PROTOCOL SUMMARY

FULL TITLE OF STUDY	A series of randomised controlled N-of 1 trials in patients who have discontinued or are considering discontinuing statin use due to muscle-related symptoms to assess if atorvastatin treatment causes more muscle symptoms than placebo		
SHORT TITLE	STATIN: WEB-BASED INVESTIGATION OF SIDE EFFECTS		
TRIAL ACRONYM	STATINWISE		
PROTOCOL /ISRCTN NUMBER	ISRCTN30952488		
EUDRACT NUMBER	2016-000141-31	**CLINICAL TRIALS.GOV**	NCT02781064

BACKGROUND: Statins are the most commonly prescribed treatment in the UK. Recently updated NICE guidelines have lowered the threshold for statin use to include all patients with a 10% or greater 10-year risk of cardiovascular disease. Previous randomised trials have established the prevalence of serious adverse effects of statins such as rhabdomyolysis, however, many patients discontinue statins due to less severe symptoms, such as muscle pain or fatigue. Randomised trials have shown no differences between those taking statin and placebo in terms of the prevalence of these side effects (approximately 9%), but currently there is no pathway of care for clinicians to empirically and objectively evaluate whether symptoms reported by a statin-user are caused by the statin itself or the so-called 'nocebo' effect (symptoms reflecting patient expectation of side effects). Given the effectiveness of statins in preventing cardiovascular disease, accurate data on the cause of symptoms experienced during statin use are needed to reliably inform patient and clinician about continuation of use. The proposed StatinWISE trial will provide definitive answers to this important uncertainty about statin therapy.

AIM: To determine whether statins cause muscle symptoms.

PRIMARY OUTCOME: Patient reported muscle symptoms (pain, weakness, tenderness, stiffness or cramp).

SECONDARY OUTCOME: Relationship between individual trial result and patient decision whether to continue statins long term.

TRIAL DESIGN: A series of randomised, double-blinded N of 1 trials.

DIAGNOSIS AND INCLUSION/EXCLUSION CRITERIA:

Inclusion criteria:

- Adults (aged 16 and over)
- Prescribed statin treatment in the last 3 years
- Stopped OR considering stopping statin treatment due to muscle symptoms
- Provided fully informed consent.

Exclusion criteria:

- Any previously documented serum alanine aminotransferase (ALT) levels at or above three times the upper limit of normal;
- Have persistent, generalised, unexplained muscle pain (whether associated or not with statin use) and have creatinine kinase (CK) levels greater than 5 times the upper limit of normal
- Any contra-indications listed in the Summary of Product Characteristics for Atorvastatin 20 mg (Appendix 8)
- Should not be using atorvastatin 20mg daily in the opinion of the general practitioner.

TEST PRODUCT, REFERENCE THERAPY, DOSE AND MODE OF ADMINISTRATION: Once daily oral atorvastatin 20mg or placebo for 12 months.

SETTING: This trial is coordinated from the Clinical Trials Unit at London School of Hygiene & Tropical Medicine and conducted in patients registered in General Practice in England and Wales.

DURATION OF TREATMENT AND PARTICIPATION: Eligible patients should be randomised as soon as possible after the screening. Treatment period is for 12 months with a final follow-up within 3 months of the end of treatment period.

CRITERIA FOR EVALUATION: Patients who enter data on muscle symptoms at least once during a treatment period with the IMP and at least once during a treatment period with placebo.

CLINICAL PHASE	4
PLANNED TRIAL START	01/09/2016
PLANNED DATE OF LAST PATIENT ENROLMENT	01/09/2017
PLANNED DATE OF LAST PATIENT FINAL FOLLOW-UP	01/10/2018