ENGOT-EN20/GOG-3083/XPORT-EC-042 A PHASE 3, RANDOMIZED, PLACEBO-CONTROLLED, DOUBLE-BLIND, MULTICENTER TRIAL OF SELINEXOR IN MAINTENANCE THERAPY FOR PATIENTS WITH P53 WILD-TYPE, ADVANCED OR RECURRENT ENDOMETRIAL CARCINOMA

Introduction/Background Molecular characterization of patients with endometrial cancer (EC) has prognostic and therapeutic implications. Wild type TP53 (TP53wt) is found in ~75% of newly diagnosed EC and 50% of advanced/recurrent tumors; there are no targeted therapies for patients with TP53wt EC. Investigational selinexor is an oral XPO1 inhibitor that drives nuclear retention and functional activation of wild type tumor suppressor proteins, such as p53. In the ENGOT-ENS/GOG-3055/SEINDO study (NCT03555422), preliminary analysis of a pre-specified exploratory subgroup of patients with TP53wt EC showed a decrease in risk for progression or death with a median PFS of 13.7 months with selinexor as maintenance therapy vs 3.7 months with placebo.

Methodology XPORT-EC-042 (NCT05611931) is a phase 3 randomized, double-blind, placebo-controlled study designed to evaluate the efficacy and safety of selinexor as maintenance therapy in patients with TP53wt primary stage IV or recurrent EC, who achieved a partial or complete response per Response Evaluation Criteria in Solid Tumors (RECIST) v1.1 after at least 12 weeks of platinum combination chemotherapy with or without immunotherapy. Among other inclusion/exclusion criteria, eligible patients must be ≥18 years of age, have histologically confirmed EC, and TP53wt tumor confirmed by NGS sequencing. Patients will be randomized 1:1 to receive selinexor 60mg PO or placebo once-weekly in 28-day cycles until progressive disease, toxicity, or 3-years if in complete response. A total of 220 patients are estimated to be enrolled globally. The primary endpoint is PFS based on RECIST v1.1 criteria as assessed by the Investigator. The key secondary endpoint is overall survival. Select secondary endpoints include safety assessments and PFS assessed by a blinded independent central review. Patient enrollment is blinded independent central review. Patient enrollment is ongoing.

