Table F-5. Study design and populations of studies comparing older versus newer antiepileptic drugs

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| Study, Year(N) | Study Design | Country | Study Funding | Quality Rating | Older AED and Dose | Newer AED and Dose | Followup |
| Reinikainen, 1987(N= 40) | Randomized Double BlindParallel Group | Finland  | Study medication provided by: Ciba-Geicy  | Fair  | CarbamazepineIncreased gradually up to 600-1200 mg/day during the first 2 or 3 weeks according to the clinical condition | OxcarbazepineIncreased gradually up to 400-800 mg/day during the first 2 or 3 weeks according to the clinical condition | 48-50 weeks |
| Danner, 1988(N=25) | RandomizedDouble BlindCross Over | Unknown | Unknown | Fair | Carbamazepine200 mg twice a dayDosages were increased to 4 tablets daily, if necessary | Oxcarbazepine300 mg twice a dayDosages were increased to 4 tablets daily, if necessary | 24 weeks |
| Dam, 1989(N=194) | RandomizedDouble Blind Parallel Group | DenmarkFinlandNorwaySweden | Ciba-Geigy Ltd. | Fair | CarbamazepineStarting Dose:200 mg/dayMean final dose: 684 mg/day Daily dose adjusted from starting dose at weekly intervals to obtain the best possible therapeutic effect associated with satisfactory tolerabilityThe titration phase was was between 4 and 8 weeks.Once the optimal dose had been determined, treatment was continued using that dose for 12 weeks (maintenance period I) and for a further 36 weeks (maintenance period II) in patients who were well controlled and willing to continue the study | OxcarbazepineStarting Dose:300 mg/dayMean final dose: 1040 mg/dayDaily dose adjusted from starting dose at weekly intervals to obtain the best possible therapeutic effect associated with satisfactory tolerabilityThe titration phase was between 4 and 8 weeks.Once the optimal dose had been determined, treatment was continued using that dose for 12 weeks (maintenance period I) and for a further 36 weeks (maintenance period II) in patients who were well controlled and willing to continue the study | 56 weeks |

| Table F-5. Study design and populations of studies comparing older versus newer antiepileptic drugs (continued) |
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| Study, Year**(N)** | **Study Design** | **Country** | **Study Funding** | **Quality Rating** | Older AED and Dose | Newer AED and Dose | **Followup** |
| Sachdeo, 1992(N=44) | RandomizedDouble BlindParallel GroupActive Control | United States | Not specified | Poor | Valproic AcidInitial dose: 15 mg/kg/day to the closest 250 mg | FelbamateTitrated to 3,600 mg/dayor the maximum tolerated dose on study day 6 | 56-day basline periodStudy day1 – one-third reduction in dosage of previous AED.Seizure calenders, vitals and clinical lab exams were obtained on days 14, 28, 42, 70, 112.Patients completed study after 112 days of double blind treatment. |
| Faught, 1993(N=111) | Randomized Double Blind Active Control Parallel Group | United States | Wallace Laboratories  | Fair | Valproic AcidConstant dosage of 15 mg/kg/day or their maximum tolerated dosage throughout the treatment periodMean dose 3600 mg/d | FelbamateDays 1-2: 1200 mg/dayDays 3-5: 2400 mg/dayRemainder of the treatment period:3600 mg/day or maximum tolerated doseMean dose 1081.8 mg/d | 16 weeks |
