lainez, 2006	N/A-Open	N/A-Open	Yes/Yes/Yes/Yes	No/No	No; excluded 31/439 (7%) for rizatriptan and 41/439 (9%) for eletriptan for secondary efficacy endpoints (Table 4) and N's not reported for 2-hour pain outcomes
Lines 2001	Yes	Yes	Yes/NR/NR/NR	Unclear/No	Excluded 7 (< 1%) who did not provide efficacy data
Loder, 2001	N/A-Open	N/A-Open	Yes/Yes/Yes/Yes	NR	Of 472 treated patients, 384 (81%) were analyzed
Mathew 2003	Yes	Yes	Yes/No/No/No	No/No	No; excluded 131 (6%) of treated patients

Evidence Table 3. Head-to-head trials: Internal validity

Author, Year Country	Post-randomization exclusions	Quality Rating	Funding
Gallagher 2000	No	Fair	Zeneca, Inc.
Garcia-Ramos 2003	No	Gair	Pfizer
Geraud 2000	No	Fair	Glaxo Wellcome
Goadsby 2000	No	Fair	Pfizer
Goadsby, 2007	No	Good	Almirall Prodesfarma
Gobel 2000	No	Fair	NR
Goldstein 1998	No	Fair	Merck
Gruffyd-Jones 2001	No	Fair	AstraZeneca
Hardebo, 1998	No	Poor	Glaxo Laboratories, Inc
Havanka 2000	No	Good	NR
Kolodny, 2004	No	Fair	NR; > 1 author w/Merck
Lainez, 2006	No	Fair	Merck
Lines 2001	No	Fair	Merck
Loder, 2001	No	Fair	NR: 8/11/authors from Merck
Mathew 2003	No	Fair	Pfizer

Evidence Table 3. Head-to-head trials: Internal validity

Internal Validity

Author, Year Country	Randomization adequate?	Allocation concealment adequate?	Groups similar at baseline?	Eligibility criteria specified?	Outcome assessors masked?
Pascual 2000	Yes, computer generated	Yes	Yes for the subgroup of 766 (87%) who were treated with study medication	Yes	Yes
Pascual 2001	Yes	Yes	Yes for the subgroup of 481 (9%) treated patients	Yes	N/A-Open
Procol 311CIL/0099 (AstraZeneca Summary Report)	NR	NR	No; there was a higher proportion of patients with severe intensity at baseline in the zolmitriptan groupr (33%) than in the naratriptan group (18%); 2-hour response analysis included adjustment for the imbalance	Yes	Yes
Sandrini 2002	NR	NR	Yes for the subgroup of 774 (77%) of treated patients	Yes	Yes
Schoenen 2005	NR	NR	Yes	Yes	N/A-Open
Spierings 2001	NR	NR	No; almotriptan patients weighed more	Yes	Yes
Steiner 2003	Yes	NR	Yes for subgroup of 1337 (84%) who received treatment	Yes	Yes
Tfelt-Hansen 1998	Yes	Yes	No; patients in rizatriptan group were statistically significantly younger than patients in the sumatriptan group (37.0 vs 39.2 years; *P*= 0.003)	Yes	Yes
Visser 1996	NR	NR	No; sumatriptan 100 mg group had significantly higher rate of patients with severe pretreatment headache severity than the rizatriptan 10 mg group overall (62% vs 46%); but differences were nonsignificant in the subgroup of patients from Dutch-only centers	Yes	Yes
Vollono, 2005	Yes	NR	Crossover study, comparison of baseline characteristics for first treatment sequence NR	Yes	No

Evidence Table 3. Head-to-head trials: Internal validity

Author, Year Country	Care provider masked?	Patient masked?	Reporting of attrition, crossovers, adherence, and contamination	Loss to follow-up: differential/high	Intention-to-treat (ITT) analysis
Pascual 2000	Yes	Yes	Yes/Yes/Yes/Yes	No/No	No; excluded 39 of 766 (5%)
Pascual 2001	N/A-Open	N/A-Open	Yes/Yes/Yes/Yes	No/No	No; excluded 5% to 7% who treated at least 1 attack
Procol 311CIL/0099 (AstraZeneca Summary Report)	Yes	Yes	Yes/No/No/No	No/No	Unclear
Sandrini 2002	Yes	Yes	Yes/No/No/No	No/No	No; excluded 29/774 (4%)
Schoenen 2005	N/A-Open	N/A-Open	Yes/NR/NR/NR	NR	Unclear
Spierings 2001	Yes	Yes	Yes/No/No/No	No/No	No; excluded 1/582 (0.2%) in sumatriptan group
Steiner 2003	Yes	Yes	Yes/No/No/No	No/No	No; excluded 107 (8%) of treated patients
Tfelt-Hansen 1998	Yes	Yes	Yes, Yes, N/A, Yes	No/No	< 1% were excluded from efficacy analyses
Visser 1996	Yes	Yes	Yes/No/No/No	No/No	Excluded 1/449 (< 1%)
Vollono, 2005	No	Yes	Yes/NR/NR/NR	No/No	No; 12/42 (28%) were excluded who did not complete the study for unspecified reasons

Evidence Table 3. Head-to-head trials: Internal validity

Author, Year Country	Post-randomization exclusions	Quality Rating	Funding
Pascual 2000	No	Fair	NR; 2 of 6 authors affiliated with Merck
Pascual 2001	No	Fair	NR; 2 of 6 authors affiliated with Merck
Procol 311CIL/0099 (AstraZeneca Summary Report)	No	Fair for 2-hour response; Poor for other outcomes	AstraZeneca
Sandrini 2002	No	Fair	Pfizer
Schoenen 2005	No	Fair	NR-3rd author w/Pfizer
Spierings 2001	No	Fair	Pharmacia
Steiner 2003	No	Fair	Pfizer
Tfelt-Hansen 1998	No	Fair	Merck
Visser 1996	No	Fair for evaluation of patients from Dutch-only centers	Merck
Vollono, 2005	No	Poor	NR

Evidence Table 4. Triptan compared with placebo: Characteristics and outcomes

Author Year Country Trial Name (Quality Score)	Study design	Eligibility criteria	Interventions
Brandes 2005 USA & Canada	RCT, DB, Parallel	IHS criteria of migraine with or without aura; aged 18-65 years; migraine history ≥1year; 1-4 attacks/month in preceding 3 months	Eletriptan (ele) 20 and 40mg Placebo (pla)

***p<0.01 vs placebo**
‡pp<0.05 vs placebo
§p<0.001 vs placebo

Evidence Table 4. Triptan compared with placebo: Characteristics and outcomes

Author Year Country Trial Name (Quality Score)	Allowed other medications/ interventions	Method of Outcome Assessment and Timing of Assessment	Age Gender Ethnicity	Other population characteristics
Brandes 2005 USA & Canada	Rescue medication permitted after 2 hours of no response (rescue medication could not be another dose of ele, another triptan, ergotamine, or ergotamine-like substance) Recurrences of headaches, after 2 hours response, were allowed a 2nd dose of study medication	Primary efficacy endpoint: proportion of patients pain free at 2 hours postdose. Secondary efficacy endpoint: proportion of patients pain free at other assessment points (30 minutes, 1 hour, 1.5 hours, 4 hours and 24 hours); relief of associated symptoms (e.g. nausea, vomitting, photophobia, and phonophobia); use of rescure medication; sustained pain free	N=565 mean age: ele 20mg=39.1 ele 40mg=38.7 pla=39.1 % female: ele 20mg=79 ele 40mg=83 pla=85 ethnicity=nr	mean duration of illness: ele 20mg=13.4 years ele 40mg=14.0 years pla=13.6 years proportion without aura: ele 20mg=73% ele 40mg=68% pla=67% mean monthly attack frequency: ele 20mg=8.3 ele 40mg=8.6 pla=8.0

***p<0.01 vs placebo**
‡pp<0.05 vs placebo
§p<0.001 vs placebo

Evidence Table 4. Triptan compared with placebo: Characteristics and outcomes

			Results
Author Year Country Trial Name (Quality Score)	**Number screened/ eligible/ enrolled**	**Number withdrawn/ lost to fu/analyzed**	**Relief at various times**
Brandes 2005 USA & Canada	799/613/565	nr/nr/565	nr

***p<0.01 vs placebo**
‡pp<0.05 vs placebo
§p<0.001 vs placebo

Evidence Table 4. Triptan compared with placebo: Characteristics and outcomes

Author Year Country Trial Name (Quality Score)	Pain Free at various times (% patients)	Presence of migraine-associated symptoms at 2 hours	Other efficacy outcomes

Brandes
2005
USA & Canada
	Pain-free at 2 Hours:
	ele 20mg=35% (p<0.01);
	ele 40mg=47% (p<0.0001) vs. pla=22%
		ele 20mg vs pla absent the following symptoms:
		nausea (83% vs 75%, p<0.05)
		photophobia (66%vs 51%, p<0.001)
		phonophobia (74% vs 55%, p<0.0001)
		
		ele 40mg vs pla absent the following symptoms:
		nausea (76% vs 75%, ns)
		photophobia (74% vs 51%, p<0.001)
		phonophobia (81% vs 55%, p<0.0001)
			Migraine Free' outcome (complete relief at 2 hours, with no associated symptoms, and normal functioning):
			ele 20mg=32% (p<0.01);
			ele 40mg=43% (p<0.0001) vs pla=20%
			
			Use of rescue medication:
			ele 20mg=22% (p<0.01);
			ele 40mg=18% (p<0.01) vs pla=44%

***p<0.01 vs placebo**
‡pp<0.05 vs placebo
§p<0.001 vs placebo

Evidence Table 4. Triptan compared with placebo: Characteristics and outcomes

Author Year Country Trial Name (Quality Score)	Method of adverse effects assessment	Adverse Effects Reported
Brandes 2005 USA & Canada	Patient report	Ele 20mg; Ele 40mg; Pla Vomiting: 4.7%; 3.8%; 3.8% Dizziness: 2.6%; 1.4%; 1.9% Asthenia: 2.1%; 1.9%; 0.5% Incidence of any adverse event: 28%; 23%; 32%

***p<0.01 vs placebo**
‡pp<0.05 vs placebo
§p<0.001 vs placebo

Evidence Table 4. Triptan compared with placebo: Characteristics and outcomes

Author Year Country Trial Name (Quality Score)	Comments
Brandes 2005 USA & Canada	

***p<0.01 vs placebo**
‡pp<0.05 vs placebo
§p<0.001 vs placebo

Evidence Table 4. Triptan compared with placebo: Characteristics and outcomes

Author Year Country Trial Name (Quality Score)	Study design	Eligibility criteria	Interventions
Cady 2006 USA	RCT, DB, parallel Multicenter	IHS criteria for migraine with or without aura, aged 18 years or older, ≥6 months history of migraines, 1 to 4 migraine attacks/month, mild at onsent attacks	Rizatriptan (R) 10mg Placebo (Pla)

***p<0.01 vs placebo**
‡pp<0.05 vs placebo
§p<0.001 vs placebo

Evidence Table 4. Triptan compared with placebo: Characteristics and outcomes

Author Year Country Trial Name (Quality Score)	Allowed other medications/ interventions	Method of Outcome Assessment and Timing of Assessment	Age Gender Ethnicity	Other population characteristics
Cady 2006 USA	Rescue medication was permitted	Primary effiacy outcome: pain freedome at 2 hours Secondary efficacy outcomes: 24-hour sustained pain freedom, pain freedom at 30, 45, 60, and 90 minutes, time to pain freedom up to 2 hours, presence of associated symptoms at 30, 45, 60, 90, and 120 minutes, use of rescue medication, presence of functional disability at 30, 45, 60, 90, and 120 minutes	Study 1 Mean age (years): R10: 43; Pla: 43 % Female: R10: 88.1; Pla: 89.3 % White: R10: 83.8; Pla: 80.2 Study 2 Mean age (years): R10: 41; Pla: 41 % Female: R10: 56.4; Pla: 91.1 % White: R10: 80.1; Pla: 77.5	Baseline associted symptoms Study 1 Photophobia: R10: 66.9%; Pla: 65.% Phonophobia: R10: 54.%; Pla: 48.6% Nausea: R10: 31.7%; Pla: 29.4% Vomiting: R10: 0.8%; Pla: 0.6% Study 2 Photophobia: R10: 60.4%; Pla: 50.9% Phonophobia: R10: 43.8%; Pla: 44.4% Nausea: R10: 35.6%; Pla: 37.9% Vomiting: R10: 1.5%; Pla: 1.8%

***p<0.01 vs placebo**
‡pp<0.05 vs placebo
§p<0.001 vs placebo

Evidence Table 4. Triptan compared with placebo: Characteristics and outcomes

			Results
Author Year Country Trial Name (Quality Score)	**Number screened/ eligible/ enrolled**	**Number withdrawn/ lost to fu/analyzed**	**Relief at various times**
Cady 2006 USA	Study 1 598/589/583 Study 2 577/570/564	Study 1 31/6/351 Study 2 41/4/331	NR

***p<0.01 vs placebo**
‡pp<0.05 vs placebo
§p<0.001 vs placebo

Evidence Table 4. Triptan compared with placebo: Characteristics and outcomes

Author Year Country Trial Name (Quality Score)	Pain Free at various times (% patients)	Presence of migraine-associated symptoms at 2 hours	Other efficacy outcomes
Cady 2006 USA	Pain Freedom at 2 Hours Study 1 R10: 57% vs Pla: 31% (p<0.001) Study 2 R10: 59% vs Pla: 31% (p<0.001) Sustained Pain Freedom at 24 Hours Study 1 R10: 43% vs Pla: 23% (p<0.001) Study 2 R10: 48% vs Pla: 25% (p<0.001)	Photophobia Study 1 R10: 23% vs Pla: 44% (p<0.05) Study 2 R10: 25% vs Pla: 40% (p<0.05) Phonophobia Study 1 R10: 18% vs Pla: 35% (p<0.05) Study 2 R10: 21% vs Pla: 34% (p<0.05) Nausea Study 1 R10: 16% vs Pla: 19% (NS) Study 2 R10: 15% vs Pla: 30% (p<0.05) Vomiting Study 1 R10: 2% vs Pla: 2% (NS) Study 2 R10: 2% vs Pla: 2% (NS)	Need for Rescue Medication at 2 Hours Study 1 R10: 35% vs Pla: 54% (p<0.05) Study 2 R10: 34% vs Pla: 53% (p<0.05) Functional Disability at 2 Hours Study 1 R10: 31% vs Pla: 54% (p<0.05) Study 2 R10: 34% vs Pla: 56% (p<0.05)

***p<0.01 vs placebo**
‡pp<0.05 vs placebo
§p<0.001 vs placebo

Evidence Table 4. Triptan compared with placebo: Characteristics and outcomes

Author Year Country Trial Name (Quality Score)	Method of adverse effects assessment	Adverse Effects Reported
Cady 2006 USA	Patient report	Incidence of adverse effects Study 1 R10: 21% vs Pla: 12.4% Study 2 R10: 21.8% vs Pla: 9.5% Dry mouth Study 1 R10: 2.8% vs Pla: 1.7% Study 2 R10: 2.4% vs Pla: 2.4% Paresthesia Study 1 R10: 2.3% vs Pla: 0% Study 2 R10: 2.1% vs Pla: 0.6% Dizziness Study 1 R10: 5.9% vs Pla: 2.3% Study 2 R10: 3.3% vs Pla: 2.4% Somnolence Study 1 R10: 3.1% vs Pla: 1.7% Study 2 R10: 3.3% vs Pla: 1.8% Fatigue Study 1 NR Study 2 R10: 3.3% vs Pla: 1.2%

