

PRESS RELEASE

For Immediate Release

Philadelphia, PA, USA, March 31, 2022 -- The GOG Foundation, Inc., (GOG) GOG Partners (GOG-P) and the European Network of Gynaecological Oncology Trial Groups (ENGOT) are pleased to share that Clovis Oncology, Inc. announced positive top-line data from the monotherapy arm of A Multicenter, Randomized, Double-Blind, Placebo- Controlled Phase 3 Study in Ovarian Cancer Patients Evaluating Rucaparib and Nivolumab as Maintenance Treatment Following Response to Front-Line Platinum-Based Chemotherapy GOG 3020/ENGOT-ov45 (ATHENA) Trial. ATHENA-MONO results will serve as the basis of a supplemental NDA for US label expansion expected to be submitted during the second quarter of 2022; European submission is planned to follow during the third quarter of 2022.

Positive top-line data from the monotherapy arm of the ATHENA (GOG 3020/ENGOT-ov45) trial (ATHENA-MONO) that Rubraca as maintenance treatment successfully achieved the primary endpoint of significantly improved investigator-assessed progression-free survival (PFS) compared with placebo. Benefit was observed in both primary efficacy analyses of newly-diagnosed patients with advanced ovarian cancer following successful treatment with platinum-based chemotherapy: those who had homologous recombination deficiency (HRD)¹, including deleterious *BRCA* mutations, as well as all patients randomized in the trial (overall intent-to-treat population (ITT)). Benefit in PFS was also seen in the exploratory subgroups of patients with HRD-negative² and *BRCA* mutant (*BRCAm*) tumors. The safety of Rubraca observed in the ATHENA-MONO study was consistent with both the US and European labels.

ATHENA is a double-blind, placebo-controlled, Phase 3 trial of rucaparib in first-line ovarian cancer maintenance treatment. It has two parts which are statistically independent. The top-line results reported today are from the ATHENA-MONO part (rucaparib vs placebo) with results from the ATHENA-COMBO part (rucaparib+nivolumab vs rucaparib) now expected in Q1 2023 based on a slower than expected event count.

ATHENA-MONO enrolled 538 women with high-grade ovarian, fallopian tube, or primary peritoneal cancer. The primary efficacy analysis evaluated two prospectively defined molecular sub-groups in a step-down manner: 1) HRD (inclusive of *BRCAm* tumors), and 2) all patients randomized (ITT) in ATHENA-MONO.

Following is a summary of the primary efficacy analyses by investigator review, the primary analysis of ATHENA-MONO.

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¹ HRD-positive may also be referred to as HR-deficient, HRD, HRD+, HRd, or biomarker positive

² HRD-negative may also be referred to as HR-proficient, HRD-, HRp, or biomarker negative

References

1: <https://pubmed.ncbi.nlm.nih.gov/34593565/>

Significant Improvement in PFS in the HRD-positive Patient Population

By investigator review, the rucaparib arm (n=185) successfully achieved statistical significance over the placebo arm (n=49) for the primary endpoint of PFS with a hazard ratio of 0.47 (95% CI: 0.31-0.72). The median PFS for the HRD-positive patient population treated with rucaparib was 28.7 months vs 11.3 months among those who received placebo (p=0.0004).

Significant Improvement in PFS in All Patients Studied (ITT or all comers)

Rucaparib also showed statistical significance in all 538 patients randomized in the study. By investigator review, the rucaparib arm (n=427) successfully achieved statistical significance over the placebo arm (n=111) for the primary endpoint of PFS with a hazard ratio of 0.52 (95% CI: 0.40-0.68). The median PFS for all patients enrolled in ATHENA-MONO and treated with rucaparib was 20.2 months vs 9.2 months among those who received placebo (p<0.0001).

Treatment Benefit in PFS Endpoint for Exploratory HRD-negative Subgroup

By investigator review, the PFS endpoint in the exploratory subgroup of HRD-negative demonstrated a hazard ratio of 0.65 (95% CI: 0.45-0.95). The median PFS for these patients treated with rucaparib (n=189) was 12.1 months vs. 9.1 months for those who received placebo (n=49) (p=0.0284).