| Brodie, 1995(N=260) | RandomizedDouble Blind Parallel Group | 8 Countries in the United Kingdom | Wellcome Foundation | Fair | CarbamazepineWeek 1: 200 mg/dayWeek 2: 200 mg twice a dayWeek 3-4: 200 mg in the morning and 40 0mg in the evening (600 mg/day)Week 6-24:The daily dose could be increased by one tablet at each visit if seizures continued and no clinically relevant adverse events had been reported provided that the drug was in the lower half of the target range or lower.Median daily dose of patients who completed the study: 600 mg | LamotrigineWeek 1: 50 mg/dayWeek 2: 50 mg twice a dayWeek 3-4: 50 mg in the morning and 100 mg in the evening (150mg/day)Week 6-24:The daily dose could be increased by one tablet at each visit if seizures continued and no clinically relevant adverse events had been reported provided that the drug was in the lower half of the target range or lower.Median daily dose of patients who completed the study: 150 mg | 52 weeks |
| Kalviainen, 1995(N=100) | Randomized Open-Label Parallel Group | Finland | Unknown | Poor | CarbamazepineTitration: Daily dose Increased to a plasma level of 35 µ mol/L (therapeutic range 20 to 50 µ mol/L) or lower in cases of complete seizure control or dose related side effectsIf clinically necessary, the doses of were regularly increased until seizures were controlled or toxic effects developed | VigabatrinTitration: Daily dose increased to a mean level of 50 mg/kg or lower in cases of complete seizure control or dose related side effectsDosages were not increased beyond 50 mg/kg, even in the cases of inadequate control because doses in excess of 50 mg/kg do not provide additional benefit | 12 months |
| Sabers, 1995(N= 52) | Prospective ObservationalObserver Blinded | Denmark | Ciba Geigy A/S DenmarkThe Danish Medical Research CouncilThe Jacob and Olga Madsen FoundationSygekassernes Helsefond | Fair | CarbamazepineMean dose: 8.4 mg/kg/day**Phenobarbital**Mean dose: 1.4 mg/kg/dayPhenytoinMean dose: 4.7 mg/kg/dayValproic AcidMean dose: 18.6 mg/kg/day | OxcarbazepineMean dose: 13.3 mg/kg/day | 16 weeks |
| Reunanen, 1996(N= 343) | Randomized Open LabelParallel Group | AustraliaCzech RepublicDenmarkEireFinlandGermanyItalyNetherlandsNorway | Unknown | Good  | CarbamazepineWeek 1-2: 200 mg/day in 2 divided dosesWeek 3-4: 400 mg/day in 2 divided dosesWeek5-30: 600 mg/day in 2 divided doses | Lamotrigine 100 mgWeek 1-2: 25 mg/dayWeek 3-4: 50 mg/dayWeek 5-30: 100 mg/dayLamotrigine 200 mgWeek 1-2: 25 mg/dayWeek 3-4: 50 mg/dayWeek 5-30: 200 mg/day | 30 weeks |
| Tanganelli, 1996(N= 51) | RandomizedResponse Conditional Cross-over  | Italy | Unknown | Poor | Carbamazepine Starting dose: 0.2 g/day Titration: the dose was progressively increased at weekly intervals by 0.2 gMaximum recommended dose: 1.4 g/day | VigabatrinStarting dose: 1.0 g/day Titration: the dose was progressively increased at weekly intervals 0.5 g at a timeMaximum recommended dose: 3.5 g/day | Run-in: 8 weeksPhase 1: Randomization to vigabatrin or Carbamazepine treatment - 16 weeksPhase 2: cross-over – 16 weeksOnly patients with intolerable seizures or adverse events switched to the cross-over phasePhase 3: combined therapy - 16 weeks |
| Bill, 1997(N=287) | Randomized Double Blind Paralell Group | ArgentinaBrazilMexicoSouth Africa | Unknown | Good | Phenytoin8-week Titration Phase:100 mg and increased bi-weekly based on clinical response to reach 150-800 mg/day at the end of the 8 weeksMean daily dose at the start of Maintenance treatment: 313.4 mg/day  | Oxcarbazepine8-week Titration Phase: 300 mg and increased bi-weekly based on clinical response to reach 450-2400 mg/day at the end of the 8 weeksMean daily dose at the start of maintenance treatment: 1028.4 mg/day  | 56 weeks |
