<table>
<thead>
<tr>
<th>NCT01623349</th>
<th>Phase I Study of the Oral PI3kinase Inhibitor BKM120 or BYL719 and the Oral PARP Inhibitor Olaparib in Patients With Recurrent Triple Negative Breast Cancer or High Grade Serous Ovarian Cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Phase</strong></td>
<td>I</td>
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<tr>
<td><strong>Drug Class</strong></td>
<td>PARP Inhibitor</td>
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<tr>
<td><strong>Drug Name</strong></td>
<td>Olaparib</td>
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<tr>
<td><strong>Alternate Drug Names</strong></td>
<td>AZD2281, KU-0059436, Lynparza</td>
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<tr>
<td><strong>Eligible Participant</strong></td>
<td>Advanced solid tumors</td>
</tr>
<tr>
<td><strong>Patients Enrolled</strong></td>
<td>118 (46 ovarian for Ola+Bup, 30 ovarian for Ola+Alp)</td>
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<tr>
<td><strong>Therapy Setting</strong></td>
<td>Recurrence</td>
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<td><strong>Study Design</strong></td>
<td>Open Label, Non-Randomized</td>
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<td><strong>Endpoints</strong></td>
<td>Recommended Phase 2 Dose (RP2D), ORR evaluated per RECIST, DCR</td>
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<td><strong>Biomarkers</strong></td>
<td>BRCA1/2 germline mutations</td>
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</table>

**Efficacy**

| RP2D: Buparlisib 50 mg QD and Olaparib 300 mg BID | Results for all doses: **ORR**: 29% (12 PR, n=41), **DCR** (>6 months): 36%

**Exploratory subgroup analysis:**

**ORR** (platinum-sensitive): 32% (6 PR, n=19), **ORR** (platinum-resistant): 27% (6 PR, n=22)

**RP2D: Alpelisib 200 mg QD and Olaparib 200 mg BID**

Results for all doses: **ORR**: 36% (10 PR, n=28) (93% platinum-resistant patients)

**Clinically Significant Adverse Events**

| Dose Limiting Toxicities Bup+Ola: depression (n=1), transaminitis (n=2), hyperglycemia (n=1)

Dose Limiting Toxicities Alp+Ola: hyperglycemia (n=2), rash (n=1), neutropenia and fewer (n=1)

Serious AE: none, Grade 3-4 AE: none

Bup+Ola: 36% and 28% of patients experienced low grade depression or anxiety, respectively

**Conclusion**

Promising activity in gBRCA MUT and gBRCA WT

**Reference**


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.
**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.