Results - Conclusion

Disclosures Ignace Vergote has received grants/research support from Oncoinvent AS (2019–2020) GRANT = CORPORATE SPONSORED RESEARCH -Amgen (2019–2020) -Roche (2019–2020); received honoraria or consulting fees from Agenus (2021) - Aksebio (2021) - Amgen (Europe) GmbH (2019) - AstraZeneca (2019–2022) - Bristol Myers Squibb (2021) - Clovis Oncology Inc. (2019–2019) -Carrick Therapeutics (2019) - Deciphera Pharmaceuticals; and Accommodations, travel expenses (2019–2020) - Amgen - MSD - Tesaro - AstraZeneca - Roche. Mansoor Raza Mirza has received grants/research supports from AstraZeneca (Inst); Boehringer Ingelheim (Inst); Pfizer (Inst); Tesaro (Inst); honoraria or consultation fees from Honoraria - Advaxis; AstraZeneca; Cerulean Pharma; Clovis Oncology; Novocure; Pfizer; Roche; tesaro Consulting or Advisory Role - AstraZeneca; BioCad; Cerulean Pharma; Clovis Oncology; Genmab; Karyopharm Therapeutics; Novocure; Pfizer; Tesaro; Stock shareholder Karyopharm Therapeutics; SeraCare; and Leadership - Karyopharm Therapeutics; SeraCare; Travel Accommodations AstraZeneca; Karyopharm Therapeutics; Pfizer; Roche; SeraCare; Tesaro. Robert J Coleman has received grants/research supports from AstraZeneca/MedImmune( Institution), Clovis Oncology (Institution), Merck (Institution), Roche/Genentech (An Immediate Family Member), Immunogen (Institution), Mirati Therapeutics (Institution), Amgen (Institution), Pfizer (Institution), Lilly (Institution), Regeneron (Institution); honoraria or consultation fees Clovis Oncology; Genentech/Roche, AstraZeneca/MedImmune, Genmab, OncoMed, Immunogen, Abbvie, Agenus, Novocure, Merck, OncXena Therapeutics, Alkermes, Gradalis, GlaxoSmithKline, Eisai, GOG Foundation, Karyopharm Therapeutics; Stock shareholder McKesson; and Employment: US Oncology-Leadership: Onxeo. Travel, Accommodations, Expenses: Merck, AstraZeneca/MedImmune, Array BioPharma, Clovis Oncology, Roche/Genentech, Research to Practice, GOG Foundation, Clovis Oncology, Soto, Vianiam Group. Alejandro Pérez Fidalgo has received grants/research supports from Pharmamar and GSK (my institution); Participation in a company sponsored speaker’s bureau Astrazeneca, GSK, Clovis, Pharmamar (myself); and honoraria or consultation fees GSK, Clovis, Astrazeneca, Pharmamar, Roche. Bradley J Monk has received honorarium and consulting fees from Acrivon, Adaptimmune, Agenus, Akeso Bio, Amgen, Bayer, Elevar, EMD Merck, Gennab/Seagen, GOG Foundation, Gradalis, Heng Rui, Immunogen, Karyopharm, Ivance, Laekna Health Care, Mersana, Myriad, Novartis, Novocure, OncoC4, Panavance, Pieris, Pfizer, Puma, Regeneron, Sorrento, US Oncology Research, VBL, Verastem, Zentasi; and Speaker/Consultant AstraZeneca, Clovis, Easai, Merck, Roche/Genentech, TESARO/GSK. Giorgio Valabrega has received Consulting or advisory: GSK, PharmaMar, Astrazeneca, MSD. Brian M. Slomovitz has received honoraria or consultation fees from AstraZeneca, Clovis, GSK, Genentech, Merck, Eisai, Lilly, Novartis, Genmab, Seagen, Immunogen, Karyopharm, Seagan. Toon Van Gorp has received grants/research supports from Amgen, AstraZeneca, Roche; Advisory board (all payed to institute): AstraZeneca, Eisai, GSK, Immunogen, MSD, OncXena, Seagen, Tubulis; Participation in a company sponsored speaker’s bureau GSK. Kathleen Moore has received grants/research supports from PTC Therapeutics, Merck, Lilly, Genentech/ROche, Verastem, GSK/Tesaro; honoraria or consultation fees Astra Zeneca, Alkemeres, Aravive, Addi, Blueprint pharma, Clovis, Eisai, EMD SErono, GSK/ Tesaro, Genentech/Roche, Hengrui, Immunogen, Inxmed, Imab, Lilly, Mereo, Mersana, Merck, Myriad, Novartis, OncXena, OncoNova, VBL Therapeutics, Verastem; and serves as Associate Director for GOG Partners; receives royalties from Up to Date. Jalid Sehouli has Advisory Board, Personal, Invited Speaker GSK, MSD, PharmaMar, novocure, Tesaro,
Astra Zeneca, Clovis, Eisai, Roche, Merck, Bayer, Molecular Health, Riemser institutional: Karyopharm, GSK, Astra Zeneca, Clovis, MSD, PharmaMar, Novartis, Tesaro, Novocure, MSD, Eisai, Roche Diagnostics, Molecular Health, Riemser. David Cibula has received honoraria from Roche Canada, GSK, Eisai, Merck; Consulting or advisory role Amgen and Eisai. Tally Levy has no conflicts of interest to disclose. Gerassimos Aravantinos received honoraria or consultation fees from Astrazeneca, Roche, BMS, and MSD. Kai Li and Pratheek Kalyanapur are employees of Karyopharm Therapeutics. Vicky Makker has received grants/research supports (Funding to institution) NIH/NCI Cancer Center Support Grant (P30 CA008748); and unpaid consultancy/unpaid advisory board membership from AstraZeneca, Clovis, Eisai, Faeth, Genentech, GSK, iTEOS, Novartis, Karyopharm, Moreo, MSD, Takeda, and Zymeworks.
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**#323**