| Christie, 1997(N=249) | RandomizedDouble Blind Parallel Group | Belgium Brazil France Germany The Netherlands South Africa Spain United Kingdom | Unknown | Fair | ValproateFlexible Titration Phase:300 mg/day increased biweekly based on clinical response during the 8 week periodMaintenance Phase: 900-2400 mg three times a day during the 48 week periodMean dose during maintenance phase: 1146.2 mg/day | OxcarbazepineFlexible Titration Phase:300 mg/day increased biweekly based on clinical response during the 8 week periodMaintenance Phase: 900-2400 mg/day three times a day during the 48 week periodMean dose during maintenance phase: 1052.8 mg/day | 56 weeks |
| Guerreiro, 1997(N=193) | RandomizedDouble Blind Parallel Group  | ArgentinaBrazil | Novartis | Fair | PhenytoinTitration: 50 mg/day increased gradually based on clinical response No fixed titration schedule except that patients were to be on a 3 times a daily regimen with daily doses from 150-800 mg/dayMaintenance:Daily dose range and 3 times daily regimen were to be continued during the maintenance period | Oxcarbazepine Titration: 150 mg/day increased gradually based on clinical responseNo fixed titration schedule except that patients were to be on a 3 times daily regimen with daily doses from 450-2400 mg/dayMaintenance:Daily dose range and 3 times daily regimen were to be continued during the maintenance period | 56 weeks |
| Chadwick, 1998(N=292) | RandomizedCarbamazepin Arm:Open-LabelGabapentin Arm: Double Blind | Europe Australia South Africa Canada  | Parke Davis | Poor | Carbamazepine600 mg/day | GabapentinGabapentin Arm A: 300 mg/dayGabapentin Arm B: 900 mg/day Gabapentin Arm C: 1800 mg/day | 24 weeks |
| Brodie, 1999a(N=150) | RandomizedDouble Blind Double DummieParallel Group | United Kingdom | Unknown | Good | CarbamazepineWeeks 1-2: 100 mg dailyWeeks 3-4: 100 mg twice a dayWeeks 5-6: 200 mg twice a dayWeeks 7-24: 200-2000 mg dailyDosage could be adjusted from week 6 onwards while maintaining the blindAfter titrating to 400 mg daily, upward adjustments by 200 mg increments were made in response to further seizures.Reductions in dosage by 100 mg decrements were allowed on the emergence of side effects | LamotrigineWeeks 1-2: 25 mg dailyWeeks 3-4: 25 mg twice a dayWeeks 5-6: 50 mg twice a dayWeeks 7-24: 75-500 mg dailyDosage could be adjusted from week 6 onwards while maintaining the blindAfter titrating to 100 mg daily, upward adjustments by 50 mg increments were made in response to further seizures. Reductions in dosage 25 mg were allowed on the emergence of side effects | 24 weeks |
| Brodie, 1999b(N=215) | Randomized Controlled Trial Parallel Group | Austria Belgium Czech Republic France Hungary Italy Netherlands Portugal Slovenia South Africa Spain United Kingdom | Unknown | Fair | Valproic AcidTitrated from 0.5 gram/day to a maintenance of 1.5 grams/day by 0.5 gram increments at 2 week intervals  | VigabatrinTitrated from an initial 1 gram/day to a standard 3 grams/day by 1 gram increments at 2 week intervals | 12 weeks |
| Chadwick, 1999(N=457) | RandomizedDouble Blind Parallel Group | 44 European Centres | Hoechst Marion Roussell | Fair | CarbamazepineWeek 1-6: 200 mg/dayMaintenance: 600 mg/dayMaximum: 1600 mg/day | VigabatrinWeek 1-6: 1000 mg/dayMaintenance: 2000 mg/dayMaximum: 4000 mg/day | 52 weeks |
| Gobbi, 1999(N=80) | ProspectiveObservationalopen-label, comparative trial | Italy | Unknown | Poor | CarbamazepineInitial dose: 9-20 mg/kg/day Mean initial dose: 17.1 mg/kg/dayMaintenance dose: 9-38 mg/kg/dayMean maintenance dose: 18.9 mg/kg/day | VigabatrinInitial dose: 20-80mg/kg/dayMean intial dose: 46.8mg/kg/dayMaintenance dose: 20-90mg/kg/dayMean maintenance dose: 50.5 mg/kg/day | 12 months |
