**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)

- 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.

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**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