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A multicentre, double-blind, randomised, phase IV clinical trial comparing the safety, tolerability and efficacy of levetiracetam versus lamotrigine and carbamazepine in the oral antiepileptic therapy of newly diagnosed elderly patients with focal epilepsy

Submission date
08/08/2006

Recruitment status
No longer recruiting

Registration date
12/09/2006

Overall study status
Completed

Last Edited
11/04/2019

Condition category
Nervous System Diseases

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)

2005-003324-19

ClinicalTrials.gov (NCT)
NCT00438451

Protocol serial number
N/A

Study information

Scientific Title
A multicentre, double-blind, randomised, phase IV clinical trial comparing the safety, tolerability and efficacy of levetiracetam versus lamotrigine and carbamazepine in the oral antiepileptic therapy of newly diagnosed elderly patients with focal epilepsy

Acronym
STEPONE05

Study objectives
Objective:
To evaluate the tolerability and efficacy of Levetiracetam (LEV) in newly diagnosed elderly patients (aged 60 years or above) with focal epilepsy compared to Lamotrigine (LTG) or Carbamazepine slow release (CBZ).

Outcome:
The primary outcome will be the 58-week retention rate measured by the number of drop outs due to adverse events or seizures from day one of treatment.

Risks for participants of this trial are:
1. To receive an antiepileptic treatment insufficient to control seizures on an individual basis
2. To be undertreated in the six weeks of titration (can be compensated by short-term benzodiazepines)
3. To obtain CBZ, which may have a less favourable safety profile compared to other drugs already licensed in monotherapy

Benefits, on the other hand, can be expected to outweigh the risks because:
1. Diagnosis and treatment indication will be made by neurologists and reviewed by expert epileptologists
2. Closer follow-up and physician contact will provide better medical supervision
3. Additional physical and cognitive testing as part of the protocol will be more sensitive to detect adverse effects in due course
4. Patients receiving LEV or LTG might benefit from better tolerability
5. Participants receiving LEV will benefit from the favourable pharmacological profile (no drug interactions, no liver enzyme induction)

Ethics approval required
Old ethics approval format

Ethics approval(s)

Ethics Commission of the National Physician Chamber of Rhineland-Palatinate, 02/11/2006. Ethics approval also received from Switzerland and Austrian sites on 17/07/2007 and 13/08 /2007, respectively.

Study design
Randomised double-blind multicentre phase IV study using a parallel-group design with three treatment groups

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Newly diagnosed focal epilepsy

Interventions
The study will consist of a six week titration phase and a 52 week maintenance phase. Patients who successfully complete the trial (final visit [V6]) will be unblinded and offered either to continue on their current drug or be changed to an alternative AED treatment of choice.

There will be three treatment group in this trial:
Group one: oral administration of LEV (500-300 mg, initial target dose 1000 mg/day)
Group two: oral administration of CBZ (200-1200 mg, initial target dose 400 mg/day)
Group three: oral administration of LTG (50-300 mg, initial target dose 100 mg/day)

Intervention Type
Drug

Phase
Phase IV

Drug/device/biological/vaccine name(s)
Levetiracetam, carbamazepine, lamotrigine

Primary outcome(s)
The primary outcome will be the 58-week retention rate measured by the number of drop outs due to adverse events or seizures from day one of treatment.

Key secondary outcome(s))
Secondary outcomes include:
1. Proportion of patients remaining seizure-free at week 30 (V4)
2. Proportion of patients remaining seizure free at week 58 (V6)
3. The time (in days) to first break-through seizure (from day one of treatment)
4. The absolute seizure frequency during the maintenance (over 52 weeks) phase
5. Proportion of seizure-free days during the maintenance phase for subjects who enter the maintenance phase
6. The frequency of adverse events (from day one of treatment)
7. Quality Of Life In Epilepsy (QOLIE-31) survey results at V6

8. Portland Neurotoxicity scale at V6
9. Results of cognitive testing (EpiTrack© by UCB)

Completion date
30/10/2008

Eligibility

Key inclusion criteria
1. Aged 60 years or above
2. New onset focal epilepsy (either at least one epileptic seizure in the last six months and focal epileptiform discharges on electroencephalogram (EEG) or a relevant lesion on computed tomography (CT)/magnetic resonance imaging (MRI) or at least two epileptic seizures, one of which occurred in the last six months prior inclusion)
3. No previous anti-epileptic drug (AED) treatment, except for a period not longer than four weeks prior to inclusion (V0)
4. Ability of subject to understand verbal and written instructions, to comply with all study requirements, and to comprehend character and individual consequences of the clinical trial
5. Written informed consent before enrolment in the trial

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Key exclusion criteria
Subjects presenting with any of the following criteria will not be included in the trial:
1. Acute symptomatic epileptic seizures occurring acutely within a two week period after the onset of an acute illness such as cerebral haemorrhage, cerebral infarct, rapid progressive malignancy or other acute brain abnormalities (i.e. encephalitis, hypoxic brain damage, trauma, metabolic derangement, following brain surgery)
2. Dementia (as defined by history)
3. Renal insufficiency as defined by glomerular filtration rate (GFR) less than 50 ml/min
4. Increased liver enzymes (glutamic-oxaloacetic transaminase [GOT], glutamic-pyruvic transaminase [GPT], gamma-glutamyl-transferase [gGT]) or increased bilirubin more than or equal to twofold the upper limit of normal (ULN)
5. Pre-treatment with valproic acid within the four weeks prior inclusion (V0)
6. Contraindication against or history of hypersensitivity to any of the investigational medicinal products or to any drug with similar chemical structure or to any excipient present in the pharmaceutical form of the investigational medicinal products
7. Participation in other clinical trials

Date of first enrolment

01/10/2006

Date of final enrolment
30/10/2008

Locations

Countries of recruitment
Austria

Germany

Switzerland

Study participating centre
University of Mainz
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Sponsor information

Organisation
University of Mainz Medical Faculty (Germany)

ROR
https://ror.org/023b0x485

Funder(s)

Funder type
Industry

Funder Name
UCB GmbH (Germany)

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/03/2015	11/04/2019	Yes	No
Basic results				No	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes