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Efficacy, safety and tolerability of MEM 1414 on allergen-induced late asthmatic response in steroid-free subjects with mild allergic asthma

Submission date
05/11/2008

Recruitment status
No longer recruiting

Registration date
28/11/2008

Overall study status
Completed

Last Edited
27/05/2015

Condition category
Respiratory

[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

Protocol serial number
MEM1414-101

Study information

Scientific Title
A multicentre, randomised, double-blind, placebo-controlled, cross-over study to evaluate the efficacy, safety and tolerability of MEM 1414 (600 mg) on the allergen-induced late asthmatic response in steroid-free subjects with mild allergic asthma

Study objectives
The purpose of this study is to evaluate the efficacy, safety and tolerability of 600 mg MEM 1414 on the allergen-induced late asthmatic response (LAR) in steroid-free subjects with mild allergic asthma.

Ethics approval required
Old ethics approval format

Ethics approval(s)
London Research Ethics Committee gave approval on the 27th November 2008 (ref: 08/H0718 /73)

Study design
Multicentre randomised double-blind placebo-controlled cross-over study

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Mild allergic asthma

Interventions
Investigational and control drugs:
Investigational: MEM 1414 tablets, 100 mg (6 tablets per day for a total of 600 mg), will be administered orally once daily for 7 consecutive days
Reference therapy (control): matching placebo tablets (6 tablets to conserve the blind) will be administered orally once daily for 7 consecutive days

Treatment arms:
Subjects will be assigned to each of the following treatments in a randomised order, each separated by a washout period of approximately 2 - 10 weeks (washout period 2):
1. 600 mg MEM 1414 once daily for 7 consecutive days (six 100 mg tablets)
2. Placebo once daily for 7 consecutive days (six placebo tablets)

Treatment assignment:
Subjects will be randomised in a 1:1 ratio to the two possible sequences of treatments:
1. MEM 1414 in treatment period A, placebo in treatment period B
2. Placebo in treatment period A, MEM 1414 in treatment period B

Subjects will be followed up 5 - 10 days after the last study drug administration.

Intervention Type
Drug

Phase
Phase II/III

Drug/device/biological/vaccine name(s)

MEM 1414

Primary outcome(s)
To assess the efficacy of MEM 1414 compared to placebo on the late asthmatic response (LAR) following an inhaled allergen challenge, as measured by changes in FEV1 compared to baseline. The LAR is defined as a fall in FEV1 of greater than 15% from baseline between 3 - 10 hours at least once following inhalation of house dust mite (HDM) extract.

Key secondary outcome(s))
1. Assess the efficacy of MEM 1414 compared to placebo on the late asthmatic response following an inhaled allergen challenge, as measured by:
1.1. Changes in allergen-induced airway hyperresponsiveness (via pre- versus 24-hour post-allergen challenge PC20 methacholine values)
1.2. Changes in the following biomarkers of allergen-induced airway inflammation compared to baseline:
1.2.1. Exhaled nitric oxide (eNO)
1.2.2. Whole blood tumour necrotising factor alpha (TNF-alpha), interleukin-6 (IL-6) and leukotriene B4 (LTB4) concentrations
2. To investigate the safety and tolerability of MEM 1414 compared to placebo in steroid-free subjects with mild allergic asthma
3. To characterise the pharmacokinetic profile of MEM 1414 in steroid-free subjects with mild allergic asthma

Completion date
14/09/2009

Eligibility

Key inclusion criteria
1. Male or female subjects between the ages of 18 and 55 years (inclusive)
2. Non- or ex-smokers who are expected to not smoke for the duration of the trial (an ex-smoker being defined as someone with less than 10 pack-year history and who has completely stopped smoking for at least 12 months before screening for this study)
3. Clinically stable, steroid-free mild allergic asthmatics who:
3.1. Have had a well-established, documented asthma diagnosis for at least 6 months prior to screening for this study
3.2. Have a forced expiratory volume in one second (FEV1) greater than or equal to 70% of predicted for age and height on screening days 1 and 2
3.3. Do not require any controller drugs for asthma
3.4. Have been on an as needed regimen of short acting beta 2-agonists
4. In the previous year or at screening, a positive allergen skin prick test (SPT) wheal response to house dust mite (HDM)
5. At screening, a demonstrated airway hyper-responsiveness to methacholine chloride, with a provocative concentration resulting in a 20% decrease in FEV1 (PC20FEV1) of 16 mg/mL or less (a PC20 methacholine value within the previous 12 months may be used to make this determination)
6. At screening, a minimum decrease in FEV1 in both early (0 - 3 hours) and late (3 - 10 hours) allergen-induced response of greater than or equal to 15% following inhaled allergen challenge
7. Due to unknown risks and potential harm to the unborn foetus, sexually active women of childbearing potential must use a reliable method of birth control while participating in this study and for a period of 90 days following the last drug administration. Reliable methods of

