

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

Submission date 28/11/2008	Recruitment status No longer recruiting	<input type="checkbox"/> Prospectively registered
		<input type="checkbox"/> Protocol
Registration date 30/01/2009	Overall study status Completed	<input type="checkbox"/> Statistical analysis plan
		<input checked="" type="checkbox"/> Results
Last Edited 20/05/2019	Condition category Cancer	<input type="checkbox"/> 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)
2008-000879-26

ClinicalTrials.gov (NCT)
NCT00751205

Protocol serial number
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-blind parallel assignment phase II safety/efficacy study

Primary study design

Interventional

Study type(s)

Treatment

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/m²) 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/m²) 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(s)

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.

Key secondary outcome(s)

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

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

Healthy volunteers allowed

No

Age group

Adult

Lower age limit

18 years

Sex

All

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 or 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

United Kingdom

England

Belgium

France

Germany

Italy

Netherlands

Study participating centre

Medical Oncology

Northwood

United Kingdom

HA6 2RN

Sponsor information

Organisation

Bayer Schering Pharma AG (Germany)

ROR

<https://ror.org/04hmn8g73>

Funder(s)

Funder type

Industry

Funder Name

Bayer Schering Pharma AG (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	01/04/2013	28/02/2019	Yes	No
Basic results			20/05/2019	No	No