ISRCTN75009754 https://doi.org/10.1186/ISRCTN75009754

Prevention of sagopilone-induced neurotoxicity with acetyl-L-carnitine (ALC)

Submission date	Recruitment status	[_] Prospectively registered
28/11/2008	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
30/01/2009	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
20/05/2019	Cancer	

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

Contact name
Prof Gordon Rustin

Contact details
Medical Oncology
The Clock Tower
Mount Vernon Hospital
Northwood
United Kingdom
HA6 2RN

Additional identifiers

EudraCT/CTIS number
2008-000879-26

IRAS number

ClinicalTrials.gov number
NCT00751205

Secondary identifying numbers
311602

Study information

Scientific Title
Double-blind, randomised phase II study to evaluate the safety and efficacy of acetyl-L-carnitine in the prevention of sagopilone-induced peripheral neuropathy

Acronym
REASON

Study objectives
Primary objective:
To demonstrate the superiority of acetyl-L-carnitine (ALC) over placebo in the prevention of sagopilone-induced peripheral neuropathy.

Secondary objectives:
1. To assess the safety and efficacy of sagopilone in combination with ALC
2. To assess the pharmacokinetics of sagopilone and ALC in this combination
3. To assess the pharmacogenomics of sagopilone in combination with ALC

Ethics approval required
Old ethics approval format

Ethics approval(s)
London Research Ethics Committee, 20/10/2008

Study design
Interventional treatment randomised double-blindparallel assignment phase II safety/efficacy study

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Only available to recruiting centres/participants

Health condition(s) or problem(s) studied
Ovarian cancer; hormone-resistant prostate cancer

Interventions
Participants will be enrolled in this study to be randomised (1:1) to one of two parallel treatment arms:

Arm 1: Experimental group -
Subjects will receive intravenous (i.v.) infusion of sagopilone (16 mg/m^2) for 3 hours on day 1 of a 3-week cycle. Duration of treatment is up to 6 courses. In addition, subjects will receive 21 weeks of prophylaxis with Acetyl-L-Carnitine (ALC) 1000 mg three times a day (TID).

Arm 2: Control group -
Subjects will receive i.v. infusion of sagopilone (16 mg/m^2) for 3 hours on day 1 of a 3-week cycle. Duration of treatment is up to 6 courses. In addition, subjects will receive 21 weeks of prophylaxis with placebo TID.

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
Sagopilone, Acetyl-L-Carnitine

Primary outcome measure
Overall incidence of peripheral neuropathy (any grade) during at most 6 cycles of sagopilone treatment, based on adverse events, timeframe based on start of treatment to end of treatment.

Secondary outcome measures
1. Efficacy of ALC:
1.1. Incidence of neuropathy of grade 3 or 4, time to onset of neuropathy, duration of neuropathy, measured from start of treatment to safety follow-up
1.2. Efficacy of ALC: percentage of discontinuations due to neuropathy, measured from start of treatment to safety follow-up
2. Safety of sagopilone in combination with ALC, measured from start of treatment to safety follow-up
3. Efficacy of sagopilone:
3.1. 'Best overall response' according to modified RECIST criteria, measured from start of treatment to end of treatment
3.2. 'Best overall response' according to CA-125 or PSA response, measured from start of treatment to end of treatment
3.3. Time to disease progression, Progression-free survival, measured from start of treatment to progression or death
3.4. Duration of response, measured from start of treatment to progression or death
3.5. WHO performance status, measured from screening to end of treatment
4. Pharmacokinetics:
4.1. Sagopilone concentrations (optional), measured on day 1, 2, 3, 5, 15 of cycle 1 and 2
4.2. ALC concentrations, measured at randomisation, day 1 of cycle 1 and 2
5. Pharmacogenomics (optional): in tumour tissue, blood and ascites, measured from blood sample at screening, tissue sample and ascites whenever available

Overall study start date
29/08/2008

Completion date
05/08/2010

Eligibility

Key inclusion criteria
1. Males or females aged 18 years or over
2. World Health Organization (WHO) performance status 0 to 1
3. Epithelial ovarian, peritoneal cavity or fallopian tube cancer (except mucinous or clear cell tumours) or adenocarcinoma of the prostate (hormone-resistant prostate cancer [HRPC])
4. At least one unidimensional measurable lesion (suitable for Response Evaluation Criteria in Solid Tumors [RECIST] evaluation) or for patients without measurable disease, CA 125 levels greater than or equal to two times the upper limit of normal (ULN) within 3 months and confirmed within 2 weeks prior to first infusion (ovarian cancer) or prostate specific antigen (PSA) value greater than or equal to 5 ng/mL (HRPC)
5. For HRPC: progression of disease despite adequate androgen-inhibiting hormone therapy. For ovarian cancer: progression of disease or symptomatic relapse after previous therapy.
6. No clinical residual neuropathy
7. Adequate recovery from previous surgery, radiation, and chemotherapy (excluding alopecia)
8. Adequate function of major organs and systems
9. Survival expectation greater than or equal to 3 months
10. Negative pregnancy test at enrolment (females of childbearing potential only)
11. Written informed consent

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
166 globally; 4 in UK

Total final enrolment
271

Key exclusion criteria
1. Candidacy for curative resection
2. Symptomatic brain metastases requiring whole-brain irradiation
3. Congenital bleeding diathesis, acquired coagulopathy or patients receiving full dose of anticoagulants for the treatment of thromboembolism
4. Any concomitant malignancy (some exceptions allowed)
5. History of organ allograft
6. Diabetes mellitus (even if controlled only by special diet)
7. History of chronic hepatitis B or C, or known human immunodeficiency virus (HIV) infection
8. Seizure disorder requiring medication (such as steroids or anti-epileptics)
9. Inability to swallow oral medications

10. Any malabsorption condition
11. Active infection
12. Breast feeding
13. Hypersensitivity to the active substance or to any of the excipients of any of the study medications
15. Concomitant use of neurotoxic drugs
16. Concomitant use of compounds that have potentially positive effects towards symptoms of neuropathy
17. Prior radiotherapy less than 4 weeks prior
18. Prior flutamide of cyproterone acetate less than 4 weeks prior
19. Prior bicalutamide or nilutamide less than 6 weeks prior
20. Anticancer chemotherapy or immunotherapy during the study or within four weeks of study entry
21. Major surgery less than 28 days prior to start of treatment
22. Prior treatment with epothilones
23. Use of any investigational drug within 4 weeks before start of study treatment

Date of first enrolment
29/08/2008

Date of final enrolment
05/08/2010

Locations

Countries of recruitment
Belgium

England

France

Germany

Italy

Netherlands

United Kingdom

Study participating centre
Medical Oncology
Northwood
United Kingdom
HA6 2RN

Sponsor information

Organisation
Bayer Schering Pharma AG (Germany)

Sponsor details
Müllerstr. 178
Berlin
Germany
D-13342
+49 30 468 1111
clinical-trials-contact@bayerhealthcare.com

Sponsor type
Industry

Website
http://www.bayerhealthcare.com

ROR
https://ror.org/04hmn8g73

Funder(s)

Funder type
Industry

Funder Name
Bayer Schering Pharma AG (Germany)

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

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				

Results article	01/04/2013	28/02/2019	Yes	No
Basic results		20/05/2019	No	No