5553

Identification of the ovarian cancer patients experiencing the highest benefit from bevacizumab in first-line setting based on their tumor intrinsic chemosensitivity (KELIM): GOG-0218 validation study

Benoit You, Christopher Purdy, Elizabeth M. Swisher, Michael A. Bookman, Gini F. Fleming, Robert L. Coleman, Leslie M. Randall, Krishnansu S. Tewari, Bradley J. Monk, Robert S. Mannel, Joan L. Walker, Fabio Cappuccini, Larry J. Copeland, Mahvish Muzaffar, David Gardner Mutch, Andrea E. Wahner-Hendrickson, Lainie P. Martin, Olivier Colomban, Robert A. Burger

Institut de Cancérologie des Hospices Civils de Lyon (IC-HCL), Lyon, France; NRG Oncology, Buffalo, NY; University of Washington School of Medicine, Seattle, WA; University of Arizona, Tucson, AZ; University of Chicago Medicine, Chicago, IL; U.S. Oncology Research, The Woodlands, TX; Virginia Commonwealth University, Richmond, VA; Division of Gynecologic Oncology, Department of Obstetrics & Gynecology, University of California, Irvine, CA; HonorHealth Research Institute, University of Arizona, Creighton University, Phoenix, AZ ; Stephenson Cancer Center, Oklahoma City, OK; The University of Oklahoma Health Sciences Center, Oklahoma City, OK; University of California-Irvine Medical Center, Orange County, CA; The Ohio State University Wexner Medical Center and James Cancer Hospital, Columbus, OH; East Carolina University/Vidant Cancer Center, Greenville, NC; Washington University School of Medicine in St. Louis, St. Louis, MO; Mayo Clinic Rochester, Rochester, MN; University of Pennsylvania, Abramson Cancer Center, Philadelphia, PA; Laboratoire EA 3738 UCBL/HCL CICLY Equipe 3, Oullins, France; Department of Obstetrics & Gynecology, Division of Gynecologic Oncology, University of Pennsylvania, Philadelphia, PA

BACKGROUND:

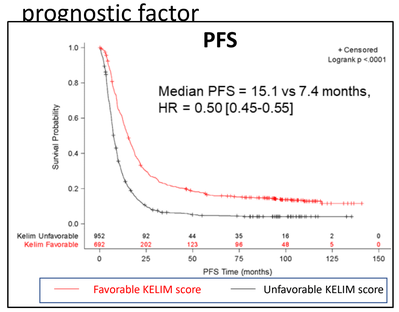
- For patients with advanced ovarian carcinoma in first-line setting
  - ↳ **How to identify those experiencing the maximum benefit from bevacizumab ?**
- Two main international phase III trials
  - **ICON-7 trial**: benefit in OS for high-risk disease (sub-optimally debulked stage III + stage IV) *(Oza et al. Lancet Oncol 2015)*
  - **GOG-0218**: benefit in OS for stage IV disease (*Tewari et al, JCO 2019*)
- The modeled CA-125 kinetic ELIMination rate constant K (**KELIM**) calculated during the first 100 days = **indicator of the tumor primary chemosensitivity** (*You et al Cancer Treatment Reviews 2021*)
  - KELIM score < 1.0 : unfavorable KELIM => poorly chemosensitive disease
  - KELIM score ≥ 1.0: favorable KELIM => highly chemosensitive disease
- **Exploratory analysis of ICON-7 => among patients with high-risk disease, only those with unfavorable KELIM might have experienced benefit from bevacizumab** (median OS, 29.7 vs 20.6 months; absolute difference, 9.1 months, HR =0.78 95%CI, 0.58-1.04)(*Colomban et al. JNCI CS 2020;4(3):pkaa026*)
  - ↳ **An external validation of these outcomes in GOG-2018 trial data was warranted**

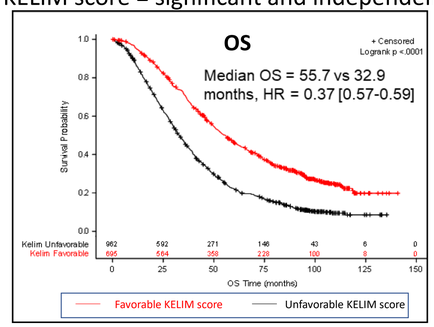
METHODS:

