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 Blind  Parallel Group | Finland | Study medication provided by: Ciba-Geicy | Fair | Carbamazepine  Increased gradually up to 600-1200 mg/day during the first 2 or 3 weeks according to the clinical condition | Oxcarbazepine  Increased 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) | Randomized  Double Blind  Cross Over | Unknown | Unknown | Fair | Carbamazepine  200 mg twice a day  Dosages were increased to 4 tablets daily, if necessary | Oxcarbazepine  300 mg twice a day  Dosages were increased to 4 tablets daily, if necessary | 24 weeks |
| Dam, 1989  (N=194) | Randomized  Double Blind  Parallel Group | Denmark  Finland  Norway  Sweden | Ciba-Geigy Ltd. | Fair | Carbamazepine  Starting Dose:  200 mg/day  Mean final dose: 684 mg/day  Daily dose adjusted from starting dose at weekly intervals to obtain the best possible therapeutic effect associated with satisfactory tolerability  The 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 | Oxcarbazepine  Starting Dose:  300 mg/day  Mean final dose: 1040 mg/day  Daily dose adjusted from starting dose at weekly intervals to obtain the best possible therapeutic effect associated with satisfactory tolerability  The 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) | Randomized  Double Blind  Parallel Group  Active Control | United States | Not specified | Poor | Valproic Acid  Initial dose: 15 mg/kg/day to the closest 250 mg | Felbamate  Titrated to 3,600 mg/dayor the maximum tolerated dose on study day 6 | 56-day basline period  Study 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 Acid  Constant dosage of 15 mg/kg/day or their maximum tolerated dosage throughout the treatment period  Mean dose 3600 mg/d | Felbamate  Days 1-2: 1200 mg/day  Days 3-5: 2400 mg/day  Remainder of the treatment period:  3600 mg/day or maximum tolerated dose  Mean dose 1081.8 mg/d | 16 weeks |
| Brodie, 1995  (N=260) | Randomized  Double Blind Parallel Group | 8 Countries in the United Kingdom | Wellcome Foundation | Fair | Carbamazepine  Week 1: 200 mg/day  Week 2: 200 mg twice a day  Week 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 | Lamotrigine  Week 1: 50 mg/day  Week 2: 50 mg twice a day  Week 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 | Carbamazepine  Titration: 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 effects  If clinically necessary, the doses of were regularly increased until seizures were controlled or toxic effects developed | Vigabatrin  Titration: Daily dose increased to a mean level of 50 mg/kg or lower in cases of complete seizure control or dose related side effects  Dosages 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 Observational  Observer Blinded | Denmark | Ciba Geigy A/S Denmark  The Danish Medical Research Council  The Jacob and Olga Madsen Foundation  Sygekassernes Helsefond | Fair | Carbamazepine  Mean dose: 8.4 mg/kg/day  **Phenobarbital**  Mean dose: 1.4 mg/kg/day  Phenytoin  Mean dose: 4.7 mg/kg/day  Valproic Acid  Mean dose: 18.6 mg/kg/day | Oxcarbazepine  Mean dose: 13.3 mg/kg/day | 16 weeks |
| Reunanen, 1996  (N= 343) | Randomized  Open Label  Parallel Group | Australia  Czech Republic  Denmark  Eire  Finland  Germany  Italy  Netherlands  Norway | Unknown | Good | Carbamazepine  Week 1-2: 200 mg/day in 2 divided doses  Week 3-4: 400 mg/day in 2 divided doses  Week5-30: 600 mg/day in 2 divided doses | Lamotrigine 100 mg  Week 1-2: 25 mg/day  Week 3-4: 50 mg/day  Week 5-30: 100 mg/day  Lamotrigine 200 mg  Week 1-2: 25 mg/day  Week 3-4: 50 mg/day  Week 5-30: 200 mg/day | 30 weeks |