***p<0.01 vs placebo**
‡pp<0.05 vs placebo
§p<0.001 vs placebo

Evidence Table 4. Triptan compared with placebo: Characteristics and outcomes

Author Year Country Trial Name (Quality Score)	Comments
Cady 2006 USA	

***p<0.01 vs placebo**
‡pp<0.05 vs placebo
§p<0.001 vs placebo

Evidence Table 4. Triptan compared with placebo: Characteristics and outcomes

Author Year Country Trial Name (Quality Score)	Study design	Eligibility criteria	Interventions
Carpay 2004 Europe *Fair quality*	RCT DB Parallel group Single attack	Between 18 and 65 years of age; at least 1-year history of migraine (IHS criteria) with or without aura; 1-6 attacks/month in preceding 2 months; history of moderate to severe migraines typically preceded by a mild-pain phase. Patients were eligible for the study regardless of previous experience with triptan therapy.	Sumatriptan rapid release (SRR) formulation 50 mg and 100 mg Placebo

***p<0.01 vs placebo**
‡pp<0.05 vs placebo
§p<0.001 vs placebo

Evidence Table 4. Triptan compared with placebo: Characteristics and outcomes

Author Year Country Trial Name (Quality Score)	Allowed other medications/ interventions	Method of Outcome Assessment and Timing of Assessment	Age Gender Ethnicity	Other population characteristics
Carpay 2004 Europe *Fair quality*	Acute migraine medication (excluding an ergo-containing medication or a triptan) allowed from 2 through 24 hours after dosing for patients who were not pain free at 2 hours or who had a return of moderate or severe pain and did not wish to take a second dose of study medication	Primary efficacy endpoint=proportion of patients who were pain free 2 hours after dosing Severity rated using 4-point scale (0=none; 1=mild; 2=moderate; 3=severe) recorded on a diary card before dosing and 30 minutes, 45 minutes, 1 hour and 2 hours after dosing	n=481 mean age=40.6 82.9% female 99% white	Without aura only=78.7% With aura only=8.3% With and without aura=13% Using triptans at study entry=75% Used triptans in past year=4.6% Used triptans sometime in past=6.2% Never used triptans=14.1% *Severity at onset* Mild=93.5% Moderate=5.3% Severe=1.1%

***p<0.01 vs placebo**
‡pp<0.05 vs placebo
§p<0.001 vs placebo

Evidence Table 4. Triptan compared with placebo: Characteristics and outcomes

		Results	
Author Year Country Trial Name (Quality Score)	**Number screened/ eligible/ enrolled**	**Number withdrawn/ lost to fu/analyzed**	**Relief at various times**
Carpay 2004 Europe *Fair quality*	nr/nr/481 randomized/432 treated a migraine attack and provided ≥ 1 postdose efficacy assessment	37(8.6%) withdrawn/9(2.1%) lost to fu/432 analyzed	nr

***p<0.01 vs placebo**
‡pp<0.05 vs placebo
§p<0.001 vs placebo

Evidence Table 4. Triptan compared with placebo: Characteristics and outcomes

Author Year Country Trial Name (Quality Score)	Pain Free at various times (% patients)	Presence of migraine-associated symptoms at 2 hours	Other efficacy outcomes
Carpay 2004 Europe *Fair quality*	SRR100 vs SRR50 vs placebo 30 minutes: 10.6* vs 3.6 vs 1.9 45 minutes: 24.6§ vs 18.2‡ vs 9.1 1-hour: 44.4§ vs 36.5* vs 18.9 2-hours: 66.2§ vs 51.1§ vs 19.6 Sustained (2-24 hours) pain-free: 32.1* vs 40.1* vs 9.8	SRR50 vs SRR100 vs placebo Nausea: 15.6* vs 22.3* vs 38.4 Photophobia: 25.4* vs 23.6* vs 48.7 Phonophobia: 23.1* vs 20.4* vs 43	SRR50vs SRR100 vs placebo Migraine-free (pain-free *AND* no associated symptoms) 30 minutes: 3.7 vs 7.1* vs 2 45 minutes: 14.7 vs 16.4* vs 7.3 1 hour: 30.1* vs 31.4* vs 17.2 2 hours: 44.9* vs 50.7* vs 17.1

***p<0.01 vs placebo**
‡pp<0.05 vs placebo
§p<0.001 vs placebo

Evidence Table 4. Triptan compared with placebo: Characteristics and outcomes

Author Year Country Trial Name (Quality Score)	Method of adverse effects assessment	Adverse Effects Reported
Carpay 2004 Europe *Fair quality*	Tolerability was assessed by calculating the incidence of specific adverse events, defined as any untoward medical occurrences, regardless of suspected cause, that were reported by a patient or noted by a clinician during the study	SRR50 vs SRR100 vs placebo (% patients) Overall drug-related adverse events: 10.2% vs 16.9* vs 5.2 Nausea and vomiting: <1 vs 5 vs 2 Chest symptoms: 2 vs 3 vs 0 Malaise and fatigue: 1 vs 3 vs <1

***p<0.01 vs placebo**
‡pp<0.05 vs placebo
§p<0.001 vs placebo

Evidence Table 4. Triptan compared with placebo: Characteristics and outcomes

Author Year Country Trial Name (Quality Score)	Comments
Carpay 2004 Europe *Fair quality*	

***p<0.01 vs placebo**
‡pp<0.05 vs placebo
§p<0.001 vs placebo

Evidence Table 4. Triptan compared with placebo: Characteristics and outcomes

Author Year Country Trial Name (Quality Score)	Study design	Eligibility criteria	Interventions
Diener 2005 Germany Diener 2005 Germany (companion paper)	RCT, DB, Parallel	IHS criteria for migraine with or without aura for ≥1 year, had experienced unsatisfactory response to sumatriptan on ≥2 occassions, experienced ≥1 moderate or severe migraine attack in each of the 2 months proceding the study	Almotriptan 12.5mg (Alm) Placebo (Pla)
Eletripan Steering Committee 2002 Japan *Fair quality*	Randomized controlled trial Multicenter Single dose	IHS criteria; 1 attack per 6-week period	Eletriptan (ele) 20, 40 and 80 mg Placebo (pla)

***p<0.01 vs placebo**
‡pp<0.05 vs placebo
§p<0.001 vs placebo

Evidence Table 4. Triptan compared with placebo: Characteristics and outcomes

Author Year Country Trial Name (Quality Score)	Allowed other medications/ interventions	Method of Outcome Assessment and Timing of Assessment	Age Gender Ethnicity	Other population characteristics
Diener 2005 Germany Diener 2005 Germany (companion paper)	Rescue medication, choosen by the investigator, was permitted	Primary efficacy outcome: pain relief at 2 hours Secondary efficacy outcome: pain-free at 2 hours, sustained pain-free, use of rescue medication within 24 hours	Mean age (years) Alm: 41.1; Pla: 41.4 % Female Alm: 88; Pla: 85.8 % White Alm: 99.4; Pla: 99.1	Mean Height (cm) Alm: 167.6; Pla: 168.1 Mean Weight (kg) Alm: 70.6; Pla: 70.47 Headache severity Severe: Alm: 69.7% Pla: 71.7% Moderate: Alm: 30.3% Pla: 28.3%
Eletripan Steering Committee 2002 Japan *Fair quality*	Rescue medication permitted nr	Primary efficacy endpoint: Proportion of patients who experienced headache response 2 hours post-dose. Patients recorded migraine severity in a diary at 0.5, 1, 2, 4, and 24 hours post-dose.	n=402 avg age 35.5 74.1% female 100% Japanese	Without aura=48.6% With aura=34.2% With and without aura=17.1% Baseline severity assessment: No pain=0% Mild pain=0% Moderate pain=75.7% Severe pain=22.4%

***p<0.01 vs placebo**
‡pp<0.05 vs placebo
§p<0.001 vs placebo

Evidence Table 4. Triptan compared with placebo: Characteristics and outcomes

			Results
Author Year Country Trial Name (Quality Score)	**Number screened/ eligible/ enrolled**	**Number withdrawn/ lost to fu/analyzed**	**Relief at various times**
Diener 2005 Germany	328/245/221	23/NR/198	Pain-reilef at 2 Hours Alm: 47.5% vs Pla: 23.2% (p<0.001)
Diener 2005 Germany (companion paper)			
Eletripan Steering Committee 2002 Japan *Fair quality*	nr/nr/402	76(18.9%) withdrawals/3(0.7%) lost to fu/321 analyzed for safety; 309 for primary endpoint; 307 for other efficacy endpoints	At .5 hour: nr At 1 hour: nr At 1.5 hours: nr At 2 hours: ele=64%; 67%; 76% pla= 51%

***p<0.01 vs placebo**
‡pp<0.05 vs placebo
§p<0.001 vs placebo

Evidence Table 4. Triptan compared with placebo: Characteristics and outcomes

Author Year Country Trial Name (Quality Score)	Pain Free at various times (% patients)	Presence of migraine-associated symptoms at 2 hours	Other efficacy outcomes
Diener 2005 Germany Diener 2005 Germany (companion paper)	Pain-free at 2 Hours Alm: 33.3% vs Pla: 14.1% (p<0.005) Sustained pain-free Alm: 20.9% vs Pla: 9% (p<0.05)	NR	Use of rescue medication Alm: 26.6% vs Pla: 46.9% (p<0.005)
Eletripan Steering Committee 2002 Japan *Fair quality*	At 2 hours: ele=24%; 22%; 28% pla=13%	*Vomiting:* ele=96%; 99%; 95%; pla=96% *Nausea:* ele=70%; 74%; 41: pla= 68% *Photophobia:* ele=84%; 83%; 86%; pla=71%	*Symptom free at 2 hours:* ele=65%; 65%; 75%; pla=54% *24 hour sustained pain-free:* ele=21%; 18%; 26%; pla=9%

***p<0.01 vs placebo**
‡pp<0.05 vs placebo
§p<0.001 vs placebo

Evidence Table 4. Triptan compared with placebo: Characteristics and outcomes

Author Year Country Trial Name (Quality Score)	Method of adverse effects assessment	Adverse Effects Reported
Diener 2005 Germany Diener 2005 Germany (companion paper)	Patient report	Treatment-emergent adverse events Alm: 7.1% vs Pla: 5.1% (p=0.77)
Eletripan Steering Committee 2002 Japan *Fair quality*	The incidence of adverse events was detected by indirect subject questioning, physical examination, and from laboratory safety data and entries in subject diaries.	Total: ele=16.3%; 32.5%; 45.5%; pla=15.5% Asthenia: ele=1.3%, 2.5%, 11.7%; pla=1.2% Parasthesia: ele=0, 3.8%, 1.3%; pla=0 Somnolence: ele=6.3%, 10.0%, 16.9%; pla=3.6%

***p<0.01 vs placebo**
‡pp<0.05 vs placebo
§p<0.001 vs placebo

Evidence Table 4. Triptan compared with placebo: Characteristics and outcomes

Author Year Country Trial Name (Quality Score)	Comments
Diener 2005 Germany	
Diener 2005 Germany (companion paper)	
Eletripan Steering Committee 2002 Japan *Fair quality*	

***p<0.01 vs placebo**
‡pp<0.05 vs placebo
§p<0.001 vs placebo

Evidence Table 4. Triptan compared with placebo: Characteristics and outcomes

Author Year Country Trial Name (Quality Score)	Study design	Eligibility criteria	Interventions
Freitag, 2008 (companion to Matew 2007)	RCT, DB, Multicenter, Parallel	IHS criteria-migraine with or without aura of moderate pain intensity for ≥ 1 year, 2-6 headaches per month for last 6 months	Almotriptan 12.5mg (Alm) Placebo (Pla)

***p<0.01 vs placebo**
‡pp<0.05 vs placebo
§p<0.001 vs placebo

Evidence Table 4. Triptan compared with placebo: Characteristics and outcomes

Author Year Country Trial Name (Quality Score)	Allowed other medications/ interventions	Method of Outcome Assessment and Timing of Assessment	Age Gender Ethnicity	Other population characteristics
Freitag, 2008 (companion to Matew 2007)	Rescue medication permitted	Functional disability assessment using 4 categories measured at 0.5, 1, 2, 4 and 24 hours MQoL questionnaire at 24 hours post treatment of each attack	40.4 yrs 87% female White: 82.2% Black: 12.1% Asian: 2.5% Hispanic : 2.9% Other: 0.3%	Weight: lbs (SD): 167.4(37.7) MiDAS Score (SD): 18.5(14.7) Height:inches (SD): 65.4 (3.2) Functional disability: perform normal activity 12.3%, disturbed but could continue work: 77.1%, bed rest required: 10.1% Migraine associated symptoms: phonophobia: 73.7%, photophobia: 75.2%, nausea: 31.4%

***p<0.01 vs placebo**
‡pp<0.05 vs placebo
§p<0.001 vs placebo

Evidence Table 4. Triptan compared with placebo: Characteristics and outcomes

			Results
Author Year Country Trial Name (Quality Score)	**Number screened/ eligible/ enrolled**	**Number withdrawn/ lost to fu/analyzed**	**Relief at various times**
Freitag, 2008 (companion to Matew 2007)	NR/NR/378	NR/NR/315	24 hour QOL social function domain p<0.05 (all 3 attacks), feelings/concern domain: p<0.05 for attack 1, p<0.01 for attack 2, p<0.001 for attack 3. Three pretreatment variables 1) functional level (p=0.011), 2) pain intensity (p=0.0089), and 3) MIDAS (p=0.0152) correlated with return to normal function at 2hr. Correlation of other pretreatment variables photophobia, phonophobia, nausea and vomiting were NS.