Treatment Benefit in PFS Endpoint for Exploratory BRCAm Subgroup

By investigator review, the PFS endpoint in the exploratory subgroup of BRCAm demonstrated a hazard ratio of 0.40 (95% CI: 0.21-0.75). The median PFS for these patients treated with rucaparib (n=91) was Not Reached vs 14.7 months for those who received placebo (n=24) (p=0.0041).

Results were consistent for the germline BRCA (n=68) and somatic BRCA (n=33) and unknown (n=14) populations.

Summary of ATHENA-MONO Safety

The safety of Rubraca observed in ATHENA-MONO was consistent with both the current US and European labels. The most common (≥5%) treatment-emergent grade 3/4 adverse events (TEAEs) among all patients treated with rucaparib in the monotherapy portion of the ATHENA study were anemia/decreased hemoglobin (28.7%), neutropenia (14.6%), ALT/AST increase (10.6%), and thrombocytopenia (7.1%). The discontinuation rate for TEAEs was 11.8% for rucaparib-treated patients and 5.5% for the placebo arm. The rate of treatment-emergent myelodysplastic syndrome (MDS)/acute myeloid leukemia (AML) in the rucaparib arm was 0.2%, and no patients on the placebo arm experienced treatment-emergent MDS/AML.

Clovis Oncology plans to provide an expanded description of the ATHENA-MONO results in a scientific session at a medical meeting later this year; these data have been submitted for presentation at the American Society of Clinical Oncology Annual Meeting in June 2022.

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Rubraca is not currently approved in the first-line ovarian cancer maintenance setting. Clovis intends to provide these data to US and European regulatory authorities and is on track to submit filings during the second and third quarters of 2022, respectively, in those geographies.

“We are thrilled to provide eligible patients with newly diagnosed ovarian cancer an additional treatment option. This trial is also emblematic of the collaboration between ENGOT and the GOG and with our partners with Clovis Oncology” said Bradley J. Monk, MD, FACOG, FACS, at GOG Foundation, HonorHealth Research Institute, University of Arizona College of Medicine, Creighton University School of Medicine, Phoenix, AZ and global primary investigator of the ATHENA trial.

“We are extremely pleased to communicate these important results from the ATHENA-MONO trial, possible only through the commitment of the women who participated, demonstrating the role of first line maintenance rucaparib as a new treatment option for advanced ovarian cancer. It has been a privilege to lead the ENGOT contribution to the ATHENA trial in this important collaboration with GOG and our partners across the rest of the world.” said Rebecca S. Kristeleit, MD, PhD, of Guy’s and St Thomas’ NHS Foundation Trust in London and lead ENGOT/NCRI National Cancer Research Institute (<https://www.ncri.org.uk/>) investigator of the ATHENA trial.

Dr. Larry J. Copeland, President of The GOG Foundation, Inc., “We are honored to have partnered with our esteemed colleagues with The European Network for Gynaecological Oncological Trial groups (ENGOT) along with Clovis Oncology to turn this scientific concept into a potential new treatment option for patients. We are deeply grateful to the patients who participated and the family members and friends who supported them along their journey.” ENGOT clinical chair Dr. Mansoor Mirza from Denmark expressed the same sentiment that “This study is another great collaboration of GOG and ENGOT together with pharmaceutical industry to bring an important drug to our patients. The results of this study will further improve the outcome of our patients.”