| Tanganelli, 1996  (N= 51) | Randomized  Response 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 g  Maximum recommended dose: 1.4 g/day | Vigabatrin  Starting dose: 1.0 g/day  Titration: the dose was progressively increased at weekly intervals 0.5 g at a time  Maximum recommended dose: 3.5 g/day | Run-in: 8 weeks  Phase 1: Randomization to vigabatrin or Carbamazepine treatment - 16 weeks  Phase 2: cross-over –  16 weeks  Only patients with intolerable seizures or adverse events switched to the cross-over phase  Phase 3: combined therapy - 16 weeks |
| Bill, 1997  (N=287) | Randomized Double Blind Paralell Group | Argentina  Brazil  Mexico  South Africa | Unknown | Good | Phenytoin  8-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 weeks  Mean daily dose at the start of Maintenance treatment: 313.4 mg/day | Oxcarbazepine  8-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 weeks  Mean daily dose at the start of maintenance treatment: 1028.4 mg/day | 56 weeks |
| Christie, 1997  (N=249) | Randomized  Double Blind Parallel Group | Belgium  Brazil  France  Germany  The Netherlands South Africa  Spain  United Kingdom | Unknown | Fair | Valproate  Flexible Titration Phase:  300 mg/day increased biweekly based on clinical response during the 8 week period  Maintenance Phase: 900-2400 mg three times a day during the 48 week period  Mean dose during maintenance phase: 1146.2 mg/day | Oxcarbazepine  Flexible Titration Phase:  300 mg/day increased biweekly based on clinical response during the 8 week period  Maintenance Phase: 900-2400 mg/day three times a day during the 48 week period  Mean dose during maintenance phase: 1052.8 mg/day | 56 weeks |
| Guerreiro, 1997  (N=193) | Randomized  Double Blind  Parallel Group | Argentina  Brazil | Novartis | Fair | Phenytoin  Titration: 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/day  Maintenance:  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 response  No fixed titration schedule except that patients were to be on a 3 times daily regimen with daily doses from 450-2400 mg/day  Maintenance:  Daily dose range and 3 times daily regimen were to be continued during the maintenance period | 56 weeks |
| Chadwick, 1998  (N=292) | Randomized  Carbamazepin Arm:Open-Label  Gabapentin Arm: Double Blind | Europe  Australia  South Africa  Canada | Parke Davis | Poor | Carbamazepine  600 mg/day | Gabapentin  Gabapentin Arm A: 300 mg/day  Gabapentin Arm B: 900 mg/day  Gabapentin Arm C: 1800 mg/day | 24 weeks |
| Brodie, 1999a  (N=150) | Randomized  Double Blind  Double Dummie  Parallel Group | United Kingdom | Unknown | Good | Carbamazepine  Weeks 1-2: 100 mg daily  Weeks 3-4: 100 mg twice a day  Weeks 5-6: 200 mg twice a day  Weeks 7-24: 200-2000 mg daily  Dosage could be adjusted from week 6 onwards while maintaining the blind  After 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 | Lamotrigine  Weeks 1-2: 25 mg daily  Weeks 3-4: 25 mg twice a day  Weeks 5-6: 50 mg twice a day  Weeks 7-24: 75-500 mg daily  Dosage could be adjusted from week 6 onwards while maintaining the blind  After 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 Acid  Titrated from 0.5 gram/day to a maintenance of 1.5 grams/day by 0.5 gram increments at 2 week intervals | Vigabatrin  Titrated 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) | Randomized  Double Blind Parallel Group | 44 European Centres | Hoechst Marion Roussell | Fair | Carbamazepine  Week 1-6: 200 mg/day  Maintenance: 600 mg/day  Maximum: 1600 mg/day | Vigabatrin  Week 1-6: 1000 mg/day  Maintenance: 2000 mg/day  Maximum: 4000 mg/day | 52 weeks |
| Gobbi, 1999  (N=80) | Prospective  Observational  open-label, comparative trial | Italy | Unknown | Poor | Carbamazepine  Initial dose: 9-20 mg/kg/day  Mean initial dose: 17.1 mg/kg/day  Maintenance dose: 9-38 mg/kg/day  Mean maintenance dose: 18.9 mg/kg/day | Vigabatrin  Initial dose: 20-80mg/kg/day  Mean intial dose: 46.8mg/kg/day  Maintenance dose: 20-90mg/kg/day  Mean maintenance dose: 50.5 mg/kg/day | 12 months |
