NCT01116648	Phase I/II Study of Cediranib and Olaparib in Combination for Treatment of Recurrent Papillary-Serous Ovarian, Fallopian Tube, or Peritoneal Cancer or for Treatment of Recurrent Triple-Negative Breast Cancer
Phase	II
Drug Class	PARP Inhibitor
Drug Name	Olaparib
Alternate Drug Names	AZD2281, KU-0059436, Lynparza
Eligible Participant	Platinum-sensitive, recurrent ovarian cancer
Patients Enrolled	162 (90 ovarian), median of 2 prior therapies
Therapy Setting	Recurrence
Study Design	Open Label, Randomized
Endpoints	**ORR** evaluated per **RECIST, PFS, OS**
Biomarkers	Exploratory analysis: germline BRCA mutations
Efficacy	**ORR**: 79.6% (olaparib + cediranib = combo) vs 47.8% (olaparib alone), (p=0.002) **PFS**: 16.5 months (combo) vs 8.2 months (olaparib alone), **HR**: 0.50 (0.30-0.83, p=0.007) **OS**: 44.2 months (combo) vs 33.3 months (olaparib alone), **HR**: 0.64 (0.36-1.11, p=0.11) <u>Exploratory gBRCA sub-group analysis: gBRCA MUT vs gBRCA WT or status unknown:</u> gBRCA MUT: **ORR**: 83% (combo) vs 63% (olaparib alone) (p=0.19) **PFS**: 16.4 mos vs 16.5 mos, **HR:** 0.75 (p=0.42), **OS**: 44.2 mos vs 40.1 mos, HR: 0.79 (p=0.55))(n=47) gBRCA WT or status unknown: **ORR**: 76% (combo) vs 32% (olaparib alone)(p=0.006) **PFS**: 23.7 mos vs 5.7 mos, **HR**: 0.32 (p=0.002), **OS**: 37.8 mos vs 23.0 mos, HR: 0.48 (p=0.074)(n=43)
Clinically Significant Adverse Events	Serious AE: none Grade 3-4 AE: overall rate (70% vs 11%), hypertension (41% vs 0), fatigue (27% vs 11%), and diarrhea (23% vs 0)
Conclusion	Improved **PFS** and **ORR** for combination therapy, particularly in BRCA WT cancer
Reference	Liu J, et al. *Combination cediranib and olaparib versus olaparib alone for women with recurrent platinum-sensitive ovarian cancer: a randomised phase 2 study* Lancet Oncol (2014) 15(11):1207-14 http://www.ncbi.nlm.nih.gov/pubmed/25218906 Liu et al. *Overall survival and updated progression-free survival results from a randomized phase 2 trial comparing the combination of olaparib and cediranib against olaparib alone in recurrent platinum-sensitive ovarian cancer* J Clin Oncol 35, 2017 (suppl; abstr 5535) http://abstracts.asco.org/199/AbstView_199_188186.html

Legend

Therapy Setting

First-line – Therapy given to patients on initial diagnosis of disease as the first, best treatment option.
Maintenance – Therapy given to patients to help keep cancer from coming back after it has responded to therapy.
Recurrence – Therapy given to patients in whom disease has returned after prior therapy.

Study Design

Randomized -- A study in which participants are assigned by chance to the separate study groups.
Non-randomized -- A study in which participants are NOT assigned by chance to the separate study groups.

Efficacy Endpoints

PFS: Progression-Free Survival—length of time during and after treatment during which the cancer does not get worse (usually reported as the time when the cancer for half –or median -- of the people in the treatment group gets worse).
OS: Overall Survival—length of time from the start of treatment that patients are still alive (usually reported as the time when half --or median-- of the people in the treatment group are still alive).
CR: Complete Response -- The disappearance of all signs of cancer in response to treatment.
PR: Partial Response -- A decrease in the size of a tumor, or in the extent of cancer in the body, in response to treatment.
SD: Stable Disease Response -- Cancer that is neither decreasing nor increasing in extent or severity.
ORR: Objective Response Rate -- Sum of complete and partial tumor responses to treatment, divided by the number of patients evaluated.
DCR: Disease Control Rate -- Sum of complete, partial and stable disease tumor responses to treatment, divided by the number of patients evaluated.
HR: Hazard Ratio--measures survival in the treatment group compared to the control group. An HR = 1 means that there is no difference in survival between the groups. An HR < 1 means that the treatment group has a lower risk of death compared to the control group. Range in parentheses is 95% Confidence Interval (CI).
RECIST: Response Evaluation Criteria in Solid Tumors -- Set of rules, based on measurements of the change in tumor size that define when cancer patients improve, stabilize, or worsen during a treatment regimen.
CA125: GCIG CA125 Criteria -- Set of rules, based on measurements of the CA125 biomarker level that define when cancer patients improve, stabilize, or worsen during a treatment regimen

Clinically Significant Adverse Events (Based on National Cancer Institute--Common Terminology Criteria for Adverse Events (CTCAE)

AE: Adverse events-- any undesirable experience associated with the use of a drug
SAE: Serious adverse events – untoward event associated with drug treatment e.g., death, life-threatening, requiring of hospitalization, persistent or significant incapacity; usually graded from 1-5.