IFAST – EFFECTS OF INTERMITTENT FASTING DURING CHEMOTHERAPY ON FATIGUE, IMMUNOLOGICAL CHANGES AND PERIPHERAL CELL DAMAGE (A RANDOMIZED-CONTROLLED, MULTICENTER TRIAL)

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10.1136/ijgc-2023-ESGO.877

Introduction/Background First-evidence exists that fasting during chemotherapy (CHT) reduces peripheral blood immunosuppressive myocard cells while increasing cytotoxic cells. Furthermore, it might protect healthy cells from damage and increases quality of life (QoL) during CHT. However, fasting periods of 60–90h are not feasible for many patients. We aim to assess the effects of short-term intermittent fasting on CHT, immunological changes and peripheral cell damage during CHT.

Methodology In this multicenter, randomized-controlled trial 110 female patients with breast/cervical/endometrial or ovarian cancer, planned to receive intravenous CHT are recruited. The intervention group will follow a 16:8h fasting regimen with a change in fatigue during 3 months of CHT. Secondary endpoints will assess the distribution of peripheral blood mononuclear cells collected at baseline, after 1 week, 7 weeks and 13 weeks of CHT and peripheral DNA cell damage (measured by yH2AX concentration) at week 0, 6 and 12 of CHT. Changes of the insulin-like growth factor 1 (IGF-1) are also measured over the course of the trial.

Results This is an ongoing trial. So far, 10 patients (2 with ovarian cancer, 8 with breast cancer) have been recruited for the study. Compliance with the intermittent fasting regimen is high.

Conclusion Intermittent fasting is a generally feasible dietary concept and has shown to reduce IGF-1 and fatigue in healthy patients, highlighting its great potential for patients receiving CHT. Should this trial be able to demonstrate reduced fatigue during CHT, or to protect healthy cells and promote the antitumor activity of the immune system, intermittent fasting could truly be a beneficial option for patients wanting to actively effect their oncological treatment and outcome.

Disclosures The authors declare no conflict of interest regarding this trial.

**#331**

G8 GERIATIC SCREENING TOOL TO IDENTIFY FRAIL WOMEN WITH ENDOMETRIAL CANCER: FIRST INTERIM ANALYSIS OF THE FRAIL-B STUDY

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10.1136/ijgc-2023-ESGO.878

Introduction/Background Endometrial cancer (EC) is the most common malignancy of the female genital tract in developed countries and is normally treated by surgery. Frail EC patients should be identified preoperatively to reduce their risk of adverse surgical outcomes. These are the first results of a systematic, preoperative frailty screening of EC patients regarding perioperative complication rates.

Methodology All EC patients with a standardized surgical treatment, regardless of their actual cancer stage and previous treatments, were screened preoperatively with the G8 geriatric screening tool. If a patient was considered to be G8-frail, multiple geriatric assessment tools followed. The main outcome measures were the relationship between perioperative laboratory results, intraoperative surgical parameters and the incidence of immediate postoperative in-hospital complications with the preoperative frailty status.

Results 42 patients with EC were included at the University Medical Centre Mainz between May 2020 and April 2023. 23.8% (n=10) of the patients were classified as G8-frail. Mean age was 67.6 (± 7.9) years. The G8-frail cohort was slightly older (71 years; p=0.43). Polypharmacy (≥ 5 medication) was found more often in the G8-frail cohort (60 vs. 18.8%; p=0.02). The G8-frail cohort showed a numerically but not statistically significant higher Clavien-Dindo-Score than the G8-non-frail cohort (grade 2 {70 vs. 87.5%}), grade ≥3 (30 vs. 12.6%); p=0.29). The G8-frail cohort seemed to have a longer mean hospital stay than the G8-non-frail cohort (27.9 (± 48.3) vs. 5.8 (±5.4) days; p=0.06). The surgical revision rate seemed to be comparable between these two cohorts. One patient in the G8-frail cohort died during the hospital stay.

Conclusion Our first interim-analysis implies that preoperative frailty assessment with the G8 geriatric screening tool for elderly patients with EC might be associated with more severe postoperative complications and a longer hospital stay. Further results will be expected in the near future.

Disclosures The authors have no conflicts of interest to declare that are relevant to the content of this article.