| Steiner, 1999  (N=181) | Randomized Double Blind  Parallel Group | United Kingdom  Germany  Belgium | Wellcome Foundation LTD | Fair | Phenytoin  Week 1-2: 200 mg/day at night Week 3-4: 300 mg/day at night  From then on, the dose of either drug could be increased by one capsule if seizure control wasinadequate and no clinically significant adverse events had occurred  Modal and maximal daily doses were 300 and 600 mg respectively | Lamotrigine  Week 1-2: 100 mg/day at night  Week 3-4: 150 mg/day at night  From 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 Blinded  Parallel Group | Netherlands | Unknown | Good | Valproic Acid  A 12-week titration interval with dosage increments of 150 mg/wk until a maximum daily dosage of 1800 mg/day or maximum tolerated dose  Mean Dose: 1384 (377.0) mg/day | Topiramate  Starting Dose: 25 mg/week  Titration: Increased weekly to at least 200mg/day during the first 8 weeks  Target Dosage Range: 200 to 400 mg/day  Mean Dose: 251.1 (101.8) mg/day | 20 weeks |
| Gillham, 2000  (N=260) | Randomized  Double Blind Parallel Group | 15 European Countries | Galxo Wellcome | Fair | Carbamazepine  Dosing not reported | Lamotrigine  Dosing not reported | 48 weeks |
| Biton, 2001  (N=133) | Controlled  Randomized Trial Parallel Group | United States | Glaxo Wellcome Incorporated | Fair | Valproic Acid  Dose Escalation Phase: starting 10-15 mg/kg/day  Maintenance Phase: target dose 20 mg/kg/day  Adjustment for clinical efficacy during maintenance phase: 10-60 mg/kg/day | Lamotrigine  Dose Escalation Phase: 25 mg/day  Maintenance Phase: target dose 200 mg/day  Adjustment in dosing for clinical efficacy during maintenance phase: 100-500 mg/day | 34 weeks |
| Cramer, 2001  (N=349) | Randomized  Double Blind  Parallel Group | United States | Abbott Laboratories | Good | Carbamazepine  Dosing not reported  Phenytoin  Dosing not reported | Tiagabine  Dosing not reported | 16 weeks |
| Kwan, 2001  (N=381) | Prospective Observational | Scotland | Unknown | Poor | Carbamazepine  Median:600 mg/day  Interquartile Range: 400-600 mg/day  Valproic Acid  Median: 1000 mg/day  Interquartile Range: 825-1500 mg/day | Lamotrigine  Median: 200 mg/day  Interquartile Range: 150-300 mg/day | 5.6 ± 3.4 years |
| Nieto-Barrera, 2001  (N=618) | Randomized  Open label  Parallel Group | Italy  Slovakia  Germany  Denmark  United Kingdom  Spain | Not specified | Good | Carbamazepine  Patients aged 2–12 years: 5-40 mg/kg/day  Patients aged 13 years or older: 100–1500 mg/day  Doses were increased until the best response was obtained according to data sheet recommendations | Lamotrigine  During 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/day  Patients 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 Acid  Dose escalation phase: starting 10-15 mg/kg/day  Maintenance phase: target dose 20 mg/kg/day  Adjustment for clinical efficacy during maintenance phase: 10-60 mg/kg/day | Lamotrigine  Dose escalation phase: 25 mg/day  Maintenance phase: target dose 200 mg/day  Adjustment in dosing for clinical efficacy during maintenance phase: 100-500 mg/day | 34 weeks  Health related quality of life evaluated at baseline, week 10 and week 32 |
| Biton, 2003  (N=38) | Randomized Parallel Group | United States | GlaxoSmithKline | Fair | Valproic Acid  Dose Escalation Phase: starting 10-15 mg/kg/day  Maintenance Phase: target dose 20 mg/kg/day  Adjustment for clinical efficacy during maintenance phase: 10-60 mg/kg/day  Mean dose during the maintenance phase: 1520 (379) mg/day | Lamotrigine  Dose Escalation Phase: 25 mg/day  Maintenance Phase: target dose 200 mg/day  Adjustment in dosing for clinical efficacy during maintenance phase: 100-500 mg/day  Mean dose during the maintenance phase: 261 (76) mg/day | 34 weeks |