| Steiner, 1999(N=181) | Randomized Double Blind Parallel Group | United KingdomGermanyBelgium | Wellcome Foundation LTD | Fair | PhenytoinWeek 1-2: 200 mg/day at night Week 3-4: 300 mg/day at nightFrom then on, the dose of either drug could be increased by one capsule if seizure control wasinadequate and no clinically significant adverse events had occurredModal and maximal daily doses were 300 and 600 mg respectively | LamotrigineWeek 1-2: 100 mg/day at nightWeek 3-4: 150 mg/day at nightFrom then on, the dose of either drug could be increased by one capsule if seizure control was inadequate and no clinically significant adverse events had occurred.Modal and maximal daily doses were 150 and 400 mg respectively | 48 weeks |
| Aldenkamp, 2000(N=53) | Randomized Observer BlindedParallel Group | Netherlands | Unknown | Good | Valproic AcidA 12-week titration interval with dosage increments of 150 mg/wk until a maximum daily dosage of 1800 mg/day or maximum tolerated doseMean Dose: 1384 (377.0) mg/day | TopiramateStarting Dose: 25 mg/weekTitration: Increased weekly to at least 200mg/day during the first 8 weeksTarget Dosage Range: 200 to 400 mg/day Mean Dose: 251.1 (101.8) mg/day | 20 weeks |
| Gillham, 2000(N=260) | RandomizedDouble Blind Parallel Group | 15 European Countries | Galxo Wellcome | Fair | CarbamazepineDosing not reported | LamotrigineDosing not reported | 48 weeks |
| Biton, 2001(N=133) | ControlledRandomized Trial Parallel Group | United States | Glaxo Wellcome Incorporated | Fair | Valproic AcidDose Escalation Phase: starting 10-15 mg/kg/dayMaintenance Phase: target dose 20 mg/kg/dayAdjustment for clinical efficacy during maintenance phase: 10-60 mg/kg/day | LamotrigineDose Escalation Phase: 25 mg/dayMaintenance Phase: target dose 200 mg/dayAdjustment in dosing for clinical efficacy during maintenance phase: 100-500 mg/day | 34 weeks |
| Cramer, 2001(N=349) | RandomizedDouble BlindParallel Group | United States | Abbott Laboratories | Good | CarbamazepineDosing not reportedPhenytoin Dosing not reported | TiagabineDosing not reported | 16 weeks |
| Kwan, 2001(N=381) | Prospective Observational | Scotland | Unknown | Poor | CarbamazepineMedian:600 mg/dayInterquartile Range: 400-600 mg/dayValproic AcidMedian: 1000 mg/dayInterquartile Range: 825-1500 mg/day | LamotrigineMedian: 200 mg/dayInterquartile Range: 150-300 mg/day | 5.6 ± 3.4 years |
| Nieto-Barrera, 2001(N=618) | Randomized Open labelParallel Group | ItalySlovakiaGermanyDenmarkUnited KingdomSpain | Not specified | Good  | CarbamazepinePatients aged 2–12 years: 5-40 mg/kg/day Patients aged 13 years or older: 100–1500 mg/dayDoses were increased until the best response was obtained according to data sheet recommendations | LamotrigineDuring the maintenance phase patients aged 2–12 years: increased by a max of 0.5-1 mg/kg every 1–2 weeks up to 2-15 mg/kg/dayPatients aged 13 years or older: Increased by a maximum of 25–50 mg every 1–2 weeks until an optimal response was achieved up to a max of 700 mg/day | 24 weeks |
| Sackellares, 2002(N= 133)  | Randomized Parallel Group | United States | Glaxo Wellcome | Fair | Valproic AcidDose escalation phase: starting 10-15 mg/kg/dayMaintenance phase: target dose 20 mg/kg/dayAdjustment for clinical efficacy during maintenance phase: 10-60 mg/kg/day | LamotrigineDose escalation phase: 25 mg/dayMaintenance phase: target dose 200 mg/dayAdjustment in dosing for clinical efficacy during maintenance phase: 100-500 mg/day | 34 weeksHealth related quality of life evaluated at baseline, week 10 and week 32 |
| Biton, 2003(N=38) | Randomized Parallel Group | United States | GlaxoSmithKline | Fair | Valproic AcidDose Escalation Phase: starting 10-15 mg/kg/dayMaintenance Phase: target dose 20 mg/kg/dayAdjustment for clinical efficacy during maintenance phase: 10-60 mg/kg/dayMean dose during the maintenance phase: 1520 (379) mg/day | LamotrigineDose Escalation Phase: 25 mg/dayMaintenance Phase: target dose 200 mg/dayAdjustment in dosing for clinical efficacy during maintenance phase: 100-500 mg/dayMean dose during the maintenance phase: 261 (76) mg/day | 34 weeks |
