Modafinil for the treatment of fatigue in advanced lung cancer

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Introduction

Patients suffering from cancer have experienced fatigue as one of the commonest and most debilitating symptoms. Over 70% of patients are affected, and it is perceived to be the symptom with the greatest negative impact on quality of life [1, 2].

Several studies have investigated the role of central nervous system (CNS) stimulant in treatment of fatigue in nonmalignant diseases. Modafinil is a CNS stimulant with a selective site of action in the brain and less side effects. It is better tolerated than the traditional stimulant such as methylphenidate. A small open labelled study showed that low doses of modafinil reduces fatigue in lung cancer patient (Spathis et al.). The aim of this study is to determine the role of modafinil in the treatment of fatigue in lung cancer patients by conducting a definitive randomised controlled trial. As a primary objective we are assessing the efficacy of modafinil in the management of fatigue in lung cancer patients. Our secondary objectives include the evaluation of the safety and tolerability of modafinil in this patient group, the dose–response relationship and finally we will be evaluating the effect of modafinil on the secondary outcomes of daytime sleepiness and depression.

Modafinil

- Manufactured by Cephalon, Inc.
- Licensed for the treatment of:
  - Excessive day time sleepiness (EDS) in narcolepsy
  - Obstructive sleep apnoea/hypopnoea syndrome (OSAHS)
  - Chronic shift work sleep disorder

- Most common adverse effects are:
  - Headache
  - Anxiety
  - Nausea
  - Dizziness

Study Design

- Multicenter, phase IV, randomised, double-blinded, placebo-controlled trial
- 206 patients will be recruited, with 103 patients in each arm
- Study treatment period is 28 days and patients will be randomised between two parallel groups:
  - Patients in the treatment arm will take modafinil:
    - 100mg on days 1-14 (one capsule)
    - 200mg from day 15 (two capsules)
  - Patients on the control arm will take matched placebo:
    - One capsule from day 1
    - Two capsules from day 15

Study population

Outpatients attending a selected oncology clinic in each of fifteen centres in London, Cambridgeshire, Thames Valley, Manchester, Wales, Wiltshire, Kent, Essex, Uxbridge, Hampshire and West Yorkshire who fulfil the eligibility criteria.

Inclusion Criteria

- Non-small cell lung cancer with confirmatory histology or cytology
- Stage 3 or 4 disease, or recurrent disease after surgery or radiotherapy
- WHO performance status between 0-2
- Screening score of 5 or more in a 10 point numerical rating scale of fatigue

Exclusion Criteria

- Received radiotherapy or chemotherapy in the last 4 weeks
- Commenced on an EGFR tyrosine kinase inhibitors e.g. Gefitinib (Iressa®) and Erlotinib (Tarceva®) within the last 6 weeks
- Commenced on antidepressants or steroids in the last 2 weeks
- Received blood transfusion in the last 2 weeks
- Currently taking warfarin
- Potentially fertile women of childbearing age
- History of major anxiety, arrhythmia, cor pulmonale or left ventricular hypertrophy
- Uncontrolled hypertension with blood pressure of more than 160/100 mmHg

Study schedule

	Day (0)	Day (14 ± 2)	Day (28 ± 2)
Time	Baseline assessment	Midpoint assessment	Endpoint assessment
Location	In clinic	By telephone or in clinic	By telephone or in clinic
Method	Randomisation Completion of baseline case record form and baseline blood test Providing patients the drug packs and instruction	Completion of follow-up case record form	Completion of follow-up case record form

Outcome measure

Change in score between baseline and 28 days of the following:

- Functional Assessment of Chronic Illness Therapy measurement system (FACIT-Fatigue)
- The Hospital Anxiety and Depression Scale (HADS)
- Epworth Sleepiness Scale (ESS)
- Quality Of Life Numerical Rating Scale (QOL-NRS)

Project management team

- Chief Investigator: Dr Bee Wee
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- Trial Data Manager: Ms Lois Sims (lois.sims@ndm.ox.ac.uk)
- Study Statistician: Ms Susan Dutton
- Other members: Dr Anna Spathis, Dr Nick Bates, Dr Kate Fife

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