Phase II, randomised, placebo controlled, multicentre, feasibility study of low dose (metronomic) cyclophosphamide with or without nintedanib (BIBF1120) in advanced ovarian cancer (METRO–BIBF)

Aim: To explore the efficacy and safety of an all oral combination of nintedanib (an inhibitor of angiogenic signalling) and metronomic cyclophosphamide in patients with multiply-relapsed advanced ovarian cancer, who have completed a minimum of two lines of previous chemotherapy and who for any reason are not suitable for further 'standard' intravenous chemotherapy treatments

Study Design – Phase II

Patients with multiply relapsed advanced ovarian cancer, in whom there are no suitable remaining IV chemotherapy options (n = 124)

Randomise

Cyclophosphamide 100 mg daily plus nintedanib 200 mg b.d. continuously n=62*

Cyclophosphamide 100 mg daily plus matched placebo b.d. continuously n=62*

* **Toxicity** of this treatment in the first 12 patients randomised will be assessed by an Independent Data Monitoring Committee

Assessments: Patients will be followed 6/52 with repeat CA125 and Quality of Life assessment. Repeat imaging every 3/12 until disease progression, death or unacceptable toxicity

Primary Objective: Overall Survival;
Secondary Objective: Toxicity, progression free survival, health related Quality of Life

CONTACT DETAILS: METRO-BIBF Trial Co-ordinator: ctc.metrobibf@ucl.ac.uk Tel: 020 7679 9857; Fax: 020 7679 9871; CR UK & UCL Cancer Trials Centre, 90 Tottenham Court Road, London W1T 4TJ

Inclusion Criteria – Summary*

- Female subjects, >18 years, histologically proven recurrent advanced epithelial ovarian, fallopian tube or primary peritoneal carcinomas
- Undergone hysterectomy or post-menopausal for 24 consecutive months
- Performance status 0-2
- Adequate organ function
- Life expectancy > 6 weeks
- Has received 2 or more lines of chemotherapy but not suitable for further IV chemotherapy
- No previous oral cyclophosphamide, nintedanib, or other tyrosine kinase inhibitors (eg cediranib, erlotinib), but can have had anti-VEGF inhibitors (e.g. Bevacizumab)
- Able to give written informed consent and to complete QoL

Exclusion Criteria – Summary*

- Malignant tumour of non-epithelial origin of the ovary, fallopian tube or the peritoneum
- Clinically relevant non-healing wound, ulcer, or bone fracture
- Symptoms or signs of GI obstruction or any GI disorders that would interfere with drug absorption
- Active brain metastases
- History of major thromboembolic event
- Known inherited or acquired bleeding disorder
- Significant cardiovascular disease
- History of CVA, TIA or subarachnoid haemorrhage within the past six months
- Lab values indicating an increased risk of adverse events
- Serious infections
- Poorly controlled diabetes mellitus
- Other malignancies diagnosed within past five years (see exceptions)
- Serious illness or concomitant non-oncological disease
- Any contraindications for treatment with cyclophosphamide

***Please consult protocol for full criteria list**