| Meador, 2003(N= 76) | Randomized Double blindPlacebo Controlled Parallel Group | Unknown | Ortho McNeal Pharmaceutical | Fair | Valproic Acid250 mg/day up to 2,250 mg/day | Topiramate50 mg/day up to 400 mg/day | 24 weeks |
| Privitera, 2003(N=613) | Randomized Double BlindParallel Group | Australia Brazil Belgium CanadaColumbia Costa RicaDenmarkFinland France Germany Israel Italy NetherlandsNew Zeland Norway United StatesUnited Kingdom South Africa Spain Sweden  | Johnson & Johnson  | Good | Carbamazepine Starting dose: 200 mg/dayincreased 200 mg every 2 weeksFinal dose: 600 mg/dayValproic Acid Starting dose: 250 mg/dayincreased weekly in 250 mg incrementsFinal dose: 1250 mg/day | Topiramate 100 mgStarting dose: 25 mg/day increased weekly in 25 mg incrementsFinal dose: 100 mg/dayTopiramate 200 mgStarting dose: 25 mg/day increased weekly to 50, 100, 150, and 200 mg/dayFinal dose: 200 mg/day | 6 months after the last patient was randomized  |
| Clemens, 2004(N=20) | ProspectiveObservational Cross-over  | Hungary | Unknown | Fair | CarbamazepineAverage daily dose during baseline period: 1100 mg/day  | OxcarbazepineAt the first evaluation after the baseline period, the patients took carbamazepine as in the baseline period.In the next week, 150 mg oxcarbazepine was substituted for every 100 mg carbamazepine, as proposed for patients with refractory seizures. | Unknown |
| Coppola, 2004(N=38) | Randomized Open Label Parallel Group | Italy | Not Sponsored by any commercial organization | Fair | Valproic AcidStarted at 10 mg/kg/day and increased by 5 mg/kg/day every 3 days until seizures were controlled or intolerable side effects occurred up to a maximum of 30 mg/kg/day given in three divided doses.Mean daily dose at 3 months: 22.6 mg/kg/dayMean daily dose at 12 months: 25.4 mg/kg/day | LamotrigineInitial dosing: 0.5 mg/kg twice a day for 2 weeks followed by 1.0 mg/kg/day for an additional 2 daysThereafter doses were increased in 1 mg/kg/day increments every 5 days until seizures were controlled, intolerable adverse effects occurred or a maximum of 12 mg/kg/day had been reachedMean daily dose at 3 months: 6.5 mg/kg/dayMean daily dose at 12 months:8.3 mg/kg/day | 12 months |
| Fakhoury, 2004(N=302) | Randomized Open-Label Parallel Group | United States | GlaxsoSmithKline | Poor | CarbamazepineDetermined by the clinician and intended to be consistent with dosing recommendations in the product labelValproic AcidDetermined by the clinician and intended to be consistent with dosing recommendations in the product label | LamotrigineAdded to prestudy AED (carbamazepine or valproic acid) according to the dosing recommendations in the product label | 28 weeks |
| Wheless, 2004 (N=613) | Randomized Double Blind | Unknown | Johnson and Johnson Pharmaceutical Research & Development | Fair  | CarbamazepineStarting dose 200 mg/day, increased 200 mg every 2 weeks to a total dose of 600 mg/dayValproic AcidStarting dose: 250 mg/day Dose increased weekly in 250mg increments to a total dose of 1250 mg/day | Topiramate 100 mgStarting dose: 25 mg/day Dose increased weekly in 25 mg incrementsTopiramate 200 mg Starting dose: 25 mg/day Dose increased weekly to 50, 100, 150 and 200 mg/day | Screening visitTitration phase- 35 daysStabilization – until patient exited or until 6 months after the last patient was enrolled.Study duration was up to 685 days.Mean duration of treatment was 307 days  |
