

Study Protocol Version 6 (01/09/16)

**TARGETING OF THE SMALL AIRWAYS IN PATIENTS WITH COPD: AIRWAY EFFECTS OF
TIOTROPIUM – Respimat vs. Handihaler**

NCT02683668

STATISTICAL ANALYSES

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EudraCT No: 2015-001615-13

REC/IRAS number: 15/LO/0982

Sample Size Calculation

The primary endpoint is the Impulse oscillometry measure of IOS R5-R20.

Each subject will act as their own control and assuming the treatment effect (ie the difference R5-R20 between baseline and 14 days) to be 0.03kPa(L/s) with an SD of 0.05, then 44 subjects will be required to achieve the said treatment effect at 1% significance and 90% power.

Statistical Analysis

t-tests/Mann-Whitney tests and linear mixed models will be used to measure overall treatment effect while adjusting for baseline variables.

The secondary endpoints are small airways (MBNW, DLCO, FVC) and large airways (FEV1, PEF) airways physiology and also the CAT score.