About the ATHENA, GOG 3020 ENGOT-ov45 Ovarian Cancer, Phase III Trial, NCT03522246

ATHENA: A Multicenter, Randomized, Double-Blind, Placebo-Controlled Phase 3 Study in Ovarian Cancer Patients Evaluating Rucaparib and Nivolumab as Maintenance Treatment Following Response to Front-Line Platinum-Based Chemotherapy

ATHENA is an international, randomized, double-blind, phase III trial consisting of two independent comparisons (ATHENA-MONO and ATHENA-COMBO) in patients with newly diagnosed platinum-sensitive ovarian cancer. Patients were randomized 4:4:1:1 to the following: oral rucaparib+ intravenous nivolumab (arm A); oral rucaparib + intravenous placebo (arm B); oral placebo+ intravenous nivolumab (arm C); and oral placebo + intravenous placebo (arm D). The starting dose of rucaparib is 600 mg orally twice a day and nivolumab 480 mg intravenously every 4 weeks for all patients. ATHENA-MONO compares arm B with arm D to evaluate rucaparib monotherapy versus placebo, and ATHENA-COMBO evaluates arm A versus arm B to investigate the effects of rucaparib and nivolumab in combination versus rucaparib monotherapy. ATHENA-MONO and ATHENA-COMBO share a common treatment arm (arm B) but each comparison is independently powered.¹

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The primary outcomes measures include:

- Investigator assessed Progression-free survival (PFS) [Timeframe: From randomization until disease progression]

Secondary Outcome Measures:

- Blinded independent central review (BICR) PFS
- Overall Survival (OS)
- Objective response rate (ORR)
- Duration of response (DOR)
- Number of participants with treatment-emergent Adverse Events (AEs) as assessed by CTCAE v4 (or higher) as a measure of safety and tolerability
- Number of participants with serious AEs as a measure of safety and tolerability]
- Number of participants with laboratory abnormalities as a measure of safety and tolerability

About Ovarian Cancer

Ovarian cancer is the 7th most common cancer in women and the 18th most common cancer overall, with **just over 313,959 new cases globally and 207,252 deaths in 2021**. A woman's lifetime risk of developing ovarian cancer is about 1 in 75, with projections for diagnosis on the rise. Ovarian cancer is a disease that affects women. In this form of cancer, certain cells in the ovary become abnormal and multiply uncontrollably to form a tumor. The ovaries are the female reproductive organs in which egg cells are produced. In about 90 percent of cases, ovarian cancer occurs after age 40, and most cases occur after age 60.

About The GOG Foundation, Inc. (www.gog.org)

The GOG Foundation, Inc. is a not-for-profit organization with the purpose of promoting excellence in the quality and integrity of clinical and translational scientific research in the field of gynecologic malignancies. The GOG Foundation is committed to maintaining the highest standards in clinical trials development, execution, analysis, and distribution of results. The GOG Foundation is the only clinical trialist group in the United States that focuses its research on patients with pelvic malignancies, such as cancer of the ovary (including surface peritoneal malignancies), uterus (including endometrium, soft tissue sarcoma, and gestational trophoblastic neoplasia), cervix, and vulva. The GOG Foundation is multi-disciplinary in its approach to clinical trials, and includes gynecologic oncologists, medical oncologists, pathologists, radiation oncologists, oncology nurses, biostatisticians (including those with expertise in bioinformatics), basic scientists, quality of life experts, data managers, and administrative personnel.

About GOG Partners

Supported by industry, GOG Partners has been structured to work directly with pharmaceutical organizations and operate clinical trials outside the National Cancer Institute (NCI) framework. The GOG Partners shares the same mission of the GOG Foundation dedicated to transforming the care in Gynecologic Oncology.

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By providing an alternative venue for patient accrual and site infrastructure support, GOG Partners has helped provide additional trials and opportunities for patients outside the national gynecologic clinical trials network.

About ENGOT (<https://engot.esgo.org>)

The European Network of Gynaecological Oncology Trial groups (ENGOT) is a platform that guarantees that the European spirit and culture is incorporated into the medical progress in gynaecological oncology, and that all European patients and countries can participate in an active way in clinical research and progress. The ultimate goal is to bring the best treatment to gynecological cancer patients through the best science and enabling every patient in every European country to access a clinical trial.

[Clovis Oncology Press Release](#), March 31, 2022

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References

1: <https://pubmed.ncbi.nlm.nih.gov/34593565/>