| Rowan, 2005(N= 593) | RandomizedDouble BlindDouble DummyParallel Group | United States | Study funding:Veteran Affairs cooperative study programStudy medication provided by: GlaxoSmithKlinePfizer  | Fair | CarbamazepineTarget dose: 600 mg/dayTitration: started at 200 mg/day and increased by 200 mg/day every every 2 weeks to 600 mg/day to the target of 600 mg/day | GabapentinTarget dose: 1500 mg/dayTitration: started at 300 mg/day and increased by 300 mg/day every 3 days to the target of 1500 mg/dayLamotrigineTarget dose: 150 mg/dayTitration: started at 25 mg/day for 2 weeks, 50 mg/day for 2 weeks, 100 mg/day for 1 week, followed by 150 mg/day  | 52 weeks |
| Sobaniec, 2005(N= 54) | Prospective Observational  | Poland | None specified | Fair | Carbamazepine18 mg/kg every 12 hours | Vigabatrin50 mg/kg every 12 hours | 24 weeks |
| Steinhoff, 2005(N=269) | Randomized Open LabelParallel Group | Germany | GlaxoSmithKline | Good | CarbamazepineDaily dose in adults: 200-400 mg/day Recommended maintenance dose in adults: 600-1200 mg/day Daily dose in patients between 11 and 15 years of age: 200-300 mg/dayRecommended maintenance dose in children between 11 and 15 years of age: 600-1000 mg/dayValproic AcidInitial dose: 5-10 mg/kg/day Titration: increased every 4-7thday by approximately 5 mg/kgRecommended daily maintenance dose for children between 6 and 14 years of age or persons with a body weight between 20-40 kg: 600-1200 mg/day Recommended daily maintenance dose for adolescents from 14 years of age or older or persons with a body weight between 40-60 kg: 600-1500 mg Recommended daily maintenance dose for adults weighing at least 60 kg: 1200-2100 mg/day | LamotrigineWeek 1-2: 25 mg/dayWeek 3-4: 50 mg/dayWeek 5 and on: 100 mg/day or 50 mg twice a dayRecommended maintenance dose: 100-200 mg/dayThe investigators were allowed to escalate the dose further for clinical reasons up to a maximum of 500 mg/day | 24 weeks |
| Babayigit, 2006(N=68) | RetrospectiveObservational(Case Control) | Turkey | Unknown | Fair | Carbamazepine15-25 mg/kg/dayValproic Acid15-40 mg/kg/day  | Oxcarbazepine15-30 mg/kg/day | 4 months |
| Brodie, 2007(N=576) | RandomizedDouble Blind Parallel Group | 12 European Countries and South Africa | UCB Pharma | Good | Carbamazepine-Controlled ReleaseTitration Period: 200 mg/dayDosing Level 1: 200 mg twice a dayPatients experiencing a seizure during the first evaluation period had their dose increased over 2 weeks with intermediate daily doses of 600 mgDosing Level 2: 400 mg twice a dayPatients experiencing a seizure at dose level 2 progressed to dose level 2 with intermediate dosing of 600 mg twice a dayDosing Level 3: 1000 mg/day | LevetiracetamTitration Period: 500 mg/dayDosing Level 1: 500 mg twice a dayPatients experiencing a seizure during the first eval period had their dose increased over 2 weeks with intermediate daily doses of 1500mg Dosing Level 2: 1000 mg twice a day Patietns experiencing a seizure at dose level 2 progressed to dose level 3 with intermediate dosing of 1500 mg twice a dayDose Level 3: 2500 mg/day | Up to 1 yearPatients achieving the primary endpoint (6-month seizure freedom) continued on treatment for a further 6-month maintenance period |
| Donati, 2007(N=112) | RandomizedOpen-label Active-Control Three-Arm Parallel Group | 7 European countries | Novartis | Poor | CarbamazepineMean daily dose: 14.4 (3.6) mg/kg/dayValproic AcidMean daily dose 20.7 (7.5) mg/kg/day | OxcarbazepineMean daily dose: 19.6 (6.4) mg/kg/day | 6 months |