birth control are considered to be: abstinence (not having sex), oral contraceptives (the "pill"), intrauterine device (IUD), Depo-Provera, Norplant, tubal ligation ("tubes tied"), or vasectomy of the partner (with confirmed negative sperm counts) in a monogamous relationship (same partner). An acceptable, although less reliable method involves the careful use of condoms and spermicidal foam or gel and/or a cervical cap or sponge. Females who do not use an acceptable contraceptive regimen will be allowed to participate in this study only if they are not considered to be of childbearing potential: females who have had a hysterectomy or tubal ligation, are clinically diagnosed infertile, or are in a menopausal state (minimum of a year without menses).
8. Pregnant women are excluded from participation in this study. Because some methods of birth control are not 100% reliable, a negative pregnancy test is required at screening.
9. Male subjects must abstain from unprotected sexual intercourse during the study and for a period of 90 days following the last drug administration
10. Are in good general health and are expected by the investigator to complete the clinical trial as designed
11. Have voluntarily provided informed consent and have signed an informed consent form (ICF) indicating that the purpose of the study has been explained, and are willing and able to adhere to the study regimen and study procedures described in the ICF

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. Any hospitalisations due to asthma in the past 3 years
2. Treatment with the following medications:
2.1. Oral corticosteroids:
2.1.1. More than once in the previous 12 months, or
2.1.2. Within 8 weeks of screening
2.2. Inhaled or nasal corticosteroids in the previous 4 weeks before screening for this study
2.3. A leukotriene receptor antagonist (LTRA), 5-lipoxygenase inhibitor, theophylline or cromones (e.g. cromolyn, nedocromil) in the previous 2 weeks before screening for this study
2.4. Long-acting beta2-agonists (LABA) or anticholinergics in the previous 7 days before screening for this study
2.5. Short-acting antihistamines and tranquilisers in the previous 7 days before screening for this study
2.6. Long-acting antihistamines in the previous 2 weeks before screening for this study
2.7. Anti-IgE in the previous 6 months before screening for this study
2.8. Previous treatment with immunotherapy
2.9. Vaccinations (e.g. anti-influenza) in the previous 3 months before screening for this study
2.10. Antidepressants within the previous 2 weeks before screening for this study

2.11. Beta-adrenoreceptor blocking agents within the previous 3 days before screening for this study
3. Significant illness or disease other than asthma
4. History of severe hypersensitivity or allergy to any drug
5. Presence of any active respiratory tract infection, whether bacterial, viral, or fungal in origin within 3 weeks of screening
6. Have unstable cardiovascular, gastrointestinal, hepatic, musculoskeletal, metabolic, endocrine, neurological or psychiatric disease or have had any clinically significant medical condition other than asthma within 1 month (30 days) prior to screening
7. Have rheumatoid arthritis, a connective tissue disorder, or any other condition known to be associated with chronic inflammation (e.g. inflammatory bowel disease)
8. Major surgery in the past 3 months before screening
9. Have evidence of significant renal insufficiency, indicated by a serum creatinine greater than the upper limit of normal at screening
10. Have either of the following liver test abnormalities at screening:
10.1. Aspartate transaminase (AST) or alanine transaminase (ALT) 1.5 times greater than the upper limit of normal
10.2. Total bilirubin greater than 1.2 times the upper limit of normal
11. Have insulin-dependent diabetes mellitus or uncontrolled diabetes mellitus, as evidenced by HbA1C level greater than or equal to 8.0% at screening
12. Have a history of malignancy other than in situ tumours
13. Have a history of bone disease (e.g., osteoporosis, osteopenia) or suffered from a bone fracture in the previous 12 months before screening
14. Have any of the following haematologic abnormalities at screening:
14.1. For females: haemoglobin less than 7.4 mmol/L
14.2. For males: haemoglobin less than 8 mmol/L
14.3. White blood cell (WBC) count less than 3.0 x 10^3/mm^3
14.4. Platelet count less than 100,000/mm^3
15. Are known to have or be a carrier of the hepatitis B surface antigen (HBsAg) or hepatitis C virus (HCV) antibody (unless confirmatory tests are negative)
16. Have significant blood loss (greater than 500 ml) or donated blood in the 30 days before screening
17. Have participated in a clinical trial evaluating an Investigational Product in the previous 3 months before screening for this study
18. Have a positive urine drug screen (UDS), which includes cotinine, at screening
19. Recent (less than 1 year) history of alcohol dependency. Subjects who have a positive alcohol breathalyser test at screening.
20. Any other reason that may preclude study participation, as determined by the Investigator

Date of first enrolment
08/12/2008

Date of final enrolment
14/09/2009

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Heart Lung Centre
London
United Kingdom
W1G 8HU

Sponsor information

Organisation
Memory Pharmaceuticals Corp. (USA)

ROR
https://ror.org/011qkaj49

Funder(s)

Funder type
Industry

Funder Name
Memory Pharmaceuticals Corp. (USA)

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	28/10/2014		Yes	No
HRA research summary			28/06/2023	No	No