***p<0.01 vs placebo**
‡pp<0.05 vs placebo
§p<0.001 vs placebo

Evidence Table 4. Triptan compared with placebo: Characteristics and outcomes

Author Year Country Trial Name (Quality Score)	Pain Free at various times (% patients)	Presence of migraine-associated symptoms at 2 hours	Other efficacy outcomes
Freitag, 2008 (companion to Matew 2007)	% of patients pain free and performing normal activities for pooled group (Attack 1) 76.9% at 0.5 hr, 94.6% at 1 hr, 91.7% at 2 hrs % of patients with mild pain and performing normal activities for pooled group (Attack 1) 27.5% at 0.5 hr, 34.0 at 1 hr , 44.8 at 2 hrs Pain free (from graph) A vs placebo at 2 hrs: 38% vs 25% (p=0.0004) at 4 hrs: 40% vs 22% (p<0.0001) 24 hrs: 43% vs 30% (p=0.0008)	% patients with normal function and no migraine assciated symptoms compared to patients with symptoms (data from graph) pooled group (p<0.0001 for each group) No phonophobia: 72% normal, with phonophobia: 19% normal No photophobia: 75% normal, with phonophobia: 20% normal No Nausea: 56% normal, with nausea: 18% normal	A vs Pla Functional disability at 2 hours: normal funtion 54.4% vs 38.1% , disturbed function 32.5% vs 45.2%, bed rest 13.1% vs 16.1% , ER hospitalization 0 vs 0.6% (p=0.007) at 4 hours: normal funtion 74.5% vs 54.3% , disturbed function 20.1% vs 29.3%, bed rest 4.7% vs 15.7% , ER hospitalization 0.7% vs 0.7% (p<0.001) Return to normal function at 2, 4 , 24 hours post treatment for pretreatment impairment group (N=276): 2 hrs: 51.1% vs 34.1% (p=0.011) 4 hrs: 64.% vs 39.4% (p<0.001) 24 hrs: 60.8% vs 47.6% (p=0.038) Normal function for whole group at 2 hours: 48.7% vs 36.5%, at 4 hours: 68.6 vs 53.7% at 24 hrs: 83.5% vs 80.4% Normal functioning p<0.0026 and <0.0007 at 2 and 4 hours (favoring Alm) for Attack 1, p=0.0003 and p=0.0112 at 1 and 4 hrs and p=0.0448 for Attack 2 at 2 hrs (p values vs placebo)

***p<0.01 vs placebo**
‡pp<0.05 vs placebo
§p<0.001 vs placebo

Evidence Table 4. Triptan compared with placebo: Characteristics and outcomes

Author Year Country Trial Name (Quality Score)	Method of adverse effects assessment	Adverse Effects Reported
Freitag, 2008 (companion to Matew 2007)	Patient report	A vs Pla: % patients reporting AE: 23% vs 23.7% treatment emergent AE with a frequency of ≥1%: 9.8% vs 6.4% Somnolence:1.1% vs 2.3% Nausea: 1.1% vs 1.7% Vomiting: 1.1% vs 0.6% Fatigue: 1.1% vs 0%

***p<0.01 vs placebo**
‡pp<0.05 vs placebo
§p<0.001 vs placebo

Evidence Table 4. Triptan compared with placebo: Characteristics and outcomes

Author Year Country Trial Name (Quality Score)	Comments
Freitag, 2008 (companion to Matew 2007)	

***p<0.01 vs placebo**
‡pp<0.05 vs placebo
§p<0.001 vs placebo

Evidence Table 4. Triptan compared with placebo: Characteristics and outcomes

Author Year Country Trial Name (Quality Score)	Study design	Eligibility criteria	Interventions
Goadsby 2008 Multinational	RCT, DB, Multicenter, Parallel	IHS criteria-with or without aura for at least 1 yrMigraine attacks of atleast moderate pain intensity within the lpat year. Avg frequency of 2-6 episodes per month during the last 3 months . History of untreated or unsuccessfully treated migraine headaces > 4 hours duration	Almotriptan 12.5mg (Alm) Placebo (Pla)

***p<0.01 vs placebo**
‡pp<0.05 vs placebo
§p<0.001 vs placebo

Evidence Table 4. Triptan compared with placebo: Characteristics and outcomes

Author Year Country Trial Name (Quality Score)	Allowed other medications/ interventions	Method of Outcome Assessment and Timing of Assessment	Age Gender Ethnicity	Other population characteristics
Goadsby 2008 Multinational	Rescue medication permitted	Primary efficacy endpoint: % of pain-free patients 2 hours , comparison between those treated early with mild pain vs moderate or severe baseline pain. Secondary endpoints: % of patients pain free at 0.25, 0.5, 1, 1.5 and 24 h post dose in the moderate-severe baseline pain arms Sustained pain-free response at 24 h, pain-free at 2 hours without return of headache and not using rescue medication in the following 24 h, % of patients taking rescue medication % patients with relapse in 24 hours and 24 and 48 hours post dose Total attack duration in hours and time lost to attack in hours Treatment satisfaction rate using VAS migraine-associated symptoms at baseline and 2 hours post treatment presence of cutaneous allodynia by questionnaire at baseline or 2 h post treatment	38.26 yrs 84.2% female Asian: 0.2% Black: 0.5% Caucasian: 98.3% Other: 1.0%	BMI (kg/m2) Mean (SD) 23.60(3.98)

***p<0.01 vs placebo**
‡pp<0.05 vs placebo
§p<0.001 vs placebo

Evidence Table 4. Triptan compared with placebo: Characteristics and outcomes

			Results
Author Year Country Trial Name (Quality Score)	**Number screened/ eligible/ enrolled**	**Number withdrawn/ lost to fu/analyzed**	**Relief at various times**
Goadsby 2008 Multinational	491/NR/491	87/NR/404	NR

***p<0.01 vs placebo**
‡pp<0.05 vs placebo
§p<0.001 vs placebo

Evidence Table 4. Triptan compared with placebo: Characteristics and outcomes

Author Year Country Trial Name (Quality Score)	Pain Free at various times (% patients)	Presence of migraine-associated symptoms at 2 hours	Other efficacy outcomes
Goadsby 2008 Multinational	1) A 12.5 (mild) 2) A 12.5 (moderate to severe) 3) Pla (mild) 4) Pla (moderate to severe) Pain free at 2 hrs: 49% vs 40% vs 25% vs 15% Differences: 1 vs. 2 NS (p=0.2154), 1 vs. 3 and 2 vs. 4 both significant (p < 0.001) Sustained pain-free (2-24 hrs) 46% vs 30% vs 16% vs 11% Differences: 1 vs. 2 significant (p=0.024), 2 vs. 4 significant (p=0.0018), 1 vs. 3 significant (p<0.0001), 3 vs. 4 NS (p=0.38) Pain-free data at 2 hours in AwM group Pain free at 2 hrs: 54% vs 38% vs 25% vs 18% Differences: 1 vs. 2 significant (p=0.02)	Therapeutic gain at 2 hours: A mild vs A moderate to severe vs placebo mild vs placebo moderate to severe: Nausea 1.8 vs 28.9 vs 9.2 vs 9.6 Vomiting -8.0 vs -1.7 vs -0.4 vs 3.1 Photophobia 17.0 vs 30.3 vs 12.5 vs 12.8 Phonophobia 17.7 vs 24.7 vs 8.5 vs 9.8 Osmophobia 6.4 vs 8.7 vs 0.4 vs 4.4	1) A 12.5 (mild) 2) A 12.5 (moderate to severe) 3) Pla (mild) 4) Pla (moderate to severe) Median duration of migraine attack from onset to resolution of pain (AwM based data): 1) 2hrs 2) 5hrs, 1 significantly shorter vs. 2 (p=0.0005) Median duration of migraine attack from time of dosing to resolution of pain (AwM based data): 1) 1.6 hr 2) 1.9 hr, 1 vs 2 NS. Median time lost in daily activities 1) 0 hr, 2) 2hr, 3) 2hr and 4) 2 hr. 3 vs. 4 difference NS , 1 vs 2 difference significant (p=0.0015) Headache recurrence within 24 hrs 6% vs. 24 % vs. 37% vs. 27% 1 vs. 2 significant difference (p=0.0124), 3 vs. 4 difference NS. Use of rescue medication 1 vs. 2 Difference NS p=0.1921 1 vs. 3, more in 3 took rescue med, p<0.0001 2 vs. 4, more in 4 took rescue med, p<0.0001 3 vs. 4, difference NS.

***p<0.01 vs placebo**
‡pp<0.05 vs placebo
§p<0.001 vs placebo

Evidence Table 4. Triptan compared with placebo: Characteristics and outcomes

Author Year Country Trial Name (Quality Score)	Method of adverse effects assessment	Adverse Effects Reported
Goadsby 2008 Multinational	Patient report	4.9% of subjects had 8 AE in the A mild group 4% of subjects had 4 AE in A moderate and severe group 4.7% of subjects had 5 AE in placebo mild group 4% of subjects had 5 AE placebo moderate to severe group

***p<0.01 vs placebo**
‡pp<0.05 vs placebo
§p<0.001 vs placebo

Evidence Table 4. Triptan compared with placebo: Characteristics and outcomes

Author Year Country Trial Name (Quality Score)	Comments
Goadsby 2008 Multinational	

***p<0.01 vs placebo**
‡pp<0.05 vs placebo
§p<0.001 vs placebo

Evidence Table 4. Triptan compared with placebo: Characteristics and outcomes

Author Year Country Trial Name (Quality Score)	Study design	Eligibility criteria	Interventions
Goldstein 2005 USA	RCT, DB, Parallel Multicenter	IHS criteria for migraine with or without aura; report 1 to 8 migraines/month; migraines are of at least moderate intensity; be able to distinguish migraines from other headaches	Sumatriptan succinate (sum) 50mg Acetaminophen 500mg, aspirin 500mg, caffeine 130mg (AAC) Placebo (pla)

***p<0.01 vs placebo**
‡pp<0.05 vs placebo
§p<0.001 vs placebo

Evidence Table 4. Triptan compared with placebo: Characteristics and outcomes

Author Year Country Trial Name (Quality Score)	Allowed other medications/ interventions	Method of Outcome Assessment and Timing of Assessment	Age Gender Ethnicity	Other population characteristics
Goldstein 2005 USA	Rescue medication permitted	Efficacy variables recorded at baseline, 0.25, 0.5, 0.75, 1, 1.5, 2, 3, and 4 hours postdose: - headache pain intensity - headache pain relief - functional disability - associated gastrointestinal and neurologic symptoms Efficacy variables without a fixed time point: - onset of meaningful migraine relief - subject global evalutation of study medication effectiveness - investigator global evalutation of study medication effectiveness - rescue medication usage	Mean age (years): 38.1 82% Female	NR

***p<0.01 vs placebo**
‡pp<0.05 vs placebo
§p<0.001 vs placebo

Evidence Table 4. Triptan compared with placebo: Characteristics and outcomes

			Results
Author Year Country Trial Name (Quality Score)	**Number screened/ eligible/ enrolled**	**Number withdrawn/ lost to fu/analyzed**	**Relief at various times**
Goldstein 2005 USA	188/171/170	0/0/170	Pain-relief (scale 0-4, with 0=no relief and 4=complete relief) At 2 Hours: AAC: 2.5 vs sum: 1.9 (p<0.05) vs pla: 1.6 At 3 Hours: ACC: 2.9 vs sum: 2.2 (p<0.05) vs pla: 1.8 At 4 Hours: ACC: 2.9 vs sum: 2.3 (p<0.05) vs pla: 1.8

***p<0.01 vs placebo**
‡pp<0.05 vs placebo
§p<0.001 vs placebo

Evidence Table 4. Triptan compared with placebo: Characteristics and outcomes

Author Year Country Trial Name (Quality Score)	Pain Free at various times (% patients)	Presence of migraine-associated symptoms at 2 hours	Other efficacy outcomes
Goldstein 2005 USA	NR	ACC group had significantly more decrease of phonophobia ($p \leq 0.044$) and photophobia ($p \leq 0.015$) than sum group No difference found for vomiting or nausea	Headache Response (baseline of moderate/severe pain reduced to mild/none): At 2 Hours: ACC: 84% vs sum: 65% ($p \leq 0.027$) vs pla: 52% At 3 Hours: ACC: 94% vs sum: 70% ($p<0.02$) vs pla: 56% At 4 Hours: ACC: 98% vs sum: 72% ($p<0.02$) vs pla: 56%

***p<0.01 vs placebo**
‡pp<0.05 vs placebo
§p<0.001 vs placebo

Evidence Table 4. Triptan compared with placebo: Characteristics and outcomes

Author Year Country Trial Name (Quality Score)	Method of adverse effects assessment	Adverse Effects Reported
Goldstein 2005 USA	Patient report	Chest tightness: sum group=1 subject Gastrointestinal complaints: AAC: 15 (21/7%) vs sum: 5 (7.5%) vs pla: 2 (5.7%)

***p<0.01 vs placebo**
‡pp<0.05 vs placebo
§p<0.001 vs placebo

Evidence Table 4. Triptan compared with placebo: Characteristics and outcomes

Author Year Country Trial Name (Quality Score)	Comments
Goldstein 2005 USA	

***p<0.01 vs placebo**
‡pp<0.05 vs placebo
§p<0.001 vs placebo

Evidence Table 4. Triptan compared with placebo: Characteristics and outcomes

Author Year Country Trial Name (Quality Score)	Study design	Eligibility criteria	Interventions
Jelinski 2006 Canada	RCT, DB, Double-dummy, placebo controlled, parallel Multicenter	IHS criteria for migraine with or without aura; aged 18 to 65 years, 1 to 6 migraines/month, moderate/severe migraine pain	Sumatriptan 50mg (S50) and 100mg (S100) Placebo (Pla)
Mathew 2007 USA	RCT, DB, Parallel Multicenter	IHS criteria for migraine with or without aura, aged 18 to 65 years, 2 to 6 migraines/month, moderate/severe migraine pain, differentiate migraines from other headaches,	Almotriptan 12.5mg (Alm) Placebo (Pla)

***p<0.01 vs placebo**
‡pp<0.05 vs placebo
§p<0.001 vs placebo

Evidence Table 4. Triptan compared with placebo: Characteristics and outcomes

Author Year Country Trial Name (Quality Score)	Allowed other medications/ interventions	Method of Outcome Assessment and Timing of Assessment	Age Gender Ethnicity	Other population characteristics
Jelinski 2006 Canada	NR	Primary efficacy outcome: proportion of patients pain-free at 1, 2, 4 and 24 hours	Pla; S50; S100 Mean age (years): 40.7; 39.8; 39.8 % Female: 83; 87; 86 % White: 92; 95; 96	Pla; S50; S100 Migraine History %without aura: 67; 63; 71 % with aura: 10; 10; 7
Mathew 2007 USA	Rescue medication was permitted	Primary efficacy outcome: proportion of patients pain-free at 2 hours Secondary efficacy outcomes (in proportions): pain-free at 0.5, 1, 4, and 24 hours; pain-relief at 0.5, 1, 2, 4, and 24 hours; modified pain-relief at 0.5,1, 2, 4, and 24 hours; sustained pain-free; use of rescue medication; level of migraine-associated symptoms at baseline at 0.5, 1, 2, 4, and 24 hours; and level of functional disability at 1, 2, 4, and 24 hours	Mean age (years): 40.4 86.8% Female 82% White	Mean weight (lbs): 167.8 Mean heaght (inches): 65.5

***p<0.01 vs placebo**
‡pp<0.05 vs placebo
§p<0.001 vs placebo

Evidence Table 4. Triptan compared with placebo: Characteristics and outcomes

Author Year Country Trial Name (Quality Score)	Number screened/ eligible/ enrolled	Number withdrawn/ lost to fu/analyzed	Results Relief at various times
Jelinski 2006 Canada	429/364/361	NR/NR/361	NR
Mathew 2007 USA	NR/NR/378	61/NR/317	Pain-relief at 1 Hour (%) Alm: 54.3 vs Pla: 41.1 (p=0.019) Pain-relief at 2 Hours (%) Alm: 72.3 vs Pla: 48.4 (p<0.001) Pain-relief at 4 Hours (%) Alm: 74.5 vs Pla: 47.4 (p<0.001) Pain-relief at 24 Hours (%) Alm: 73.4 vs Pla: 48.4 (p<0.001)

***p<0.01 vs placebo**
‡pp<0.05 vs placebo
§p<0.001 vs placebo

Evidence Table 4. Triptan compared with placebo: Characteristics and outcomes

Author Year Country Trial Name (Quality Score)	Pain Free at various times (% patients)	Presence of migraine-associated symptoms at 2 hours	Other efficacy outcomes
Jelinski 2006 Canada	Pain-Free at 1 Hour S50: 24% Pla: 7% (p<0.001) S100: 24% vs Pla: 7% (p<0.001) Pain-Free at 2 Hours S50: 40% vs Pla: 16% (p<0.001) S100: 50% vs Pla: 16% (p<0.001) Pain-Free at 4 Hours S50: 50% vs Pla: 17% (p<0.001) S100: 56% vs Pla: 17% (p<0.001) Pain-Free at 24 Hours S50: 37% vs Pla: 15% (p<0.001) S100: 45% vs Pla: 15% (p<0.001)	Nausea reported at 2 Hours: S50: 26% vs S100: 26% vs Pla: 38%	NR
Mathew 2007 USA	Pain-free at 1 Hour Alm: 16.7 vs Pla: 8.4 (p=0.026) Pain-free at 2 Hours Alm: 37 vs Pla:23.9 (p=0.01) Pain-free at 4 Hours Alm: 42 vs Pla: 21.9 (p<0.001) Pain-free at 24 Hours Alm: 38.9 vs Pla: 27.1 (p=0.031)	Phonophobia At 2 to 4 hours and 4 to 24 hours after treatment, Alm group was significantly lower than Pla group (p=0.002, p<0.001, respectively) Photophobia At 2 to 4 hours and 4 to 24 hours after treatment, Alm group was significantly lower than Pla group (p<0.001 for both time periods) Nausea At 4 to 24 hours after treatment, Alm group was significantly lower than Pla group (p=0.014)	Functionality Of those reporting functional disability at time of treatment, proportion reporting normal functioning at 2 Hours: Alm: 54.4 vs Pla: 38.1 (p=0.007) At 4 Hours: Alm: 74.5 vs Pla: 54.3 (p<0.001)

