Final study report

Title:

The effect of a humanised monoclonal anti-IgE antibody (omalizumab) on disease control and bronchial mucosal inflammation in non-atopic ("intrinsic") asthma

Study acronym: None

EudraCT: 2009-009154-25

REC number: 09/H0804/43

Co-Sponsors: Guy's and St Thomas NHS Foundation Trust & King's College London

IMP: Omalizumab

Indication studied: Asthma

Study design: Randomised double-blind placebo controlled trial

Study initiation date: 12th & 20th May 2010

Date of early termination: 1st Oct 2015

Chief Investigator: Prof Chris Corrigan

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Date of Report: 29 November 2016

The trial was conducted in compliance with the principles of the Declaration of Helsinki (1996), the principles of GCP and in accordance with all applicable regulatory requirements including, but not limited to, the Research Governance Framework and the Medicines for Human Use (Clinical Trial) Regulations 2004, as amended in 2006 and any subsequent amendments. The study and amendments were reviewed by an independent ethics committee: NRES Committee – London Bridge

SYNOPSIS

Study Title	The effect of a humanised monoclonal anti-IgE antibody (omalizumab) on disease control and bronchial mucosal inflammation in non-atopic ("intrinsic") asthma
Study Centres	Guy's & St Thomas' NHS Foundation Trust
First patient's first visit	14 -June -2010
Last patient's last visit	12- July -2013
Last dose of IMP taken by a subject	12 –July - 2013
Date of early termination	01-Oct-2015
Phase	III
Design summary	A randomised, double blind, proof of concept study was performed to assess the effect of omalizumab/placebo on disease control and IgE expressing effector cells (utilising immunohistochemistry) in a group of severe, non-atopic asthmatics. This incorporated a "stable" phase of omalizumab/placebo treatment during which existing anti-asthma medications were not altered followed by a phase in which they were systematically reduced
Primary objective	The primary aim of the study was to obtain proof of principle that omalizumab therapy maintained lung function, symptom control and quality of life in a group of non-atopic, moderate/severe asthmatics whose regular anti-asthma therapy was uniformised and reduced for an 8 week period following omalizumab/placebo therapy, while the latter therapy was continued
Secondary objectives	A secondary aim was to see whether omalizumab, as compared with placebo therapy reduced bronchial inflammation and local IgE production in the bronchial mucosa of this same group of asthmatics.
Primary endpoint	Pre-bronchodilator FEV_1
Secondary endpoints	Morning and evening peak expiratory flow Day and night Symptom scores Validated asthma Quality of life scores Exhaled nitric oxide Rescue medication use

	Total dosages of rescue β2 agonist Total symptom free days
Summary of eligibility criteria	**Inclusion criteria** Males and females aged 18 to 75 years inclusive Moderate/severe non-atopic asthma treated with inhaled corticosteroid, with or without oral corticosteroids (oral, up to 20mg/day prednisolone or equivalent) for at least 3 months prior to screening Written, informed consent provided **Exclusion criteria** Smoking within the last 3 months or total smoking history ≥ 10 pack years Pregnant or lactating females or those at risk of pregnancy. Patients taking >20mg of prednisolone daily. Hospitalisation for asthma or exacerbation requiring systemic corticosteroid therapy within 3 months of the screening visit. History of life-threatening asthma, defined as an asthma episode that required intubation and/or was associated with hypercapnia, respiratory arrest and/or hypoxic seizures within the 6 months prior to screening. Pre bronchodilator FEV1 < 40% of the predicted. Patients in whom, in the opinion of the study investigators, omalizumab therapy might normally require precaution (current or suspected malignancy, current or suspected autoimmune disease, renal or hepatic impairment, hyperimmunoglobulin E syndrome, allergic bronchopulmonary aspergillosis , diabetes mellitus, current immunosuppressive therapy and known Churg-Strauss or hypereosinophilic syndrome
Primary efficacy parameter	Pre-bronchodilator FEV1
Patient information and consent	Informed consent was obtained before the start of visit 1

	(screening visit).
IMPs	Omalizumab / placebo Terbutaline sulphate Budesonide/formoterol
Dosing regimen	Omalizumab: Based on the approved omalizumab dosing table for allergic asthma (Omalizumab SmPC): subcutaneous injections every 2 or 4 weeks according to weight and serum total IgE (5 or 9 injections in total). Terbutaline sulphate (500µ g per inhalation): 1-2 puffs as needed for symptoms from visit 6 Budesonide/formoterol (budesonide 100µg and formoterol 6µg per inhalation): 2 puffs twice daily from visit 6, reducing to 1 puff daily from visit 8
Sample size	40
No. participants recruited	18
No. withdrawals	2 (+1 loss of follow up after screening)
No. participants completing study	15
SAEs reported	Yes; (2 in total, both R06, asthma exacerbations)
IMP Dosing and recoded adverse events / important medical events	None
Protocol deviations	No significant deviations
Reason for early termination	i) Interim analysis showed significant positive trend in the primary outcome (FEV1) ii) Paucity of funding to continue the study
Conclusions	Omalizumab therapy of non-atopic asthmatics reduces bronchial mucosal IgE+ mast cells and improves lung function despite withdrawal of conventional therapy

Prof Chris Corrigan

Chief Investigator

SIGNATURE:

DATE: 29/11/16