| Meador, 2003  (N= 76) | Randomized Double blind  Placebo Controlled Parallel Group | Unknown | Ortho McNeal Pharmaceutical | Fair | Valproic Acid  250 mg/day up to 2,250 mg/day | Topiramate  50 mg/day up to 400 mg/day | 24 weeks |
| Privitera, 2003  (N=613) | Randomized  Double Blind  Parallel Group | Australia  Brazil  Belgium  Canada  Columbia  Costa Rica  Denmark  Finland  France  Germany  Israel  Italy  Netherlands  New Zeland  Norway  United States  United Kingdom  South Africa Spain  Sweden | Johnson & Johnson | Good | Carbamazepine  Starting dose: 200 mg/day  increased 200 mg every 2 weeks  Final dose: 600 mg/day  Valproic Acid  Starting dose: 250 mg/day  increased weekly in 250 mg increments  Final dose: 1250 mg/day | Topiramate 100 mg  Starting dose: 25 mg/day increased weekly in 25 mg increments  Final dose: 100 mg/day  Topiramate 200 mg  Starting dose: 25 mg/day increased weekly to 50, 100, 150, and 200 mg/day  Final dose: 200 mg/day | 6 months after the last patient was randomized |
| Clemens, 2004  (N=20) | Prospective  Observational Cross-over | Hungary | Unknown | Fair | Carbamazepine  Average daily dose during baseline period: 1100 mg/day | Oxcarbazepine  At 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 Acid  Started 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/day  Mean daily dose at 12 months: 25.4 mg/kg/day | Lamotrigine  Initial dosing: 0.5 mg/kg twice a day for 2 weeks followed by 1.0 mg/kg/day for an additional 2 days  Thereafter 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 reached  Mean daily dose at 3 months: 6.5 mg/kg/day  Mean 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 | Carbamazepine  Determined by the clinician and intended to be consistent with dosing recommendations in the product label  Valproic Acid  Determined by the clinician and intended to be consistent with dosing recommendations in the product label | Lamotrigine  Added 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 | Carbamazepine  Starting dose 200 mg/day, increased 200 mg every 2 weeks to a total dose of 600 mg/day  Valproic Acid  Starting dose: 250 mg/day  Dose increased weekly in 250mg increments to a total dose of 1250 mg/day | Topiramate 100 mg  Starting dose: 25 mg/day  Dose increased weekly in 25 mg increments  Topiramate 200 mg  Starting dose: 25 mg/day  Dose increased weekly to 50, 100, 150 and 200 mg/day | Screening visit  Titration phase- 35 days  Stabilization – 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) | Randomized  Double Blind  Double Dummy  Parallel Group | United States | Study funding:  Veteran Affairs cooperative study program  Study medication provided by: GlaxoSmithKline  Pfizer | Fair | Carbamazepine  Target dose: 600 mg/day  Titration: 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 | Gabapentin  Target dose: 1500 mg/day  Titration: started at 300 mg/day and increased by 300 mg/day every 3 days to the target of 1500 mg/day  Lamotrigine  Target dose: 150 mg/day  Titration: 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 | Carbamazepine  18 mg/kg every 12 hours | Vigabatrin  50 mg/kg every 12 hours | 24 weeks |
| Steinhoff, 2005  (N=269) | Randomized  Open Label  Parallel Group | Germany | GlaxoSmithKline | Good | Carbamazepine  Daily 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/day  Recommended maintenance dose in children between 11 and 15 years of age: 600-1000 mg/day  Valproic Acid  Initial dose: 5-10 mg/kg/day  Titration: increased every 4-7th  day by approximately 5 mg/kg  Recommended 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 | Lamotrigine  Week 1-2: 25 mg/day  Week 3-4: 50 mg/day  Week 5 and on: 100 mg/day or 50 mg twice a day  Recommended maintenance dose: 100-200 mg/day  The 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) | Retrospective  Observational  (Case Control) | Turkey | Unknown | Fair | Carbamazepine  15-25 mg/kg/day  Valproic Acid  15-40 mg/kg/day | Oxcarbazepine  15-30 mg/kg/day | 4 months |