***p<0.01 vs placebo**
‡pp<0.05 vs placebo
§p<0.001 vs placebo

Evidence Table 4. Triptan compared with placebo: Characteristics and outcomes

Author Year Country Trial Name (Quality Score)	Method of adverse effects assessment	Adverse Effects Reported
Jelinski 2006 Canada	Patient report	S100: paraesthesias, chest symptoms, and throat contstriction reported by 3% of subjects
Mathew 2007 USA	Patient report	Somnolence Alm: 1.1% vs Pla: 2.3% Nausea Alm: 1.1% vs Pla: 1.7% Vomiting Alm: 1.1% vs Pla: 0.6% Fatigue Alm: 1.1% vs Pla 0%

***p<0.01 vs placebo**
‡pp<0.05 vs placebo
§p<0.001 vs placebo

Evidence Table 4. Triptan compared with placebo: Characteristics and outcomes

Author Year Country Trial Name (Quality Score)	Comments
Jelinski 2006 Canada	
Mathew 2007 USA	

***p<0.01 vs placebo**
‡pp<0.05 vs placebo
§p<0.001 vs placebo

Evidence Table 4. Triptan compared with placebo: Characteristics and outcomes

Author Year Country Trial Name (Quality Score)	Study design	Eligibility criteria	Interventions
Sakai 2002 Japan *Fair quality*	Randomized controlled trial Multicenter Single dose	IHS criteria of migraine with or without aura; age of migraine onset <50 years; migraine history ≥1 year; 1-6 attacks/month in preceding 3 months	Zolmitriptan (zol) 1, 2.5, 5 mg Placebo (pla)
Sheftell 2005 USA	RCT, DB, Parallel, 2 studies	aged between 18-65 years, ≥ 6 month history f migraine with/without aura, 1-6 migraines per month during the 3 months before screening, previous thistory of tripatn therapy was not an exclusion criteria	Fast-disintegrating, rapid release sumatriptan 50 mg: N=902 Fast-disintegrating, rapid release sumatriptan 100 mg: N=902 Placebo: 892

***p<0.01 vs placebo**
‡pp<0.05 vs placebo
§p<0.001 vs placebo

Evidence Table 4. Triptan compared with placebo: Characteristics and outcomes

Author Year Country Trial Name (Quality Score)	Allowed other medications/ interventions	Method of Outcome Assessment and Timing of Assessment	Age Gender Ethnicity	Other population characteristics
Sakai 2002 Japan *Fair quality*	Type(s) of rescue medication approved 4-hours post-dose nr	Primary efficacy endpoint: proportion of patients with headache response at 2h post-dose. Patients recorded migraine intensity on diary cards at 0.5, 1, 2, and 4h post-dose.	n=289 avg age 38.3 74.2% female 100% Japanese	Without aura=64% Associated symptoms: Nausea=90% Vomiting=54% Photophobia=56% Phonophobia=45% Severity: Moderate=73%
Sheftell 2005 USA	Recurrence of headache were allowed a second dose of study medication, patients with no relief after 2 hours weer allowed an nonprohibited acute migraine medication	Primary efficacy endpoint was time to onset of pain relief. Responses recorded every 2 hours between after dosing for 24 hour periods. Patients rated pain relief and recurrence.	Studies combined: N= 2696 Mean age: 40 years Female: 85% White: 92%	History of triptan use: Study 1: S50: 77% vs S100: 79% vs placebo: 78% Study 2: S50: 84% vs S100: 84% vs placebo: 84% History of migraine without aura only: Study 1: S50: 72% vs S100: 68% vs placebo: 71% Study 2: S50: 65% vs S100: 70% vs placebo: 67%

***p<0.01 vs placebo**
‡pp<0.05 vs placebo
§p<0.001 vs placebo

Evidence Table 4. Triptan compared with placebo: Characteristics and outcomes

Author Year Country Trial Name (Quality Score)	Number screened/ eligible/ enrolled	Number withdrawn/ lost to fu/analyzed	Results Relief at various times
Sakai 2002 Japan *Fair quality*	nr/nr/289	58/289(20%) did not take medication; a further 29/287(10%) were excluded from efficacy analysis due to protocol deviations/lost to fu nr/202 analyzed	At .5 hour: zol=8.5%; 9.8%; 13.7% pla= 12.2% At 1 hour: zol=30.4%; 28.3%; 32.7% pla=26.5% At 1.5 hours: nr At 2 hours: zol=53.3%; 55.6%; 65.4% pla=37.5%
Sheftell 2005 USA	NR/NR/3331	73/NR/2696	Pain-relief at 2 Hours: S50: 67% vs S100: 72% vs placebo: 42%; p< 0.05 for both doses vs placebo

***p<0.01 vs placebo**
‡pp<0.05 vs placebo
§p<0.001 vs placebo

Evidence Table 4. Triptan compared with placebo: Characteristics and outcomes

Author Year Country Trial Name (Quality Score)	Pain Free at various times (% patients)	Presence of migraine-associated symptoms at 2 hours	Other efficacy outcomes
Sakai 2002 Japan *Fair quality*	At 2 hours: zol=17.8%; 18.5%; 23.1% pla=14.6%	*Vomiting:* zol=95.6%; 98.1%; 98%; pla=95.8% *Nausea:* ele=53.3%; 61.1%; 64.7: pla= 54.2% *Photophobia:* ele=82.2%; 83.3%; 78.4%; pla=77.1%	*Symptom free at 2 hours:* nr *24 hour sustained pain-free:* Complete response (headache response at 2h and then no recurrence or use of escape medication within 24h) zol=37.8%, 46.3%, 46.2% pla=22.9%
Sheftell 2005 USA	Pain-free at 2 Hours: S50: 40% vs S100: 47% vs placebo: 15%; p< 0.001	NR	NR

***p<0.01 vs placebo**
‡pp<0.05 vs placebo
§p<0.001 vs placebo

Evidence Table 4. Triptan compared with placebo: Characteristics and outcomes

Author Year Country Trial Name (Quality Score)	Method of adverse effects assessment	Adverse Effects Reported
Sakai 2002 Japan *Fair quality*	The assessment of tolerability was based on the reporting of adverse events in patient diaries.	Asthenia: zol=1.9%, 1.6%, 7.0%; pla=1.7% Parathesia: zol=0, 0, 5.3%; pla=0 Somnolence: zol=0, 3.3%, 5.3%; pla=1.7%
Sheftell 2005 USA	Patient report	Any drug-related adverse event: Study 1: S50: 8% vs S100: 12% vs placebo: 3% Study 2: S50: 12% vs S100: 19% vs placebo: 5% Nausea (drug-related): Study 1: S50: <1% vs S100: <1% vs placebo: 0 Study 2: S50: 1% vs S100: 3% vs placebo: 1% Paresthesia (drug-related): Study 1: S50: <1% vs S100: <1% vs placebo: 0 Study 2: S50: 1% vs S100: 3% vs placebo: <1%

***p<0.01 vs placebo**
‡pp<0.05 vs placebo
§p<0.001 vs placebo

Evidence Table 4. Triptan compared with placebo: Characteristics and outcomes

Author Year Country Trial Name (Quality Score)	Comments
Sakai 2002 Japan *Fair quality*	
Sheftell 2005 USA	

***p<0.01 vs placebo**
‡pp<0.05 vs placebo
§p<0.001 vs placebo

Evidence Table 4. Triptan compared with placebo: Characteristics and outcomes

Author Year Country Trial Name (Quality Score)	Study design	Eligibility criteria	Interventions
Silberstein 2008 US	RCT, DB, Parallel	Men and women aged 18 to 65 years with ≥6 month history of migraine with or without aura as defined by the ICHD-2, and had experienced 2-6 migraine attacks per month in last 3 months.	Sumatriptan 85/mg/day + naproxen sodium 500mg/day (Sum) Placebo (Pla)

Sumatriptan Rapid Release formulation

***p<0.01 vs placebo**
‡pp<0.05 vs placebo
§p<0.001 vs placebo

Evidence Table 4. Triptan compared with placebo: Characteristics and outcomes

Author Year Country Trial Name (Quality Score)	Allowed other medications/ interventions	Method of Outcome Assessment and Timing of Assessment	Age Gender Ethnicity	Other population characteristics
Silberstein 2008 US	Rescue medications were allowed	Patients rated pain severity (0=none, 3=severe) in diaries	Mean age (years): 40.4 88.7% Female 86.5% White	Mean attacks per month: 3.8 Mean age of onset: 22.4 years Previous triptan use: 66.2%

Sumatriptan Rapid Release formulation

***p<0.01 vs placebo**
‡pp<0.05 vs placebo
§p<0.001 vs placebo

Evidence Table 4. Triptan compared with placebo: Characteristics and outcomes

			Results
Author Year Country Trial Name (Quality Score)	**Number screened/ eligible/ enrolled**	**Number withdrawn/ lost to fu/analyzed**	**Relief at various times**
Silberstein 2008 US	NR/1305/1122	11/NR/1111	NR

Sumatriptan Rapid Release formulation

***p<0.01 vs placebo**
‡pp<0.05 vs placebo
§p<0.001 vs placebo

Evidence Table 4. Triptan compared with placebo: Characteristics and outcomes

Author Year Country Trial Name (Quality Score)	Pain Free at various times (% patients)	Presence of migraine-associated symptoms at 2 hours	Other efficacy outcomes
Silberstein 2008 US	**Study 1** Pain free at 30 min Sum: 5% vs Pla: 2% (p=0.016) Pain free at 1 hr Sum: 20% vs Pla: 7% (p<0.001) Pain free at 2 hr Sum: 52% vs Pla: 17% (p<0.001) Pain free at 4 hr Sum: 70% vs Pla: 25% (p<0.001) Pain free 2-24 hr Sum: 45% vs 12% (p<0.001) **Study 2** Pain free at 30 min Sum: 6% vs Pla: 2% (p=0.021) Pain free at 1 hr Sum: 24% vs Pla: 7% (p<0.001) Pain free at 2 hr Sum: 51% vs Pla: 15% (p<0.001) Pain free at 4 hr Sum: 67% vs Pla: 25% (p<0.001) Pain free 2-24 hr Sum: 40% vs Pla: 14% (p<0.001)	Nausea Study 1: Sum: 17% vs Pla: 24% (p=0.018) Study 2: Sum: 19% vs 31% (p<0.001) Photophobia Study 1: Sum: 31% vs Pla: 57% (p<0.001) Study 2: Sum: 22% vs Pla: 55% (p<0.001) Phonophobia Study 1: Sum: 26% vs Pla: 54% (p<0.001) Study 2: Sum: 20% vs Pla: 46% (p<0.001) Neck pain/discomfort Study 1: Sum: %35 vs Pla: 44% (p=0.001) Study 2: Sum: 28% vs 54% (p<0.001) Sinus pain/pressure Study 1: Sum: 19% vs Pla: 33% (p<0.001) Study 2: Sum: 23% vs 38% (p<0.001)	NR

Sumatriptan Rapid Release formulation

***p<0.01 vs placebo**
‡pp<0.05 vs placebo
§p<0.001 vs placebo

Evidence Table 4. Triptan compared with placebo: Characteristics and outcomes

Author Year Country Trial Name (Quality Score)	Method of adverse effects assessment	Adverse Effects Reported
Silberstein 2008 US	Patient report	Incidence of AEs reported Study 1: Sum: 11% vs Pla: 7% Study 2: Sum: 14% vs 9%

Sumatriptan Rapid Release formulation

***p<0.01 vs placebo**
‡pp<0.05 vs placebo
§p<0.001 vs placebo

Evidence Table 4. Triptan compared with placebo: Characteristics and outcomes

Author Year Country Trial Name (Quality Score)	Comments
Silberstein 2008 US	2 studies reported in one publication. Same methods for both studies.

Sumatriptan Rapid Release formulation

***p<0.01 vs placebo**
‡pp<0.05 vs placebo
§p<0.001 vs placebo

Evidence Table 4. Triptan compared with placebo: Characteristics and outcomes

Author Year Country Trial Name (Quality Score)	Study design	Eligibility criteria	Interventions
Tepper 2006 USA	RCT, DB, Parallel Multicenter	IHS criteria for migraine without aura, aged 18 to 65 years, met either headache pain criteria or associated symptom criteria, triptan- and ergot-naïve	Sumatriptan (S) 25, 50, or 100mg Placebo (Pla)
Tfelt-Hansen 2006 Denmark	RCT, DB, Parallel	Patients between 18 and 65 years suffering from migraines with or without aura as defined by the 1988 IHS criteria for ≥ 1 year and had a history of 6-12 migraine attacks/year, those who had the experience that the headache became moderate or severe following a mild phase, were able to differentiate migraine from other headaches and had not treated a migraine with a triptan within the last 6 months.	Sumatriptan 50mg (Sum) Placebo (Pla)

***p<0.01 vs placebo**
‡pp<0.05 vs placebo
§p<0.001 vs placebo

Evidence Table 4. Triptan compared with placebo: Characteristics and outcomes

Author Year Country Trial Name (Quality Score)	Allowed other medications/ interventions	Method of Outcome Assessment and Timing of Assessment	Age Gender Ethnicity	Other population characteristics
Tepper 2006 USA	Rescue medication was permitted	Primary efficacy outcome: % with headache relief at 2 hours Secondary efficacy outcomes: % with headache relief at 0.5, 1, 1.5, and 4 hours, % pain free at 0.5, 1, 1.5, 2, and 4 hours; % with nausea, photophobia and phonophobia at 0.5, 1, 1.5, 2, and 4 hours	Pla; S25; S50; S100 Mean age (years): 37.8; 37.9; 39.1; 39.3 % Female: 80; 68; 74; 73 % White: 73; 71; 71; 75	Previous headache treatment with OTC analgesics (%): Pla: 93 S25: 93 S50: 95 S100: 94
Tfelt-Hansen 2006 Denmark	Rescue medication was permitted	Primary efficacy endpoint: % pain free after 2 hours Patients recorded their pain severity and symptoms at 30 minutes, 1 hour, 2 hours, and 24 hours after taking study medication	Mean age (years): Sum: 40 (males) & 36 (females); Pla: 48 (males) & 36 (females) 78.2% females Ethnicity: NR	Migraine with aura: 10.9% Migraine without aura: 80.2% Migraine with and without aura: 8.9% Previous triptan use: 11.9% Concurrent medications: 66.3%

