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Trial comparing the effectiveness and cost effectiveness of levetiracetam and zonisamide versus standard treatments for epilepsy: a comparison of Standard And New Antiepileptic Drugs

Submission date
03/07/2012

Recruitment status
No longer recruiting

Registration date
03/07/2012

Overall study status
Completed

Last Edited
22/12/2021

Condition category
Nervous System Diseases

[X] Prospectively registered

[X] Protocol

[_] Statistical analysis plan

[X] Results

[_] Individual participant data

Plain English summary of protocol

Background and study aims
Epilepsy is a condition that affects the brain and causes repeated seizures. Antiepileptic drugs (AED) are the mainstay of treatment and may have to be taken for life. The ultimate goal of treatment is to maximise quality of life by eliminating seizures at drug doses that do not cause side effects. However, for many patients there is a necessary trade-off between effective seizure control and side effects, which can diminish quality of life. Over the past 20 years, a number of new AED drugs have become available and have been approved for NHS use on the basis of information from short-term studies, but these studies do not provide information about the longer term outcomes. The aim of this study is to compare the effectiveness and cost-effectiveness of the AEDs levetiracetam and zonisamide compared with the standard treatments for epilepsy (lamotrigine and valproate).

Who can participate?
Children aged 5 or older and adults with epilepsy

What does the study involve?
This study is essentially two studies run in parallel. Patients with untreated focal onset seizures (affecting a small part of the brain) are randomly allocated to be treated with either lamotrigine, levetiracetam or zonisamide. Patients with generalised onset seizures (affecting both halves of the brain) or seizures that are difficult to classify are randomly allocated to be treated with either levetiracetam or valproate.

What are the possible benefits and risks of participating?
Not provided at time of registration

Where is the study run from?
University of Liverpool (UK)

When is the study starting and how long is it expected to run for?
August 2012 to February 2018

Who is funding the study?
NIHR Health Technology Assessment program (HTA) (UK)

Who is the main contact?
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Study website
http://www.sanad2.org.uk/

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
2012-001884-64

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
12477

Study information

Scientific Title

A pragmatic randomised controlled trial comparing the effectiveness and cost effectiveness of levetiracetam and zonisamide versus standard treatments for epilepsy: a comparison of Standard And New Antiepileptic Drugs (SANAD-II)

Acronym
SANAD-II

Study objectives
SANAD-II is a phase IV multicentre pragmatic randomised controlled trial comparing the effectiveness and cost-effectiveness of levetiracetam and zonisamide versus standard treatments (lamotrigine and valproate) for epilepsy.

More details can be found at http://public.ukcrn.org.uk/search/StudyDetail.aspx?StudyID=12477

Ethics approval required
Old ethics approval format

Ethics approval(s)
NRES Committee North West Liverpool East, First MREC approval date 07/06/2012, ref: 12/NW /0361

Study design
Randomised; Interventional; Design type: Treatment

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Patient information sheets can be downloaded from http://www.sanad2.org.uk/families.html

Health condition(s) or problem(s) studied
Topic: Medicines for Children Research Network, Neurological; Subtopic: All Diagnoses, Neurological (all Subtopics); Disease: Nervous system disorders

Interventions
SANAD-II will essentially be two randomised controlled trials run in parallel. Arm A of SANAD-II will compare lamotrigine, levetiracetam and zonisamide in patients with untreated focal onset seizures. Arm B of SANAD-II will compare levetiracetam and valproate in patients with generalised onset seizures or seizures that are difficult to classify. It will aim to accrue about 1510 patients (children aged 5 or older and adults) over a 3.5 year period and follow up will continue for a further two years (a maximum time a patient will receive randomised treatment is 5.5 years). There will be economy of scale given that the protocols and data structure are almost

identical and that the same group of collaborators will be recruiting patients to both trials. There will be no competition for patients between Arm A and Arm B as the inclusion criteria are mutually exclusive. All treatments will be issued as per routine NHS.

Arm A: Patients randomised to receive lamotrigine, levetiracetam or zonisamide
Arm B: Patients randomised to receive levetiracetam or valproate
Trial interventions will follow the usual clinical practice

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Lamotrigine, levetiracetam, zonisamide, valproate

Primary outcome measure
Time to 12 month remission from seizures. This is a time to event outcome, measured during the entirity of follow-up.

Secondary outcome measures
1. Adverse events at 3 months, 6 months, 1 year, 2 years, 3 years, 4 years and 5 years
2. Quality of Life (QOL) outcomes at 3 months, 6 months, 1 year, 2 years, 3 years, 4 years and 5 years
3. Time to 24 month remission. This is a time to event outcome, measured during the entirity of follow-up
4. Time to first seizure. This is a time to event outcome, measured during the entirity of follow-up
5. Time to treatment failure due to inadequate seizure control. This is a time to event outcome, measured during the entirity of follow-up
6. Time to treatment failure due to unacceptable adverse events. This is a time to event outcome, measured during the entirity of follow-up
7. Time to treatment failure. This is a time to event outcome, measured during the entirity of follow-up

Overall study start date
01/08/2012

Completion date
30/11/2019

Eligibility

Key inclusion criteria
1. Male and female aged 5 years or older
2. Two or more spontaneous seizures that require antiepileptic drug treatment
3. Untreated and not previously treated with antiepileptic drugs

4. Antiepileptic drug monotherapy considered the most appropriate option
5. Willing to provide consent (patients parent/legal representative willing to give consent where the patient is aged under 16 years of age)

Participant type(s)
Patient

Age group
Child

Lower age limit
5 Years

Sex
Both

Target number of participants
Planned Sample Size: 1510; UK Sample Size: 1510

Total final enrolment
1510

Key exclusion criteria
1. Provoked seizures (e.g. alcohol)
2. Acute symptomatic seizures (e.g. acute brain haemorrhage or brain injury)
3. Currently treated with antiepileptic drugs
4. Progressive neurological disease (e.g. known brain tumour)

Date of first enrolment
01/08/2012

Date of final enrolment
01/02/2018

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
University of Liverpool
Liverpool
United Kingdom
L9 7LJ

Sponsor information

Organisation
University of Liverpool (UK)

Sponsor details
Health Services Research
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Sponsor type
University/education

ROR
https://ror.org/04xs57h96

Funder(s)

Funder type
Government

Funder Name
NIHR Health Technology Assessment program (HTA) (UK)

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date
30/11/2020

Individual participant data (IPD) sharing plan
Not provided at time of registration

IPD sharing plan summary
Not provided at time of registration

Study outputs

	Date	Date	Peer	Patient-

Output type	Details	created	added	reviewed?	facing?
Protocol article	protocol	26/08/2020	02/09/2020	Yes	No
Results article	results for newly diagnosed focal epilepsy	10/04/2021	13/04/2021	Yes	No
Results article	results for newly diagnosed generalised and unclassifiable epilepsy	10/04/2021	13/04/2021	Yes	No
Other publications	sub study on methods	05/07/2021	07/07/2021	Yes	No
Results article	HTA report	01/12/2021	22/12/2021	Yes	No
HRA research summary			28/06/2023	No	No