| Kang, 2007(N=112) | Randomized Observer BlindedOpen-labelParallel Group | Korea | Johnson & Johnson | Fair | CarbamazepineInitial dose: 10 mg/kg.dayTitration dose: 20 mg/kg/day over 4 weeksMaximum dose: 30 mg/kg/dayAverage daily dose during maintenance phase: 3.4 (1.6) mg/kg/day  | TopiramateInitial dose: 12.5 mg/dayTitration dose: to at least 50 mg/day in patients < 30 kg and 75 mg/day in patients > 30 kg over 4 weeksMaximum dose: 4 mg/kg/dayAverage daily dose during maintenance phase: 21.6 (3.2) mg/kg/day | 28 weeks |
| Kim, 2007(N=33) | Prospective Observational | Korea | Unknown | Poor | CarbamazepineDose not reportedValproic AcidDose not reported | LamotrigineDose not reported | 6 months |
| Levisohn, 2007(N= 28) | Randmoized,Open LabelParallel Group | United States | Unknown | Poor | Valproic AcidMedian daily dose: 750 mg/day | TopiramateMedian daily dose: 250 mg/day | 26 weeks |
| Marson, 2007SANAD Arm A(N= 1721) | RandomizedOpen Label Parallel Group | United Kingdom | Health Technology Assessment ProgramGlaxoSmithKlineJanssen-CilagNovartisPfizerSanofi-SynthelaboWellcome Trust | Fair | CarbamazepineMaintenance dose (above 16 years of age): 600 mg/dayMaintenance dose (children under 16 years of age): 15-20 mg/kg/day | LamotrigineMaintenance dose (above 16 years of age): 150 mg/dayMaintenance dose (children under 16 years of age): 3-6 mk/gk/dayGabapentinMaintenance dose (above 16 years of age): 1200 mg/dayMaintenance dose (children under 16 years of age): 30-45 mg/kg/dayTopiramateMaintenance dose (above 16 years of age): 150 mg/dayMaintenance dose (children under 16 years of age): 3-6 mg/kg/day OxcarbazepineMaintenance dose (above 16 years of age): 900 mg/dayMaintenance dose (children under 16 years of age): 15-30mg/kg/day | Primary outcome measures:1.) time from randomization to treatment failure (stopping randomized drug because of inadequate seizure control, intolerable side-effects, or both; or the addition of other antiepileptic drugs, whichever was earliest)2.) the time from randomization to a 1-year period of remission of seizuresSecondary outcome measures:1.) time from randomization to a first seizure2.) time to achieve a 2-year period of remission of seizures |
| Marson, 2007SANAD Arm B(N= 716) | RandomizedOpen Label Parallel Group | United Kingdom | Health Technology Assessment ProgramGlaxoSmithKlineJanssen-CilagNovartisPfizerSanofi-SynthelaboWellcome Trust | Fair | Valporic AcidMaintenance dose (above 16 years of age): 1000 mg/dayMaintenance dose (children under 16 years of age): 20-30 mg/kg/day | LamotrigineMaintenance dose (above 16 years of age): 150 mg/dayMaintenance dose (children under 16 years of age): 3-6 mk/gk/dayTopiramateMaintenance dose (above 16 years of age): 150 mg/dayMaintenance dose (children under 16 years of age): 3-6 mk/gk/day | Primary outcome measures:1.) time from randomization to treatment failure (stopping randomized drug because of inadequate seizure control, intolerable side-effects, or both; or the addition of other antiepileptic drugs, whichever was earliest)2.) the time from randomization to a 1-year period of remission of seizuresSecondary outcome measures:1.) time from randomization to a first seizure2.) time to achieve a 2-year period of remission of seizures |
| Saetre, 2007(N= 186) | Randomized Double Blind Double Dummy Parallel Group  | CroatiaFinlandFranceItaly Norway | GlaxoSmithKline | Good | CarbamazepineInitial dose: 100 mg/dayMaintenance dose: 400 mg/dayMaximum dose: 2000 mg/dayTitration: 100 mg/day for 2 weeks increased to 100 mg twice a day for 2 weeks, then increased to 200 mg twice a day up to a max of 1000 mg twice a day | LamotrigineInitia dose: 25 mg/dayMaintenance dose: 100 mg/dayMaximum dose: 500 mg/day Titration: 25mg/day for 2 weeks increased to 25 mg twice a day for 2 weeks, then increased to 50 mg twice a day up to a max of 250 mg twice a day | 40 weeks |