***p<0.01 vs placebo**
‡pp<0.05 vs placebo
§p<0.001 vs placebo

Evidence Table 4. Triptan compared with placebo: Characteristics and outcomes

Author Year Country Trial Name (Quality Score)	Number screened/ eligible/ enrolled	Number withdrawn/ lost to fu/analyzed	Results Relief at various times
Tepper 2006 USA	NR/NR/677	74/22/581	Headache relief at 2 Hours (%) S25: 57 vs S50: 53 vs S100: 59 vs Pla: 47% (p=0.053 for S100 vs Pla) Headache relief at 4 Hours (%) S25: 49 vs S50: 57 vs S100: 64 vs Pla: 40 (p<0.01 for S50 vs Pla and S100 vs Pla)
Tfelt-Hansen 2006 Denmark	158/150/101	2/NR/99	NR

***p<0.01 vs placebo**
‡pp<0.05 vs placebo
§p<0.001 vs placebo

Evidence Table 4. Triptan compared with placebo: Characteristics and outcomes

Author Year Country Trial Name (Quality Score)	Pain Free at various times (% patients)	Presence of migraine-associated symptoms at 2 hours	Other efficacy outcomes
Tepper 2006 USA	Pain-free at 2 Hours S25: 31 vs S50: 28 vs S100: 32 vs Pla: 25 (NS) Pain-free at 4 Hours S25: 39 vs S50: 41 vs S100: 49 vs Pla: 26 (p<0.023 for all comparisons)	Nausea Baseline: 14% to 20% of each group 2 Hours: 20% to 50% of baseline reporters still had nausea Photophobia Baseline: 41% to 47% of each group 2 Hours: 50% of baseline reporters still had photophobia Phonophobia Baesline: 34% to 46% of each group 2 Hours: 50% of baseline reporters still had phonophobia	Pla group took 2nd dose or rescue medication significantly earlier compared with S100 group (p=0.002)
Tfelt-Hansen 2006 Denmark	Pain free at 2 hours Sum: 39% vs Pla: 18% Sustained pain free response Sum: 33% vs Pla: 13%	Stated no difference between groups, but data not presented	NR

***p<0.01 vs placebo**
‡pp<0.05 vs placebo
§p<0.001 vs placebo

Evidence Table 4. Triptan compared with placebo: Characteristics and outcomes

Author Year Country Trial Name (Quality Score)	Method of adverse effects assessment	Adverse Effects Reported
Tepper 2006 USA	Patient report	Incidence of adverse events Pla: 4%; S25: 11%; S50: 14%; S100: 17% Nausea Pla: 0%; S25: 4%; S50: 5%; S100: 6% Dizziness Pla: 0%; S25: <1%; S50: 3%; S100: 2% Vomiting Pla: <1%; S25: 0%; S50: <1%; S100: 3%
Tfelt-Hansen 2006 Denmark	Patient report	Patients with AEs Sum: 51% vs Pla: 15% Most common AEs Nausea (N=5) Paraesthesia (N=4 Fatigue (N=3) Chest pressure sensation (N=2)

***p<0.01 vs placebo**
‡pp<0.05 vs placebo
§p<0.001 vs placebo

Evidence Table 4. Triptan compared with placebo: Characteristics and outcomes

Author Year Country Trial Name (Quality Score)	Comments
Tepper 2006 USA	
Tfelt-Hansen 2006 Denmark	

***p<0.01 vs placebo**
‡pp<0.05 vs placebo
§p<0.001 vs placebo

Evidence Table 4. Triptan compared with placebo: Characteristics and outcomes

Author Year Country Trial Name (Quality Score)	Study design	Eligibility criteria	Interventions
Wendt 2006 USA	RCT, DB Multicenter	IHS criteria for migraine with or without aura, aged 18 to 60 years, presented with acute migrain attack with moderate or severe pain	Sumatriptan (S) 4mg Inj Placebo (Pla)

***p<0.01 vs placebo**
‡pp<0.05 vs placebo
§p<0.001 vs placebo

Evidence Table 4. Triptan compared with placebo: Characteristics and outcomes

Author Year Country Trial Name (Quality Score)	Allowed other medications/ interventions	Method of Outcome Assessment and Timing of Assessment	Age Gender Ethnicity	Other population characteristics
Wendt 2006 USA	Rescue medication was permitted	Primary efficacy outcomes: migraine symptoms and severity of headache pain just prior to treatment administration, then at 10, 20, 30, 40, 50, 60, 90, and 120 minutes after dosing	Mean age (years): S4: 38.3; Pla: 38.1 % Female: S4: 86; Pla: 88 % White: S4: 95; Pla: 91	Migraine with aura: S4: 8%; Pla: 8% Migraine without aura: S4: 65%; Pla: 68% Migraine with or without aura: S4: 27%; Pla: 24% Use of migraine prophylaxis (%): S4: 56; Pla: 66 Severity of pain(%) Mild: S4: <1%; Pla: 1% Moderate: S4: 47%; Pla: 51% Severe: S4: 53%; Pla: 48%

***p<0.01 vs placebo**
‡pp<0.05 vs placebo
§p<0.001 vs placebo

Evidence Table 4. Triptan compared with placebo: Characteristics and outcomes

			Results
Author Year Country Trial Name (Quality Score)	**Number screened/ eligible/ enrolled**	**Number withdrawn/ lost to fu/analyzed**	**Relief at various times**
Wendt 2006 USA	NR/NR/577	NR/NR/577	Pain-relief at 10 minutes (%) S4: 11% vs Pla: 6% (p=0.039) Pain-relief at 20 minutes (%) S4: 27% vs Pla: 11% (p<0.001) Pain-relief at 30 minutes (%) S4: 43% vs 18% (p<0.001) Pain-relief at 40 minutes (%) S4: 56% vs Pla: 23% (p<0.001) Pain-relief at 50 minutes (%) S4: 62% vs Pla: 24% (p<0.001) Pain-relief at 1 hour (%) S4: 67% vs Pla: 25% (p<0.001) Pain-relief at 90 minutes (%) S4: 69% vs Pla: 26% (p<0.001) Pain-relief at 2 hours (%) S4: 70% vs Pla: 22% (p<0.001)

***p<0.01 vs placebo**
‡pp<0.05 vs placebo
§p<0.001 vs placebo

Evidence Table 4. Triptan compared with placebo: Characteristics and outcomes

Author Year Country Trial Name (Quality Score)	Pain Free at various times (% patients)	Presence of migraine-associated symptoms at 2 hours	Other efficacy outcomes
Wendt 2006 USA	Pain-free at 10 minutes S4: 1% vs Pla: 1% (NS) Pain-free at 20 minutes S4: 5% vs Pla: 2% (NS) Pain-free at 30 minutes S4: 10% vs 3% (p<0.001) Pain-free at 40 minutes S4: 18% vs Pla: 4% (p<0.001) Pain-free at 50 minutes S4: 26% vs Pla: 6% (p<0.001) Pain-free at 1 hour S4: 34% vs Pla: 7% (p<0.001) Pain-free at 90 minutes S4: 43% vs Pla: 9% (p<0.001) Pain-free at 2 hours S4: 50% vs Pla: 11% (p<0.001)	Nausea 30 minutes: S4: 39% vs Pla: 49% (p=0.021) 2 hours: S4: 12% vs Pla: 37% (p<0.001) Photophobia 10 minutes: S4: 80% vs Pla: 87% (P=0.046) 2 hours: S4: 27% vs Pla: 56% (p<0.001)	Use of rescue medication S4: 22% vs Pla: 45%

***p<0.01 vs placebo**
‡pp<0.05 vs placebo
§p<0.001 vs placebo

Evidence Table 4. Triptan compared with placebo: Characteristics and outcomes

Author Year Country Trial Name (Quality Score)	Method of adverse effects assessment	Adverse Effects Reported
Wendt 2006 USA	Patient report and lab tests	Incidence of adverse events S4: 69% vs Pla: 39% (p<0.001) Injection site reaction S4: 43% vs Pla: 15% Tingling S4: 12% vs Pla: 3% Dizziness or vertigo S4: 10% vs Pla: 5% Warm or hot sensation S4: 8% vs Pla: 2% Nausea, vomiting, or both S4: 7% vs Pla: 8%

***p<0.01 vs placebo**
‡pp<0.05 vs placebo
§p<0.001 vs placebo

Evidence Table 4. Triptan compared with placebo: Characteristics and outcomes

Author Year Country Trial Name (Quality Score)	Comments
Wendt 2006 USA	

***p<0.01 vs placebo**
‡pp<0.05 vs placebo
§p<0.001 vs placebo

Evidence Table 4. Triptan compared with placebo: Characteristics and outcomes

Author Year Country Trial Name (Quality Score)	Study design	Eligibility criteria	Interventions
Winner 2006 USA	RCT, DB, Parallel Multicenter 2 studies	IHS criteria for migraine with or without aura, aged 18 to 65 years, 1 to 6 migraines/month, awakened with moderate to severe migraine pain ≥1 in last 3 months	Sumatriptan succinate (S) 6mg Inj Placebo (pla)

***p<0.01 vs placebo**
‡pp<0.05 vs placebo
§p<0.001 vs placebo

Evidence Table 4. Triptan compared with placebo: Characteristics and outcomes

Author Year Country Trial Name (Quality Score)	Allowed other medications/ interventions	Method of Outcome Assessment and Timing of Assessment	Age Gender Ethnicity	Other population characteristics
Winner 2006 USA	Rescue medication was permitted	Primary efficacy endpoints: % pain-free at 2 hours; % migraine free at 2 hours; % at normal functioning level at 2 hours; % using rescue medication	Study 1 Mean age (years): S6: 40.2; Pla: 41.4 S6: 84% Female; Pla: 82% Female S6: 83% White; Pla: 78% White Study 2 Mean age (years): S6: 38.8; Pla: 39.3 S6: 93% Female; Pla: 81% Female S6:81% White; Pla: 89% White	Migraines without aura Study 1: S6: 59%; Pla: 62% Study 2: S6: 76%; Pla: 71% Migraines with aura Study 1: S6: 17%; Pla: 18% Study 2: S6: 14%; Pla: 12% Migrains with or without aura Study 1: S6: 24%; Pla: 20% Study 2: S6: 11%; Pla: 17%

***p<0.01 vs placebo**
‡pp<0.05 vs placebo
§p<0.001 vs placebo

Evidence Table 4. Triptan compared with placebo: Characteristics and outcomes

			Results
Author Year Country Trial Name (Quality Score)	**Number screened/ eligible/ enrolled**	**Number withdrawn/ lost to fu/analyzed**	**Relief at various times**
Winner 2006 USA	Study 1 NR/NR/357 Study 2 NR/NR/351	Study 1 1/NR/297 Study 2 1/NR/287	NR

***p<0.01 vs placebo**
‡pp<0.05 vs placebo
§p<0.001 vs placebo

Evidence Table 4. Triptan compared with placebo: Characteristics and outcomes

Author Year Country Trial Name (Quality Score)	Pain Free at various times (% patients)	Presence of migraine-associated symptoms at 2 hours	Other efficacy outcomes
Winner 2006 USA	At 2 Hours Study 1: S6: 48% vs Pla: 18% (p<0.001) Study 2: S6: 57% vs Pla: 19% (p<0.001) Sustained pain-free Study 1: S6: 32% vs Pla: 14% (p<0.001) Study 2: S6: 34% vs Pla: 15% (p<0.001)	% with symptoms Nausea Study 1: S6: 20% vs Pla: 38% (p<0.001) Study 2: S6: 17% vs Pla: 39% (p<0.001) Vomiting Study 1: S6: 1% vs Pla: 7% (NS) Study 2: S6: 1% vs Pla: 5% (NS) Photophobia Study 1: S6: 30% vs Pla: 50% (p<0.001) Study 2: S6: 27% vs Pla: 62% (p<0.001) Phonophobia Study 1: S6: 26% vs Pla: 43% (p<0.001) Study 2: S6: 20% vs Pla: 56% (p<0.001)	NR

***p<0.01 vs placebo**
‡pp<0.05 vs placebo
§p<0.001 vs placebo

Evidence Table 4. Triptan compared with placebo: Characteristics and outcomes

Author Year Country Trial Name (Quality Score)	Method of adverse effects assessment	Adverse Effects Reported
Winner 2006 USA	Patient report	Nausea Study 1: S6: 6% vs Pla: 2% Study 2: S6: 4% vs Pla 2% Injection site reaction Study 1: S6: 5% vs Pla: 2% Study 2: S6: 5% vs Pla: 1%

***p<0.01 vs placebo**
‡pp<0.05 vs placebo
§p<0.001 vs placebo

Evidence Table 4. Triptan compared with placebo: Characteristics and outcomes

Author Year Country Trial Name (Quality Score)	Comments
Winner 2006 USA	2 studies Morning migraines

***p<0.01 vs placebo**
‡pp<0.05 vs placebo
§p<0.001 vs placebo

Evidence Table 5. Triptan compared with placebo: Triptans with none or few head-to-head trials

Author, Year	Drug/Dose	Sample Size Age (mean yrs) Gender	Results at 1 hour	Results at 2 hours
Eletriptan				
Farkkila, 2003	40, 80mg	N=446 41 87.3% Female	Relief at 1 hour: E40: 40% E80: 48% Placebo: 15% (p<0.0005) Pain-free at 1 Hour: E80: 15% Placebo: 3% (p<0.05)	Relief at 2 hours: E40: 59% E80: 70% Placebo: 30% P-Value for E40, E80 vs Placebo: p<0.0001 P-Value for E40 vs E80: p<0.05 Pain-Free at 2 hours: E40: 35% E80: 42% Placebo: 7% (p<0.0001)

Evidence Table 5. Triptan compared with placebo: Triptans with none or few head-to-head trials

Author, Year	Disability, Return to Normal Function
Eletriptan	
Farkkila, 2003	Recurrance of pain within 24 Hours: E40: 26% E80:32% Placebo: 50% Need for rescue medication at 1 Hr: E40: 24% E80: 14% Placebo: 63% Nausea at 1 hour: E40: 41% E80: 44% Placebo: 62% Sustained response: E40: 39% E80: 45% Placebo: 14%

Evidence Table 5. Triptan compared with placebo: Triptans with none or few head-to-head trials

Author, Year	Drug/Dose	Sample Size Age (mean yrs) Gender	Results at 1 hour	Results at 2 hours
Frovatriptan				
Goldstein, 2002	2.5, 5, 10, 20, 40	N=- 598 41.3 84.9% Female	Relief at 2 hours: F2.5: 38% P<.05 vs placebo Placebo: 25% F5: 37% F0.5: 48% 5mg: 68% Pain-Free at 2 Hours: F2.5: 15% F5: 15% Placebo: 5%	Continued relief at 12 hrs post-dose: F: 76%-91% vs Placebo: 64% at 24 hrs: F: 80-88% vs Placebo: 83% % Patients requiring rescue medication within 24 hrs: Placebo: 48.3% F0.5: 33.3% F1: 33.3% F2.5: 28.6% F5: 29.2% % Patients rating meds as "good", "excellent": F0.5: 28% F1: 30% F2.5: 44% F5: 48%

Evidence Table 5. Triptan compared with placebo: Triptans with none or few head-to-head trials

Author, Year	Disability, Return to Normal Function
Frovatriptan	
Goldstein, 2002	

Evidence Table 5. Triptan compared with placebo: Triptans with none or few head-to-head trials

Author, Year	Drug/Dose	Sample Size Age (mean yrs) Gender	Results at 1 hour	Results at 2 hours
Rapoport, 2002	2.5-40mg	N=1453 40.6 86% Female	Relief at 2 hours: P-value= F vs Placebo 0.5mg: 28% (p=.346) 1mg: 25% (p= .726) 2.5mg: 40% (p<.001) 5mg: 38% (p= .002) 10mg: 41% (p<.001) 20mg: 48% (p<.001) 40mg: 42% (p<.001) Pain-Free at 2 Hours: P-value= F vs Placebo 0.5mg: 4% (p=.771) 1mg: 4% (p=.687) 2.5mg: 14% (p<.001) 5mg: 15% (p<.001) 10mg: 14% (p<.001) 20mg: 19% (p<.001) 40mg: 21% (p<.001)	Patients with headache recurrance within 24 hrs: Placebo: 27% 0.5mg: 9% 1mg: 16% 2.5mg: 14% 5mg: 15% 10mg: 12% 20mg: 13.8% 40mg: 11.8% Patients able to work/function normally at 2; and 4 Hours: Placebo: 20%; 38% 0.5mg: 22%; 39% 1mg: 20%; 41% 2.5mg: 34%; 48% 5mg: 31%; 51% 10mg: 25%; 53% 20mg: 31%; 57% 40mg: 31%; 49% Median time to relief: Placebo: 8.5hrs 0.5mg: 5.2hrs 1mg: 6.0hrs 2.5mg: 4.0hrs 5mg: 3.8hrs 10mg: 3.6hrs 20mg: 3.2hrs 40mg: 3.7hrs

Evidence Table 5. Triptan compared with placebo: Triptans with none or few head-to-head trials

Author, Year	Disability, Return to Normal Function
Rapoport, 2002	

Evidence Table 5. Triptan compared with placebo: Triptans with none or few head-to-head trials

Author, Year	Drug/Dose	Sample Size Age (mean yrs) Gender	Results at 1 hour	Results at 2 hours
Sumatriptan				
Brandes, 2007 Study 1	85mg	N=1441 Mean age (years) SNS:40.3; S: 40.1; NS: 39.4; Pla: 40 % Female SNS: 87; S: 86; NS: 86; Pla: 84 % White SNS: 90; S: 86; NS: 89; Pla: 88	NR	Headache relief SNS: 65% vs S: 55% vs NS: 44% vs Pla: 28% (p=0.009 for SNS vs S and p<0.001 for SNS vs Pla) Pain free SNS: 34% vs S: 25% vs NS: 15% vs Pla: 9% (p=0.009 for SNS vs S and p<0.001 for SNS vs Pla)
Brandes, 2007 Study 2	85mg	N=1470 Mean age (years) SNS: 39.4; S: 40.3; NS: 40.4; Pla: 40.6 % Female SNS: 87; S: 87; NS: 89; Pla: 89 % White SNS: 89; S: 89; NS: 90; Pla: 89	NR	Headache relief SNS: 57% vs S: 50% vs NS: 43% vs Pla: 29% (p=0.03 for SNS vs S and p<0.001 for SNS vs Pla) Pain free SNS: 30% vs S: 23% vs NS: 16% vs Pla: 10% (p=0.02 for SNS vs S and p<0.001 for SNS vs Pla)

Evidence Table 5. Triptan compared with placebo: Triptans with none or few head-to-head trials

Author, Year	Disability, Return to Normal Function
Sumatriptan	
Brandes, 2007 Study 1	NR
Brandes, 2007 Study 2	NR

Evidence Table 5. Triptan compared with placebo: Triptans with none or few head-to-head trials

Author, Year	Drug/Dose	Sample Size Age (mean yrs) Gender	Results at 1 hour	Results at 2 hours
Nasal Formulations: Sumatripan				
Diamond, 1998	5, 10, 20 mg	N=1086 41.1 87.7% Female	Relief at 1 Hour: 5mg: 34% (P<.05 vs placebo) 10mg: 40% (P<.05 vs placebo, 10mg vs 5mg) 20mg: 42% (P<.05 vs placebo, 20mg vs 5mg) Placebo: 25%	Relief at 2hrs: 5mg: 44% (P<.05 vs placebo) 10mg: 54% (P<.05 vs placebo, 10mg vs 5mg) 20mg: 60% (P<.05 vs placebo, 20mg vs 5mg) Placebo: 32% Patient-defined meaningful Relief at 2 hrs: 5mg: 41% (P<.05 vs placebo) 10mg: 50% (P<.05 vs placebo) 20mg: 56% (P<.05 vs placebo, 20mg vs 5mg) Placebo: 31%

Evidence Table 5. Triptan compared with placebo: Triptans with none or few head-to-head trials

Author, Year	Disability, Return to Normal Function
Nasal Formulations	
Diamond, 1998	Clinical Disability scores at 2 hours: 5mg: 57%-No/Mild Impairment 10mg: 67%-No/Mild Impairment 20mg: 70%-No/Mild Impairment Placebo: 50%-No/Mild Impairment

Evidence Table 5. Triptan compared with placebo: Triptans with none or few head-to-head trials

Author, Year	Drug/Dose	Sample Size Age (mean yrs) Gender	Results at 1 hour	Results at 2 hours
Peikert, 1999	2.5, 5, 10, 20mg	N=544 41.4 64.5% Female	Results at 60 Min NR	% with mod/severe headache improving to mild/none after 2hrs: 5mg: 49% (P<0.01 vs placebo) 10mg: 46% (P<0.01 vs placebo) 20mg: 64% (P<0.01 vs placebo, P<0.05 vs 10mg and 5mg) Placebo: 25% Pain-free at 2 hrs: 10mg: 24% (P<0.05 vs placebo) 20mg: 42% (P<0.001 vs placebo, P<0.003 vs 10mg) Placebo: 11%
Ryan, 1997	10, 20mg	N=845 40.7 86.1% Female	Results at 60 Min NR	Pain Relief at 2 hrs- pain reduced from severe/mod to mild/none: 10mg: 43-54% 20mg: 62-63% (P<0.05 vs placebo) Placebo: 29-35%

Evidence Table 5. Triptan compared with placebo: Triptans with none or few head-to-head trials

Author, Year	Disability, Return to Normal Function
Peikert, 1999	Report of grade 0-1 for clinical disability: 2.5mg: 39% 5mg: 53% (P<0.02 vs placebo) 10mg: 51% (P<0.05 vs placebo) 20mg: 65% (P<0.001 vs placebo, P<0.005 vs 10mg) Placebo: 28%
Ryan, 1997	Clinical Disability at 2 hrs, reported as none/mild: 10mg: 56-68% 20mg: 72-74% Placebo: 47-58%

Evidence Table 5. Triptan compared with placebo: Triptans with none or few head-to-head trials

Author, Year	Drug/Dose	Sample Size Age (mean yrs) Gender	Results at 1 hour	Results at 2 hours
Salonen, 1994	1,5,10,20,40mg	N=455 41.8 81% Female	Results at 60 Min NR	Pain relief at 2 hrs: One-nostril study Sumatriptan: 78% Placebo: 35% Two-nostril study Sumatriptan: 74% Placebo: 42%
Salonen, 1991	2 doses of 20mg, 15 minutes apart	N=74 40 85% Female	Relief at 1 Hour: Sumatriptan: 64% vs Placebo: 30% p=0.004	Relief at 2 Hours: Sumatriptan: 75% vs Placebo: 32% p=0.001

Evidence Table 5. Triptan compared with placebo: Triptans with none or few head-to-head trials

Author, Year	Disability, Return to Normal Function
Salonen, 1994	Clinical Disability at 2 hrs: Grade 0=no disability 5-40mg Sumatriptan: 0.9-1.3 Placebo: 1.7
Salonen, 1991	Clinical Disability at baseline vs 1 hr vs 2 hrs: grade 0=no pain Sumatriptan: 2.4 vs 1.1 vs 0.8 Placebo: 2.2 vs 1.8 vs 1.6

Evidence Table 5. Triptan compared with placebo: Triptans with none or few head-to-head trials

Author, Year	Drug/Dose	Sample Size Age (mean yrs) Gender	Results at 1 hour	Results at 2 hours
Dowson, 2003	0.5, 1, 2.5, 5mg	N=1093 41.25 81.9% Female	Pain-Free at 1 hour (Proportion of attacks:%): 0-90 days: 29.0% 91-180 days: 29.9% 181-270 days: 29.8% 271-360 days: 30.9% >360 days: 24.8% Relief at 1 Hour: 0-90 days: 56.2% 91-180 days: 57.3% 181-270 days: 57.9% 271-360 days: 55.7% >360 days: 46.2%	Pain Free at 2 Hours: 0.5mg: 21.8% 1mg: 24.7% 2.5mg: 48.1% 5mg: 51.5% Relief at 2 Hours: 0.5mg: 41.5% 1mg: 49.9% 2.5mg: 70.5% 5mg: 73.2%
Carpay 2004 Europe Fair quality	50 mg and 100 mg	n=481 40.6 82.9% female	Relief at 1 Hour: SRR100: 44.4% SRR50: 36.5% Placebo: 18.9%	Migraine-related symptoms at 2 hours: SRR50 vs SRR100 vs placebo Nausea: 15.6* vs 22.3* vs 38.4 Photophobia: 25.4* vs 23.6* vs 48.7 Phonophobia: 23.1* vs 20.4* vs 43

Evidence Table 5. Triptan compared with placebo: Triptans with none or few head-to-head trials

Author, Year	Disability, Return to Normal Function
Dowson, 2003	Resumption of Normal Activities at 1 Hour: 0-90 days: 40.4% 91-180 days: 40.9% 181-270 days: 40.4% 271--360 days: 37.3% >360 days: 24.8% at 2 Hours: 0-90 days: 59.7% 91-180 days: 62.2% 181-270 days: 61.6% 271-360 days: 58.0% >360 days: 56.1%
Carpay 2004 Europe Fair quality	SRR50vs SRR100 vs placebo Migraine-free (pain-free AND no associated symptoms) 30 minutes: 3.7 vs 7.1* vs 2 45 minutes: 14.7 vs 16.4* vs 7.3 1 hour: 30.1* vs 31.4* vs 17.2 2 hours: 44.9* vs 50.7* vs 17.1

Evidence Table 5. Triptan compared with placebo: Triptans with none or few head-to-head trials

Author, Year	Drug/Dose	Sample Size Age (mean yrs) Gender	Results at 1 hour	Results at 2 hours
Nasal Formulations: Zolmitripan				
Dodick, 2005	5mg	N=1868 40.7 86.7% Female	Relief at 1 Hour: Zolmitriptan: 53.2% vs Placebo: 30.6% Pain-Free at 1 Hour: Zolmitriptan: 21.3% vs Placebo: 7.9%	Relief at 2 Hours: Zolmitriptan: 66.2% vs Placebo: 35% (p< 0.001) Pain-Free at 2 Hours: Zolmitriptan: 35.6% vs Placebo: 13.7%

Evidence Table 5. Triptan compared with placebo: Triptans with none or few head-to-head trials

Author, Year	Disability, Return to Normal Function
Nasal Formulations	
Dodick, 2005	No recurrance/requirement for rescue meds: Zolmitriptan: 2.6% vs Placebo: 24.4% (p<0.0001) Return to normal activities at 1 Hour: Zolmitriptan: 60.8% vs Placebo: 47.3% (p<0.001) at 2 Hours: Zolmitriptan: 71.5% vs Placebo: 51.5% (p<0.001) Resolution of Nausea at 1 hour: Zolmitriptan: 55.1% vs Placebo: 38.3% (p<0.001) at 2 Hours: Zolmitriptan: 67.2% vs Placebo: 45.4% (p<0.001) Resolution of Vomiting: at 1 Hour: Zolmitriptan: 73.7% vs Placebo: 58.8% at 2 Hours: Zolmitriptan: 82.1% vs Placebo: 68.5%

Evidence Table 5. Triptan compared with placebo: Triptans with none or few head-to-head trials

Author, Year	Drug/Dose	Sample Size Age (mean yrs) Gender	Results at 1 hour	Results at 2 hours
Gawel, 2005	5mg Nasal	N=1044 41.6 87.5% Female	Relief at 1 Hour: Z5: 14.5% vs Placebo: 5.1% P<.0001	Relief at 2 hours: Z5: 32.6% vs Placebo: 8.5% P<.0001 Relief at 2 Hours for Moderate Pain: Z5: 67.1% vs Placebo: 28.0% P<.0001 for Severe Pain: Z5: 59.0% vs Placebo: 12.4% Pain Free at 2 Hours: Z5: 35.7% vs Placebo: 9% P<.0001

Evidence Table 5. Triptan compared with placebo: Triptans with none or few head-to-head trials

Author, Year	Disability, Return to Normal Function
Gawel, 2005	Relief at 10 minutes: Z5: 15.1% vs Placebo: 9.1% P=.0079 Relief at 30 Minutes: Z5: 7.7% vs Placebo: 3.2% P=.0039 Sustained Relief at 24 Hours: Z5: 23.9% vs Placebo: 7.4% (P<.0001) Back to Normal Activities in 2 Hours: Z5: 46.7% vs 18.7% P<.0001 Mild: Z5: 67.9% vs Placebo: 21.2% Moderate: 44.4% vs Placebo: 18.5% Severe: 56.7% vs 18.4%; P<.0001

Evidence Table 6. Triptans compared with placebo controls: Assessment of internal validity

Author Year Country	Randomization adequate?	Allocation concealment adequate?	Groups similar at baseline?	Eligibility criteria specified?	Outcome assessors masked?	Care provider masked?	Patient masked?	Reporting of attrition, crossovers, adherence, and contamination	Attrition: differential/high
Eletriptan Steering Committee in Japan, 2002	Adequate	Unclear; pre-packaged drug kits supplied using randomization codes	Yes	Yes	nr	nr	nr	Yes nr nr nr	No No
Sakai, 2002	nr	nr	Yes	Yes	nr	nr	nr	Yes nr nr nr	No No
Carpay 2004 Europe	nr	nr	yes	yes	yes	yes	yes	yes nr nr nr	no no

Evidence Table 6. Triptans compared with placebo controls: Assessment of internal validity

Author Year Country	Intention-to-treat (ITT) analysis	Post-randomization exclusions	Quality Rating	Funding
Eletriptan Steering Committee in Japan, 2002	Difference of 19 patients (6.8%) between evaluable population=326(81%) and analyzed population=307(76%)	yes	Fair	Pfizer, Ltd. Role nr
Sakai, 2002	Difference of 29 (12.5%) between evaluable population=231/289(79.9%) and analyzed population=202/289(69.9%)	yes	Fair	nr
Carpay 2004 Europe	yes	49 (10.2%) withdrawn post-randomization due to not being treated	Fair	nr

Evidence Table 6. Triptans compared with placebo controls: Assessment of internal validity

Author Year Country	Randomization adequate?	Allocation concealment adequate?	Groups similar at baseline?	Eligibility criteria specified?	Outcome assessors masked?	Care provider masked?	Patient masked?	Reporting of attrition, crossovers, adherence, and contamination	Attrition: differential/high
Cady 2006 USA	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes/NR/Yes/NR	No No
Brandes 2005 USA & Canada	Yes	Yes	Yes	Yes	NR	Yes	Yes	Yes/NR/Yes/NR	No No

Evidence Table 6. Triptans compared with placebo controls: Assessment of internal validity

Author Year Country	Intention-to-treat (ITT) analysis	Post-randomization exclusions	Quality Rating	Funding
Cady 2006 USA	Yes	Study 1 35 (1%) and Study 2 45 (11%) withdrawn post-randomization due to not being treated, withdrew consent, or lost to follow-up	Good	Merck
Brandes 2005 USA & Canada	NR	23 (<1%) withdrawn post-randomization for not having an attack and/or recording necessary information in diary	Fair	Pfizer

Evidence Table 6. Triptans compared with placebo controls: Assessment of internal validity

