1002TiP BAROCCO: A randomized phase II study of weekly paclitaxel vs cediranib-olaparib with continuous schedule vs cediranib-olaparib with intermittent schedule in advanced platinum resistant ovarian cancer

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Background: Cediranib and olaparib have shown efficacy in ovarian cancer (OC) throughout several clinical settings. A phase II study demonstrated that the combination of the two drugs increased progression free survival (PFS) in women with recurrent platinum sensitive OC with respect to olaparib (Liu et al, 2014). The greatest benefit from the combination was observed in wild-type/unknown BRCA patients, therefore suggesting a possible effect of the combination in platinum resistant OC which are mainly BRCA proficient tumors. The most frequent grade ≥ 3 AEs with the combination were hypertension, diarrhea and fatigue, suggesting an amplificatory effect caused by cediranib. The purpose of this study is to test the efficacy of olaparib/cediranib combination in platinum resistant disease, comparing this regimen with weekly paclitaxel, and to identify a more tolerable schedule for this combination treatment.

Trial design: This is a randomized multicenter phase II open label study. Patients with platinum resistant OC will be randomized in a 1:1:1 ratio in a control and two experimental arms. Control treatment consists of administration of 80 mg/m^2 weekly paclitaxel, up to a maximum of 24 weeks or to progression. Combination therapy is administered up to progression with two different schedules: i. Continuous with 600 mg olaparib (tablets) and 20 mg cediranib given every day; ii. Intermittent with 600 mg olaparib (tablets) given every day and 20 mg cediranib given 5 days/week. The study has two primary endpoints: 1) PFS, to compare the efficacy between control and experimental arms with a 80% power to detect a benefit ≥ 3.3 months and, 2) the number of evacuations/day in the first 28 days of the combination therapy as tolerability indicator. If both experimental arms show superiority - in terms of PFS - to control treatment, these will be compared for tolerability. The study is registered at clinicaltrials.gov (NCT03314740) and is currently recruiting. Eighty-seven patients out of 100 planned have already been enrolled from 6 experimental sites in Italy in 11 months.

Clinical trial identification: EudraCT: 2016-003964-38; NCT03314740.

Legal entity responsible for the study: IRCCS Istituto di Ricerche Farmacologiche Mario Negri di Milano.

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