| Brodie, 2007  (N=576) | Randomized  Double Blind Parallel Group | 12 European Countries and South Africa | UCB Pharma | Good | Carbamazepine-Controlled Release  Titration Period: 200 mg/day  Dosing Level 1: 200 mg twice a day  Patients experiencing a seizure during the first evaluation period had their dose increased over 2 weeks with intermediate daily doses of 600 mg  Dosing Level 2: 400 mg twice a day  Patients experiencing a seizure at dose level 2 progressed to dose level 2 with intermediate dosing of 600 mg twice a day  Dosing Level 3: 1000 mg/day | Levetiracetam  Titration Period: 500 mg/day  Dosing Level 1: 500 mg twice a day  Patients 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 day  Dose Level 3: 2500 mg/day | Up to 1 year  Patients achieving the primary endpoint (6-month seizure freedom) continued on treatment for a further 6-month maintenance period |
| Donati, 2007  (N=112) | Randomized  Open-label  Active-Control Three-Arm  Parallel Group | 7 European countries | Novartis | Poor | Carbamazepine  Mean daily dose: 14.4 (3.6) mg/kg/day  Valproic Acid  Mean daily dose 20.7 (7.5) mg/kg/day | Oxcarbazepine  Mean daily dose: 19.6 (6.4) mg/kg/day | 6 months |
| Kang, 2007  (N=112) | Randomized  Observer Blinded  Open-label  Parallel Group | Korea | Johnson & Johnson | Fair | Carbamazepine  Initial dose: 10 mg/kg.day  Titration dose: 20 mg/kg/day over 4 weeks  Maximum dose: 30 mg/kg/day  Average daily dose during maintenance phase: 3.4 (1.6) mg/kg/day | Topiramate  Initial dose: 12.5 mg/day  Titration dose: to at least 50 mg/day in patients < 30 kg and 75 mg/day in patients > 30 kg over 4 weeks  Maximum dose: 4 mg/kg/day  Average daily dose during maintenance phase: 21.6 (3.2) mg/kg/day | 28 weeks |
| Kim, 2007  (N=33) | Prospective  Observational | Korea | Unknown | Poor | Carbamazepine  Dose not reported  Valproic Acid  Dose not reported | Lamotrigine  Dose not reported | 6 months |
| Levisohn, 2007  (N= 28) | Randmoized,  Open Label  Parallel Group | United States | Unknown | Poor | Valproic Acid  Median daily dose: 750 mg/day | Topiramate  Median daily dose: 250 mg/day | 26 weeks |
| Marson, 2007  SANAD Arm A  (N= 1721) | Randomized  Open Label  Parallel Group | United Kingdom | Health Technology Assessment Program  GlaxoSmithKline  Janssen-Cilag  Novartis  Pfizer  Sanofi-Synthelabo  Wellcome Trust | Fair | Carbamazepine  Maintenance dose (above 16 years of age): 600 mg/day  Maintenance dose (children under 16 years of age): 15-20 mg/kg/day | Lamotrigine  Maintenance dose (above 16 years of age): 150 mg/day  Maintenance dose (children under 16 years of age): 3-6 mk/gk/day  Gabapentin  Maintenance dose (above 16 years of age): 1200 mg/day  Maintenance dose (children under 16 years of age): 30-45 mg/kg/day  Topiramate  Maintenance dose (above 16 years of age): 150 mg/day  Maintenance dose (children under 16 years of age): 3-6 mg/kg/day  Oxcarbazepine  Maintenance dose (above 16 years of age): 900 mg/day  Maintenance 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 seizures  Secondary outcome measures:  1.) time from randomization to a first seizure  2.) time to achieve a 2-year period of remission of seizures |