Author Year Country	Randomization adequate?	Allocation concealment adequate?	Groups similar at baseline?	Eligibility criteria specified?	Outcome assessors masked?	Care provider masked?	Patient masked?	Reporting of attrition, crossovers, adherence, and contamination	Attrition: differential/high
Goldstein 2005 USA	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes/NR/NR/NR	No No
Jelinski 2006 Canada	NR	Yes	Yes	Yes	NR	Yes	Yes	Yes/NR/NR/NR	No No
Mathew 2007 USA	NR	NR	Unclear; excluded 30/347 (9%) who did not have 2-hour pain intensity data	Yes	NR	Yes	Yes	Yes/NR/Yes/NR	No No

Evidence Table 6. Triptans compared with placebo controls: Assessment of internal validity

Author Year Country	Intention-to-treat (ITT) analysis	Post-randomization exclusions	Quality Rating	Funding
Goldstein 2005 USA	Yes	18 (<1%) withdrawn post-randomization for not taking study medication to treat an attack	Good	BMS
Jelinski 2006 Canada	Yes	4 (<1%) withdrawn post-randomization for not treating a migraine attack		GSK
Mathew 2007 USA	No; excluded 30/347 (9%) who did not have 2-hour pain intensity data	No	Fair	NR

Evidence Table 6. Triptans compared with placebo controls: Assessment of internal validity

Author Year Country	Randomization adequate?	Allocation concealment adequate?	Groups similar at baseline?	Eligibility criteria specified?	Outcome assessors masked?	Care provider masked?	Patient masked?	Reporting of attrition, crossovers, adherence, and contamination	Attrition: differential/high
Tepper 2006 USA	Yes	Yes	Yes	Yes	NR	Yes	Yes	Yes/NR/Yes/NR	No No
Winner 2006 USA	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes/NR/Yes/NR	No No
Wendt 2006 USA	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes/NR/Yes/NR	No No

Evidence Table 6. Triptans compared with placebo controls: Assessment of internal validity

Author Year Country	Intention-to-treat (ITT) analysis	Post-randomization exclusions	Quality Rating	Funding
Tepper 2006 USA	Yes	73 (10%) withdrawn post-randomization for not treating a migraine attack	Good	GSK
Winner 2006 USA	Yes	Study 1 58 (16%) Study 2 63(17%) withdrawn post-randomizatoin for not treating a migraine attack	Good	NR
Wendt 2006 USA	NR	NR	Fair	GSK

Evidence Table 6. Triptans compared with placebo controls: Assessment of internal validity

Author Year Country	Randomization adequate?	Allocation concealment adequate?	Groups similar at baseline?	Eligibility criteria specified?	Outcome assessors masked?	Care provider masked?	Patient masked?	Reporting of attrition, crossovers, adherence, and contamination	Attrition: differential/high
Diener 2005 Germany	Yes	Yes	Yes	Yes	NR	Yes	Yes	Yes/NR/NR/NR	No No
Diener 2005 Germany (companion paper)									
Silberstein 2008 US	Yes	Yes	Yes	Yes	NR	Yes	Yes	Yes/NR/Yes/NR	No No
Tfelt-Hansen 2006 Denmark	Unclear, authors mention "randomized in blocks of 6"	Implied, but NR	Yes	Yes	NR	NR	Yes	Yes/NR/Yes/NR	No No

Evidence Table 6. Triptans compared with placebo controls: Assessment of internal validity

Author Year Country	Intention-to-treat (ITT) analysis	Post-randomization exclusions	Quality Rating	Funding
Diener 2005 Germany Diener 2005 Germany (companion paper)	Yes	23 (10%) withdrawn post-randomization for not treating a migraine attack	Good	Bayer HealthCare
Silberstein 2008 US	Yes	183 (14%) withdrawn post-randomization for not treating a migraine attack	Good	Pozen, Inc and GlaxoSmithKline
Tfelt-Hansen 2006 Denmark	Yes	49 (32.6%) excluded post randomization for not treating a migraine attack	Fair	GSK

Evidence Table 6. Triptans compared with placebo controls: Assessment of internal validity

Author Year Country	Randomization adequate?	Allocation concealment adequate?	Groups similar at baseline?	Eligibility criteria specified?	Outcome assessors masked?	Care provider masked?	Patient masked?	Reporting of attrition, crossovers, adherence, and contamination	Attrition: differential/high
Loder 2001	Yes	Yes	Crossover	Yes	No, open	No, open	No, open	Yes/Yes/Yes/Yes	No No
Pascual 2001	Yes	Yes	Crossover	Yes	No, open	No, open	No, open	Yes/Yes/Yes/Yes	No No
Merck Protocol 39-Unpublished	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes, Yes, N/A, Yes	No No
Ahrens 1999	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes/Yes/Yes/Yes	No No
Goadsby 2008	NR	NR	Yes	Yes	Yes	Yes	Yes	Yes/No/No/No	No No

Evidence Table 6. Triptans compared with placebo controls: Assessment of internal validity

Author Year Country	Intention-to-treat (ITT) analysis	Post-randomization exclusions	Quality Rating	Funding
Loder 2001	No; excluded 88/472 (19%) who only treated 1 attack	No	Fair	Merck
Pascual 2001	No; excluded 32/481 (7%) for sumatriptan and 25/481 (5%) for rizatriptan in headache relief analysis	No	Fair	Merck
Merck Protocol 39-Unpublished	Yes	No	Good	Merck
Ahrens 1999	No; excluded 2/188 (1%) from rizatriptan and 5/185 (3%) from placebo groups that discontinued for "other" reasons	No	Good	Merck
Goadsby 2008	Yes	No	Fair	NR

Evidence Table 7. Triptan compared with placebo: Sumatriptan SC - pain outcomes

Author	Sumatriptan Dosage (mg)	Notes	30-min outcomes	1-hour outcomes	2-hour outcomes	Earliest relief (min)
Akpunonu 1995	6mg	Time to discharge: 60 vs 96 min	NR	NR	NR	43 vs 66 min
Anonymous 1991	6mg, 8mg		Relief: 51 vs 15	Relief: 73 vs 26 Free: 45 vs 8	NR	30
Bousser 1993	6mg	EARLY MORNING	NR	Relief: 71 vs 21 Free: 33 vs 10	Relief: 78 vs 28 Free: 44 vs 18	NR
Cady 1991 (JAMA)	6mg	Pooled results from 2 studies	NR	Relief: 70 vs 22 Free: 49 vs 9	NR	10
Cady 1993 (Neurology)	6mg		Relief: 54 vs 11	Relief: 80 vs 18	NR	
Cady 1998 PRODUCTIVITY	6mg	Sumatriptan naïve (any form); Only generalizable to patients that are working 8-hour shifts and have a migraine w/I the 1st 4 hours of a shift	NR	NR	NR	
Cull 1997	S 6 mg	Tx of recurrences	NR	NR	NR	

Evidence Table 7. Triptan compared with placebo: Sumatriptan SC - pain outcomes

Author	Earliest pain free	24-hr sustained S>P	↓ in related sx	AEs: S=P
Akpunonu 1995			N, pht, phn	Dizziness, tingling, chest tightness
Anonymous 1991	30	Recurrence higher in S groups	Y	Injection site reaction; nausea/vomiting; flushing;
Bousser 1993	NR	Recurrence: S=P	N and V	Parasthesia, injection site reactions; flushes
Cady 1991 (JAMA)	10	Pain-free at 24 hrs	Nausea (20 min); photophobia (60 min)	
Cady 1993 (Neurology)		Y: 30-40 vs 3-12	N, Pht, Phn @ 90	Injection site reaction (79 vs 24); tingling (23 vs 1)
Cady 1998 PRODUCTIVITY				
Cull 1997				

Evidence Table 7. Triptan compared with placebo: Sumatriptan SC - pain outcomes

Author	Sumatriptan Dosage (mg)	Notes	30-min outcomes	1-hour outcomes	2-hour outcomes	Earliest relief (min)
Dahlof 1992	S 8 mg	8 mg General well-being (MSEP): S>P	NR	NR	NR	30
Diener 1999	6mg		NR	NR	Relief: 91.2 vs 23.8 Free: 76.3 vs 14.3	
Diener 2001	S 6 mg	Focused on comparison between S and alnitidan	NR	NR	NR	
Ensink 1991	1-3mg, 1-8mg	2 protocols, pooled	NR	NR	NR	30
Gross 1994	S 6 mg (novel self-injector)		NR	NR	NR	
Henry 1993	S 6 mg	100% concomitant use of DHE	NR	NR	NR	
Jensen, 1995	S6	Sumatriptan naïve	NR	NR	NR	
Mathew 1992	1mg, 2mg,3mg,4mg,6mg,8 mg		NR	Relief: 73 vs 24	NR	20
Mushet 1996 (Study 1)	6mg (using Imitrex Stat-Dose System)	S-SC naïve	NR	NR	Relief: 73 vs 28	10
Mushet 1996 (Study 2)	6mg (using Imitrex Stat-Dose System)	S-SC naïve	NR	NR	Relief: 79 vs 37	30
Pfaffenrath 1991	6mg		NR	Relief: 77 vs 26	Relief: 83 vs 30 Free: 62 vs 13	60
Russell 1994	6mg		NR	NR	NR	
Thomson 1993	4mg		Relief: 64 vs 27	NR	NR	30
Visser 1992	S 1, 2, or 3 mg	up to 3 mg only	NR	NR	NR	30

Evidence Table 7. Triptan compared with placebo: Sumatriptan SC - pain outcomes

Author	Earliest pain free	24-hr sustained S>P	↓ in related sx	AEs: S=P
Dahlof 1992			N, Pht	
Diener 1999		recurrence: 23.1 vs 20	N, Pht, Phn	
Diener 2001		30	Y at 60- and 120-min (any associated)	S>P
Ensink 1991				
Gross 1994			Y	
Henry 1993				
Jensen, 1995				
Mathew 1992			nausea, pht @ 60	Injection site reaction, tingling, flushing
Mushet 1996 (Study 1)	40	NR	N, Pht, Phn all w/l 60 min; V NR	X
Mushet 1996 (Study 2)	40	NR	N, Pht, Phn all w/l 60 min; V NR	X
Pfaffenrath 1991	60	48-hr recurrence: S=P	X	S>P in some
Russell 1994				
Thomson 1993	30	24-hr recurrence only recorded in a limited of pts	X	
Visser 1992			Y	

Evidence Table 7. Triptan compared with placebo: Sumatriptan SC - pain outcomes

Author	Sumatriptan Dosage (mg)	Notes	30-min outcomes	1-hour outcomes	2-hour outcomes	Earliest relief (min)
Winner, 2006 (Study 1)	S 6mg	Morning migraines	NR	NR	Free: 48 vs 18	10
Winner, 2006 (Study 2)	S 6mg	Morning migraines	NR	NR	Free: 57 vs 19	10
Wendt, 2006	S 4mg	Acute migraine attacks in clinic	Relief: 43 vs 18 Free: 10 vs 3	Relief: 67 vs 25 Free: 34 vs 7	Relief: 70 vs 22 Free: 50 vs11	10

Evidence Table 7. Triptan compared with placebo: Sumatriptan SC - pain outcomes

Author	Earliest pain free	24-hr sustained S>P	↓ in related sx	AEs: S=P
Winner, 2006 (Study 1)	20	Pain-free at 24 hrs	N, Pht, Phn all w/in 2 hours	NS
Winner, 2006 (Study 2)	20	Pain-free at 24 hrs	N, Pht, Phn all w/in 2 hours	NS
Wendt, 2006	10	NR	N, Pht, Phn all by 2 hours	S>P

Evidence Table 8. Triptan compared with placebo: Summary of quality-of-life results

Author	Dose	Sample size Age(years) % Female	Special characteristics	Functional capacity
Almotriptan				
Freitag, 2008	Almotriptan 12.5mg (Alm) Placebo (Pla)	N=378 Age: 40.4 yrs 87% female	Functional disability and QOL	A vs Pla Functional disability at 2 hours: normal funtion 54.4% vs 38.1% , disturbed function 32.5% vs 45.2%, bed rest 13.1% vs 16.1% , ER hospitalization 0 vs 0.6% (p=0.007) at 4 hours: normal funtion 74.5% vs 54.3% , disturbed function 20.1% vs 29.3%, bed rest 4.7% vs 15.7% , ER hospitalization 0.7% vs 0.7% (p<0.001) Normal function for whole group at 2 hours: 48.7% vs 36.5%, at 4 hours: 68.6 vs 53.7% at 24 hrs: 83.5% vs 80.4% Normal functioning p<0.0026 and <0.0007 at 2 and 4 hours (favoring Alm) for Attack 1, p=0.0003 and p=0.0112 at 1 and 4 hrs and p=0.0448 for Attack 2 at 2 hrs (p values vs placebo)
Eletriptan				
Wells, 2000	40, 80mg	N=692 NR 84% Female	Time loss assessments	

Evidence Table 8. Triptan compared with placebo: Summary of quality-of-life results

Author	QOL/Work-related outcomes
Almotriptan	
Freitag, 2008	24 hour QOL social function domain p<0.05 (all 3 attacks), feelings/concern domain: p<0.05 for attack 1, p<0.01 for attack 2, p<0.001 for attack 3.
Eletriptan	
Wells, 2000	Total Time Loss: Median Hours E40: 4.0 E80: 4.0 Placebo: 9.0 Work Time Loss: Median Hours E40: 2.5 E80: 3.0 Placebo: 4.0

Evidence Table 8. Triptan compared with placebo: Summary of quality-of-life results

Author	Dose	Sample size Age(years) % Female	Special characteristics	Functional capacity
Martin 2005	40mg	N=160 37 85% Female	Patients who failed on Fiorinal and/or Fioricet Open label	Normal functioning at 2 Hours 69% of E40
Silberstein, 2006	20, 40mg	N=613 Mean age (years) E20: 39.1; E40: 38.7 % Female E20: 79; E40: 83	Work productivity outcomes	Functional response based on FIS criteria E40: 75% vs Pla: 45% (p<0.001)
Rizatriptan				
Santanello, 1997	R2.5, R5, R10	N=247 38.2 89.7% Female		
Sumatriptan-SC				
Akpunonu 1995	6mg	N=136 39.8 87%	Patients admitted to the ER	Time to discharge: 60 vs 96 min

Evidence Table 8. Triptan compared with placebo: Summary of quality-of-life results

Author	QOL/Work-related outcomes
Martin 2005	MSQ Scores Pre-treatment: 57.4 vs Post-treatment: 65.0 (change of +7.5)
Silberstein, 2006	Mean FAIM-IMMF Improvement scores E20: +20.8 vs E40: +22.1 vs Pla: +12.9 (p<0.01 for both E20 vs Pla and E40 vs Pla) Mean PQ-7 Improvement scores E20: +21.8 vs E40: +22.4 vs Pla: +11.8 (p<0.01 for both E20 vs Pla and E40 vs Pla) Mean FAIM-A&P Improvement scores E20: +22.4 vs E40: +26.3 vs Pla: +13.8 (p<0.05 for E20 vs Pla and p<0.001 for E40 vs Pla)
Rizatriptan	
Santanello, 1997	Need for Escape Medication at 4 Hours: R5: 8.1% R10: 11.8% Placebo: 17.1% R2.5: 32.6%
Sumatriptan-SC	
Akpunonu 1995	

Evidence Table 8. Triptan compared with placebo: Summary of quality-of-life results