| Stephen, 2007(N=225) | Randomized Open-label Parallel Group | United Kingdom | Unknown | Good | Valproic AcidTitration:Weeks 1-2: 500 mg/day Weeks 3-4: 500 mg twice dailyWeeks 5-6: -Weeks 7-8: -Weeks 9-10: -Target dose: 1000 mg/dayDosage adjustments: 200-500 mg/day | LamotrigineTitration:Weeks 1-2: 25 mg/dayWeeks 3-4: 25 mg twice dailyWeeks 5-6: 50mg twice dailyWeeks 7-8: 50 mg/100 mgWeeks 9-10: 100 mg twice dailyTarget dose: 200 mg/dayDosage adjustments 25-50 mg/day | 1 year |
| Morrell, 2008(N=447) | Randomized Open labelParallel Group | AsiaEuropeNorth AmericaSouth America | GlaxoSmithKline | Good | Valproic AcidTarget maintenance dose: 1000 mg/day. | Lamotrigine The target maintenance dose was 100 to 200 mg/day with the dose not to exceed 500 mg/day. The target doses for lamotrigine added to enzyme-inducing AED and nonenzyme inducing AED were 200 to 400mg/day and 100 to 200mg/day, respectively | 1 year |
| Pack, 2008(N=93) | ProspectiveObservationalCross Sectional  | United States | National Institute of Health GlaxoSmithKline | Poor | CarbamazepineDose not specified PhenytoinDose not specified ValproateDose not specified | LamotrigineDose not specified | 1 year |
| Perry, 2008(N=86) | RetrospectiveObservational Cohort study | United States | UCB, Inc | Fair | CarbamazepineDose not specified  | LevetiracetamDose not specified  | Mean duration of followup for the carbamazepine group in months: 33.5 (17.8) Meanduration of followup for the levetiracetam group in months: 23.1 (12.7) |
| Kim, 2009(N=146) | Prospective Observational | Korea | Unknown | Poor  | CarbamazepineMean dose: 12.8 (3.2) mg/kg/day | TopiramateMean dose: 4.9 (2.5) mg/kg/day | 48 months |
| Kwan, 2009(N= 81) | RandmoizedOpen LabelParallel Group  | China | Unknown | Poor | Valproic AcidInitial dose: 400 mg/dayMaintenance dose: 800 mg/dayMean daily dose: 796 mg/day  | LamotrigineStarting dose: 25 mg/dayMaintenance dose: 100 mg/day Mean daily dose: 108 mg/day | 12 months |
| Ma, 2009(N= 497) | ProspectiveObservational | China | Foundation | Fair | CarbamazepineDaily dose required required by the majority of patients: 12.59 (4.76) mg/kg/dayValproic AcidDaily dose required by the majority of patients: 21.12 (6.74) mg/kg/day | TopiramateDaily dose required by the majority of patients: 4.68 (0.85) mg/kg/day | 1 year |
| Glauser, 2010(N= 451) | Randomized Double Blind Active Comparator  | United States | Study Funding: National Institute of HealthMedications provided by:PfizerAbbott LaboratoriesGlaxoSmithKline | Good | EthosuximideMean dose 33.5 (15.3)mg/kg/dayValproic AcidMean dose 34.9 (15.8)mg/kg/day | LamotrigineMean dose 9.7 (6.3) mg/kg/day | 16 weeks |
| Helmstaedter, 2010 (N=222) | Prospective ObservationalOpen-label Non-interventional ControlledSurveillance Study  | Germany | Industry: UCB Pharma | Poor | Carbamazepine Choice of drug and dose was left to the doctorsMean dose at baseline: 717 ± 300 mg/dayMean dose at followup: 789 ± 357 mg/day | Levetiracetam Choice of drug and dose was left to the doctorsMean dose at baseline: 1261 ± 460Mean dose at followup: 1311 ± 500 | 6 months |
| Ramsay, 2010(N=261) | RandomizedDouble Blind Double Dummie Active Comparator  | United States | Ortho-McNeil Janssen  | Good | PhenytoinInitial target dose: 1000 mg, given as 3 divided doses on Day 1 (400, 300 and 300 mg, respectively, at 2-hour intervals)Maintenance Period: 300 mg/day | TopiramateIntial target dose: 100 mg/day, given as 3 divided doses on Day 1 (50, 25 and 25 mg, respectively, at 2-hour intervals)Maintenance Period: 50 mg twice a day  | 4 weeks |

AED = antiepileptic drug; N = sample size