| Marson, 2007  SANAD Arm B  (N= 716) | Randomized  Open Label  Parallel Group | United Kingdom | Health Technology Assessment Program  GlaxoSmithKline  Janssen-Cilag  Novartis  Pfizer  Sanofi-Synthelabo  Wellcome Trust | Fair | Valporic Acid  Maintenance dose (above 16 years of age): 1000 mg/day  Maintenance dose (children under 16 years of age): 20-30 mg/kg/day | Lamotrigine  Maintenance dose (above 16 years of age): 150 mg/day  Maintenance dose (children under 16 years of age): 3-6 mk/gk/day  Topiramate  Maintenance dose (above 16 years of age): 150 mg/day  Maintenance 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 seizures  Secondary outcome measures:  1.) time from randomization to a first seizure  2.) time to achieve a 2-year period of remission of seizures |
| Saetre, 2007  (N= 186) | Randomized Double Blind Double Dummy Parallel Group | Croatia  Finland  France  Italy  Norway | GlaxoSmithKline | Good | Carbamazepine  Initial dose: 100 mg/day  Maintenance dose: 400 mg/day  Maximum dose: 2000 mg/day  Titration: 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 | Lamotrigine  Initia dose: 25 mg/day  Maintenance dose: 100 mg/day  Maximum 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 Acid  Titration:  Weeks 1-2: 500 mg/day  Weeks 3-4: 500 mg twice daily  Weeks 5-6: -  Weeks 7-8: -  Weeks 9-10: -  Target dose: 1000 mg/day  Dosage adjustments: 200-500 mg/day | Lamotrigine  Titration:  Weeks 1-2: 25 mg/day  Weeks 3-4: 25 mg twice daily  Weeks 5-6: 50mg twice daily  Weeks 7-8: 50 mg/100 mg  Weeks 9-10: 100 mg twice daily  Target dose: 200 mg/day  Dosage adjustments 25-50 mg/day | 1 year |
| Morrell, 2008  (N=447) | Randomized  Open label  Parallel Group | Asia  Europe  North America  South America | GlaxoSmithKline | Good | Valproic Acid  Target 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) | Prospective  Observational  Cross Sectional | United States | National Institute of Health  GlaxoSmithKline | Poor | Carbamazepine  Dose not specified  Phenytoin  Dose not specified  Valproate  Dose not specified | Lamotrigine  Dose not specified | 1 year |
| Perry, 2008  (N=86) | Retrospective  Observational Cohort study | United States | UCB, Inc | Fair | Carbamazepine  Dose not specified | Levetiracetam  Dose 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 | Carbamazepine  Mean dose: 12.8 (3.2) mg/kg/day | Topiramate  Mean dose: 4.9 (2.5) mg/kg/day | 48 months |
| Kwan, 2009  (N= 81) | Randmoized  Open Label  Parallel Group | China | Unknown | Poor | Valproic Acid  Initial dose: 400 mg/day  Maintenance dose: 800 mg/day  Mean daily dose: 796 mg/day | Lamotrigine  Starting dose: 25 mg/day  Maintenance dose: 100 mg/day  Mean daily dose: 108 mg/day | 12 months |
| Ma, 2009  (N= 497) | Prospective  Observational | China | Foundation | Fair | Carbamazepine  Daily dose required required by the majority of patients: 12.59 (4.76) mg/kg/day  Valproic Acid  Daily dose required by the majority of patients: 21.12 (6.74) mg/kg/day | Topiramate  Daily 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 Health  Medications provided by:  Pfizer  Abbott Laboratories  GlaxoSmithKline | Good | Ethosuximide  Mean dose 33.5 (15.3)mg/kg/day  Valproic Acid  Mean dose 34.9 (15.8)mg/kg/day | Lamotrigine  Mean dose 9.7 (6.3) mg/kg/day | 16 weeks |
| Helmstaedter, 2010  (N=222) | Prospective  Observational  Open-label  Non-interventional Controlled  Surveillance Study | Germany | Industry: UCB Pharma | Poor | Carbamazepine  Choice of drug and dose was left to the doctors  Mean dose at baseline: 717 ± 300 mg/day  Mean dose at followup: 789 ± 357 mg/day | Levetiracetam  Choice of drug and dose was left to the doctors  Mean dose at baseline: 1261 ± 460  Mean dose at followup: 1311 ± 500 | 6 months |
| Ramsay, 2010  (N=261) | Randomized  Double Blind Double Dummie Active Comparator | United States | Ortho-McNeil Janssen | Good | Phenytoin  Initial 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 | Topiramate  Intial 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