Author	Dose	Sample size Age(years) % Female	Special characteristics	Functional capacity
Anonymous 1991	6mg, 8mg	N=639 NR 81.5%		Normal function at 60: 45 vs 9; p<0.001
Bousser 1993	6mg	N=96 41 22.5%	EARLY MORNING	
Cady 1991 (JAMA)	6mg	N=1104 39.2 32%	Pooled results from 2 studies	
Cady 1998	6mg	N=135 40 85%	Sumatriptan naïve (any form); Patients working 8-hr shifts + have migraine w/i the 1st 4 hours of a shift	
Dahlof 1992	S 8 mg	N=27 45 81.4%	General well-being	Normal function at 30, 60, 90 and 120 min: S>P; p<0.01 for all
Diener 1999	6mg	N=278 91.6 80.2%		
Diener 2001	S 6 mg	N=924 NR NR		% pts whose functional capacity was severely impaired or who required bed-rest at 1 hr: 18.2% vs 48.4%; p<0.001

Evidence Table 8. Triptan compared with placebo: Summary of quality-of-life results

Author	QOL/Work-related outcomes
Anonymous 1991	
Bousser 1993	Duration of inability to work: 5 h 40 m vs. 9 h 37 m; p<0.05
Cady 1991 (JAMA)	Return to normal/slightly impaired working ability at 20 min: S>P; p<0.001
Cady 1998	Mean productivity loss at 2 hrs/across shift; mean time lost because of reduced effectiveness while working with symptoms: 55.2 m vs 108.8 m; mean time lost due to missing work because of migraine symptoms: 31.3 m vs 69.3 m
Dahlof 1992	
Diener 1999	Time to working ability (hrs): 8.2 vs 19.4; p<0.009
Diener 2001	

Evidence Table 8. Triptan compared with placebo: Summary of quality-of-life results

Author	Dose	Sample size Age(years) % Female	Special characteristics	Functional capacity
Gross 1994	S 6 mg (novel self-injector)	N=86 43.5 78%	Self-injected at home	
Henry 1993	S 6 mg	N=76 43 86.8%	100% concomitant use of DHE	
Jensen, 1995	S6	N=138 43 90%	Sumatriptan naïve patients; self-injector	Improvement in clinical disability at 1 Hr: S > P
Mathew 1992	1mg, 2mg,3mg,4mg,6 mg,8mg	N=242 38 86.5%		Improvement in clinical disability at 60 minutes: S > P at all doses; p<0.05-0.001
Mushet 1996 (Study 1)	6mg (using Imitrex Stat-Dose System)	N=158 39.1 86.5%	Subcutaneous sumatriptan naïve	% of patients with no or mild clinical disability at 20 minutes onward: S > P; p<0.05
Mushet 1996 (Study 2)	6mg (using Imitrex Stat-Dose System)	N=78 40.2 87%	Subcutaneous sumatriptan naïve	% of patients with no or mild clinical disability at 30 minutes onward: S > P; p<0.05
Pfaffenrath 1991	6mg	N=264 41 82.5%	Auto-injector	

Evidence Table 8. Triptan compared with placebo: Summary of quality-of-life results

Author	QOL/Work-related outcomes
Gross 1994	Ability to return to work within 2 hours: 61% vs 27%; p=0.0084
Henry 1993	Time to return to work/carry out normal activities (hrs): 10 vs 14; p=0.05
Jensen, 1995	
Mathew 1992	
Mushet 1996 (Study 1)	
Mushet 1996 (Study 2)	
Pfaffenrath 1991	% Patients Able to Return to Work or Carry Out Usual Activities By 6 Hours: S: 75% vs Placebo: 39%; p<0.0001

Evidence Table 8. Triptan compared with placebo: Summary of quality-of-life results

Author	Dose	Sample size Age(years) % Female	Special characteristics	Functional capacity
Russell, 1994	6mg	N=230 44 82% Female	Auto-injector	Improvement of severity of headache: S6 had 48% more success than Placebo at both 1 and 2 hours; (p<0.001) Need for rescue medication: S6: 30% vs Placebo: 79%; (p<0.001)
Schulman, 2000	6mg	N=116 39.7 89% Female		Relief at 1 Hour: S6: 63% vs Placebo: 33%; (p=.004) % Patients experiencing meaningful relief after treatment: S6: 88% vs Placebo: 55%; (p<.001)
Thomson 1993	4mg	N=51 41 86%		% pts with improved clinical disability at 30 min: S > P; p=0.03
Visser 1992	1, 2, or 3 mg	N=685 39.7 76%		Normal or only mildly impaired at 30 min: 62% vs 32%; p<0.001

Evidence Table 8. Triptan compared with placebo: Summary of quality-of-life results

Author	QOL/Work-related outcomes
Russell, 1994	Headache: none/mild after treatment: S6: 29% vs Placebo: 9%
Schulman, 2000	Productivity loss in min. after treatment: S6: 36.8 vs Placebo: 72.6; (p=.001) % of Patients able to return to normal work performance after 2 Hours: S6: 70% vs Placebo: 30%; across the work shift: S6: 84% vs Placebo: 58%; (p<.001) Recurrence of headache during work shift: S6: 12% vs Placebo: 36%
Thomson 1993	
Visser 1992	

Evidence Table 9. Triptan compared with placebo: Summary of orally disintegrating drug results

Author, Year	Dose	Sample Size Mean age (yrs) % Female	Results at 1 Hour	Results at 2 hours	Functional/Return to Normal
Zolmitriptan					
Loder, 2005	2.5mg	N=565 41.3 85.3% Female	Pain-Free at 1 hour vs Placebo: Z2.5: 13% vs Placebo: 8%; p=0.004	Pain-Free at 2 hours vs Placebo: Z2.5: 40% vs placebo: 20%; p<0.001	Return to Normal Activities at 1 hour: Z2.5 vs Placebo: p=0.004
Spierings, 2004	5mg	N=670 42 86.5% Female	Headache Relief Z5 vs Placebo; P-Value at 1 hour: 41.1% vs 22.9%; p<0.0001 Pain-Free Z5 vs Placebo; P-Value at 1 Hour: 10.6% vs 4.4%; p=0.0002	Headache Relief Z5 vs Placebo; P-Value at 2 hours: 59% vs 30.6%; p<0.0001 Pain-Free Z5 vs Placebo; P-Value at 2 hours: 31.1% vs 11%; p<0.0001	Sustained relief at 24 Hours Z5: 42.5% vs Placebo: 16.4%; p<0.0001 Return to Activities: at 1 hour: Z5: 35.7% vs Placebo: 18.9%; p<0.0001 at 2 hours: Z5: 51.8% vs Placebo: 25.7%; p<0.0001
Rizatriptan					
Ahrens, 1999	5, 10mg	N=555 42.4 88.3% Female	Results at 1 Hour: NR	Relief at 2 Hours: R5: 59% R10: 74% Placebo: 28% Pain-Free at 2 Hours: R5: 35% R10: 42% Placebo: 10%	% of Patients with No Functional Disability: R5: 37.6% R10: 46.2% Placebo: 14.5%

Evidence Table 10. Triptan compared with placebo: Summary of early treatment results

Author, Date	Dose	Sample size Mean Age (yrs) % Female	Results at 1 hour	Results at 2 hours	Functional/Return to Normal Activities
Almotriptan					
Mathew, 2007	12.5mg	N=317 40.4 86.8% Female	Pain-relief at 1 Hour (%) Alm: 54.3 vs Pla: 41.1 (p=0.019) Pain-free at 1 Hour (%) Alm: 16.7 vs Pla: 8.4 (p=0.026)	Pain-relief at 2 Hours (%) Alm: 72.3 vs Pla: 48.4 (p<0.001) Pain-free at 2 Hours (%) Alm: 37 vs Pla:23.9 (p=0.01)	Of those reporting functional disability at time of treatment, proportion reporting normal functioning at 2 Hours: Alm: 54.4 vs Pla: 38.1 (p=0.007) At 4 Hours: Alm: 74.5 vs Pla: 54.3 (p<0.001)

Evidence Table 10. Triptan compared with placebo: Summary of early treatment results

Author, Date	Dose	Sample size Mean Age (yrs) % Female	Results at 1 hour	Results at 2 hours	Functional/Return to Normal Activities
Goadsby, 2008	Almotriptan 12.5mg (Alm) Placebo (Pla)	491 38.26 yrs 84.2% female	NR	1) A 12.5 (mild) 2) A 12.5 (moderate to severe) 3) Pla (mild) 4) Pla (moderate to severe) Pain free at 2 hrs: 49% vs 40% vs 25% vs 15% Differences: 1 vs. 2 NS (p=0.2154), 1 vs. 3 and 2 vs. 4 both significant (p < 0.001) Sustained pain-free (2-24 hrs) 46% vs 30% vs 16% vs 11% Differences: 1 vs. 2 significant (p=0.024), 2 vs. 4 significant (p=0.0018), 1 vs. 3 significant (p<0.0001), 3 vs. 4 NS (p=0.38) Pain-free data at 2 hours in AwM group Pain free at 2 hrs: 54% vs 38% vs 25% vs 18% Differences: 1 vs. 2 significant (p=0.02)	1) A 12.5 (mild) 2) A 12.5 (moderate to severe) 3) Pla (mild) 4) Pla (moderate to severe) Use of rescue medication 1 vs. 2 Difference NS p=0.1921 1 vs. 3, more in 3 took rescue med, p<0.0001 2 vs. 4, more in 4 took rescue med, p<0.0001 3 vs. 4, difference NS.

Evidence Table 10. Triptan compared with placebo: Summary of early treatment results

Author, Date	Dose	Sample size Mean Age (yrs) % Female	Results at 1 hour	Results at 2 hours	Functional/Return to Normal Activities
Eletriptan					
Olesen, 2004	80mg	N=43 40 78% Female	Need for second dose: E80: 44% vs Placebo: 34%	Relief: E80: 54% vs Placebo: 53%	Use of rescue medication: E80: 28% vs Placebo: 53%
Brandes, 2005	20mg	N=183 39.1 79% Female	NR	Pain-Free: E20: 35% vs Placebo: 22% (p<0.01)	'Migraine free' at 2 hours: E20: 32% vs Placeb: 20% (p<0.01)
Brandes, 2005	40mg	N=207 38.7 85% Female	NR	Pain-Free: E40: 47% vs Placebo: 22% (p<0.0001)	'Migraine free' at 2 hours: E40: 43% vs Placeb: 20% (p<0.0001)

Evidence Table 10. Triptan compared with placebo: Summary of early treatment results

Author, Date	Dose	Sample size Mean Age (yrs) % Female	Results at 1 hour	Results at 2 hours	Functional/Return to Normal Activities
Frovatriptan					
Cady, 2004	2.5mg	N=275 41.5 86.9% Female	Pain-Free at 1 Hour: F early dose: 11% vs Placebo: 8%	Pain-Free at 2 Hours: F early dose: 28% vs Placebo: 20%; (p=0.04)	% of Patients Rating Frovatriptan As "excellent"/"good": F: 57% vs Placebo: 46% % of Patients Requiring Second Dose after Early Dose: F: 50% vs Placebo: 68%; (p<0.001) Need for Rescue Medication: F: 20%; Placebo:NR 24 Hour Sustained Relief F-early dose vs late dose: 40% vs 31%; (p<0.05) Functional Impairment Scores: F early: 0.82 at 1 hr -0.54 at 4 Hr vs Placebo: 0.88 at 1 hr - 0.94 at 4 Hr
Rizatriptan					
Cady 2006 Study 1	10mg	N=351 43 88% Female	NR	Pain Freedom at 2 Hours R10: 57% vs Pla: 31% (p<0.001)	Functional Disability at 2 Hours R10: 31% vs Pla: 54% (p<0.05)

Evidence Table 10. Triptan compared with placebo: Summary of early treatment results

Author, Date	Dose	Sample size Mean Age (yrs) % Female	Results at 1 hour	Results at 2 hours	Functional/Return to Normal Activities
Cady 2006 Study 2	10mg	N=331 41 88% Female	NR	Pain Freedom at 2 Hours R10: 59% vs Pla: 31% (p<0.001)	Functional Disability at 2 Hours R10: 34% vs Pla: 56% (p<0.05)
Sumatriptan					
Melchart, 2003	6mg-Inj	N=179 44.4 86% Female	Pain-Free at 1 Hour: S:10% vs Placebo: 0% (p=0.012)	Pain-Free at 2 Hours: S: 24% vs Placebo: 0% (p<0.001) Relief at 2 Hours after Full Attack/ Second Treatment: S: 55% with 1st Dose Sumatriptan S: 80% with 1st Dose Placebo	Full attack prevented with early dose, at 48 hours: S: 36% vs Placebo: 18% (95% CI, 0.62-0.98)
Winner, 2003	50 mg, 100 mg	N=691 41.4 88% Female	NR	Pain-free at 2 Hours: S50: 43% vs S100: 49% vs placebo: 24%	Migraine-free at 2 Hours: S50: 43% vs S100: 57% vs placebo: 29%
Goldstein, 2005	50mg-Inj	N=67 NR NR	Pain-relief (scale 0-4, with 0=no relief and 4=complete relief): S: 1.2 vs Placebo: 0.9	Pain-relief (scale 0-4, with 0=no relief and 4=complete relief): S: 1.9 vs Placebo: 1.6	NR

Evidence Table 10. Triptan compared with placebo: Summary of early treatment results

Author, Date	Dose	Sample size Mean Age (yrs) % Female	Results at 1 hour	Results at 2 hours	Functional/Return to Normal Activities
Jelinski, 2006	50 & 100mg	N=361 40 85	Pain-Free at 1 Hour S50: 24% Pla: 7% (p<0.001) S100: 24% vs Pla: 7% (p<0.001)	Pain-Free at 2 Hours S50: 40% vs Pla: 16% (p<0.001) S100: 50% vs Pla: 16% (p<0.001)	NR
Silberstein, 2008	85mg	N=1111 40.4 88.7% Female	**Study 1** Pain free at 1 hr Sum: 20% vs Pla: 7% (p<0.001) **Study 2** Pain free at 1 hr Sum: 24% vs Pla: 7% (p<0.001)	**Study 1** Pain free at 2 hr Sum: 52% vs Pla: 17% (p<0.001) **Study 2** Pain free at 2 hr Sum: 51% vs Pla: 15% (p<0.001)	NR
Tfelt-Hansen, 200	50mg	N=101 Mean age (years): Sum: 40 (males) & 36 (females); Pla: 48 (males) & 36 (females) 78.2% females	NR	Pain free at 2 hours Sum: 39% vs Pla: 18%	NR

Evidence Table 10. Triptan compared with placebo: Summary of early treatment results

Author, Date	Dose	Sample size Mean Age (yrs) % Female	Results at 1 hour	Results at 2 hours	Functional/Return to Normal Activities
Zolmitriptan					
Klapper, 2004	2.5mg	N=280 41.7 86% Female	Pain Free Rates After Early Dose vs Placebo: 30 min: Z2.5: 5.7% vs Placebo: 1.8% 1 hour: Z2.5: 18.9% vs Placebo: 10.9% 90 min: Z2.5: 43.4% vs Placebo: 16.4% (p<0.01)	Pain-Free at 2 hours: Z2.5: 43.4% vs Placebo: 18.4%; (p<0.0001) Pain Free at 2 hours after early dose (15 min): E2.5: 57% vs Placebo: 20%; (p<0.001) Increase of Pain at 2 Hours: Z2.5: 53.7% vs Placebo: 70.4%; (p<0.0001)	Need for Rescue Medication after Early Dose: Z2.5: 41.5% vs Placebo: 69.6%; (p<0.01) Able to perform Normal Activities at 2 Hours: early dose vs non-early dose: Z2.5: 54.3% vs 28.2% Placebo: 63.5% vs 27.3%