SYNOPSIS

Name of Sponsor: Imperial College London
Name of Finished Product: Irosustat
Name of Active Ingredient: Micronised irosustat
Title of Study: A Phase II study to assess the safety and efficacy of the steroid sulfatase inhibitor Irosustat when added to an aromatase inhibitor in ER positive locally advanced or metastatic breast cancer patients.
Investigators: Professor C Palmieri, Chief Investigator, University of Liverpool; Professor C Coombes, Principal Investigator Site IRIS001; Dr S Barrett, Principal Investigator Site IRIS002; Dr L Haywood, Principal Investigator Site IRIS003; Dr R Stein, Principal Investigator Site IRIS004; Dr R Ahmad, Principal Investigator Site IRIS005; Dr S Howell, Principal Investigator Site IRIS006; Dr S Skaria, Principal Investigator Site IRIS008; Dr A Jones, Principal Investigator Site IRIS009; Mr C Holcombe, Principal Investigator Site IRIS010
Study centres: IRIS001: Charing Cross Hospital, Imperial College Healthcare NHS Trust, UK; IRIS002: The Beatson West of Scotland Cancer Centre, NHS Greater Glasgow and Clyde, UK; IRIS003: Western General Hospital, NHS Lothian, UK; IRIS004: University College London NHS Foundation Trust, UK; IRIS005: West Middlesex University Hospital, Chelsea and Westminster Hospital NHS Foundation Trust, UK; IRIS006: The Christie NHS Foundation Trust, UK; IRIS008: Broomfield Hospital, Mid Essex Hospital Services NHS Trust, UK; IRIS009: Royal Free London NHS Foundation Trust, UK; IRIS010: The Royal Liverpool and Broadgreen University Hospitals NHS Trust, UK
Publication: Publication is currently being prepared
Study period: 09.02.2013 - 17.12.2014 **Phase of development:** II
Objectives: ***Primary Objective:*** To assess the efficacy of Irosustat when added to existing aromatase inhibitor (AI) therapy in patients who have progressed on an AI based on clinical benefit rate (CBR). ***Secondary Objectives:*** • To assess the efficacy of the addition of Irosustat to an AI based on duration of clinical benefit. • To assess the efficacy of the addition of Irosustat to an AI based on Objective Response Rate (ORR). • To assess the efficacy of the addition of Irosustat to an AI based on Progression Free Survival (PFS). • To assess the safety and tolerability of the addition of Irosustat to an AI. • To assess the Pharmacodynamic (PD) profile of the addition of Irosustat to an AI.
Methodology: A multi-centre, single arm, open label, non-randomised, phase II study
Number of patients (planned and analysed): 27
Diagnosis and main criteria for inclusion: Postmenopausal women with ER+ve locally advanced or metastatic breast cancer who have progressed during 1st line treatment with an AI and fulfil all study eligibility criteria.

Test product, dose and mode of administration, batch number: Irosustat, 40mg O.D orally, Batches E01548, F18208, G01359, H05468.
Duration of treatment: Until disease progression, unacceptable toxicity or withdrawal
Reference therapy, dose and mode of administration, batch number: Not applicable
Criteria for Evaluation: ***Efficacy:*** Clinical benefit rate, duration of clinical benefit, objective response rate, progression free survival, serum concentrations of circulating steroid hormones ***Safety:*** Adverse events
Statistical Methods: The Simon's minimax two-stage design of phase II clinical trials was utilised, setting the one-sided alpha and beta errors as 0.05 and 0.20, respectively, and defining the maximum unacceptable activity (p0) for the experimental treatment as a clinical benefit rate (CBR) of 5%. Assuming the experimental treatment is able to achieve a minimal acceptable activity (p1) of at least 20% CBR, to test the alternative one-sided hypothesis with 80% power that the CBP (p1) is greater than p0, at least 4 patients with clinical benefit will have to be reported among the final sample size of 27 patients.
Summary Conclusions: Irosustat when added to first-line aromatase inhibitor (AI) on progression resulted in clinical benefit, and was well tolerated. These data provide evidence that blocking sulfatase in ER positive advanced breast cancer can result in clinical activity. Larger studies are now needed to investigate further the activity of Irosustat in ER+ metastatic BC.
Date of Report: 21/03/2016