- Retrospective analysis of GOG-0218 (NCT00262847) comparing carboplatin-paclitaxel +/- bevacizumab followed by bevacizumab maintenance for 15 months
- KELIM was calculated by Lyon University team (EA 3738 CICLY, France) with the model implemented online https://www.biomarker-kinetics.org/
- The prognostic and predictive value of KELIM score was assessed by NRG GOG statistics team
- Using univariate and multivariate survival analyses
- Survival analyses with landmark timepoint at 100 days

RESULTS: *Prognostic value of KELIM regarding PFS and OS*

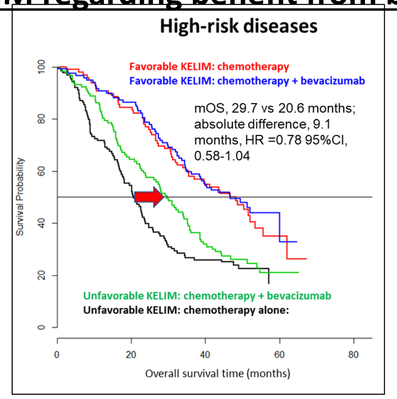
- In univariate and multivariate analyses, KELIM score = significant and independent prognostic factor



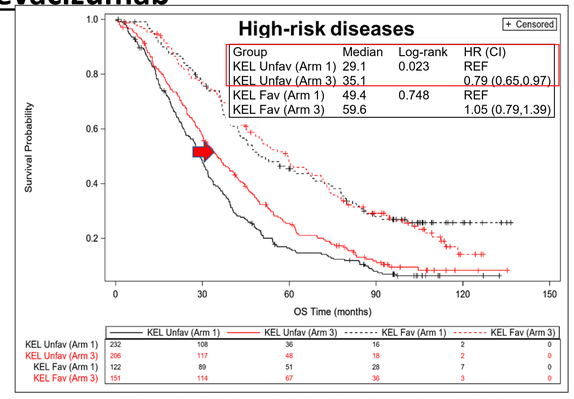


RESULTS: Predictive value of KELIM regarding benefit from bevacizumab

Among patients with **high-risk diseases**, only those with **unfavorable KELIM** had OS benefit from bevacizumab

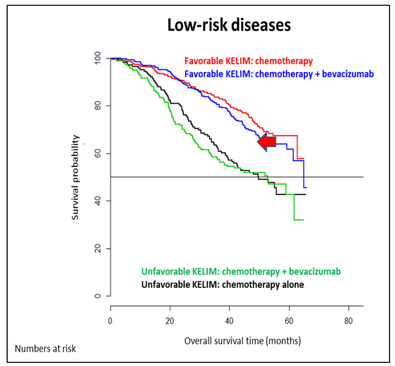


Initial study in ICON-7 phase III trial
Colomban et al. JNCI CS 2020;4(3):pkaa026

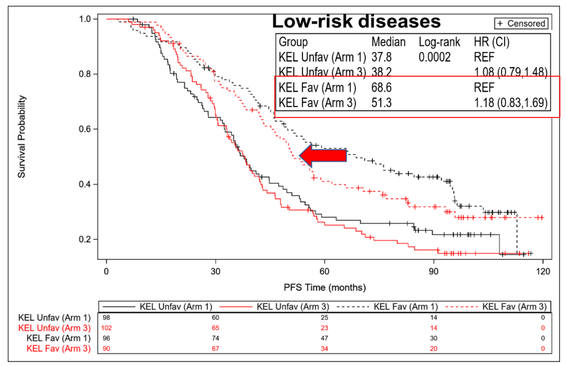


External validation study in GOG-0218 phase III trial

Among patients with **low-risk diseases**, potentially lower OS with bevacizumab in patients with favorable KELIM



Initial study in ICON-7 phase III trial
Colomban et al. JNCI CS 2020;4(3):pkaa026



External validation study in GOG-0218 phase III trial

CONCLUSION:

- Bevacizumab should be prioritized in patients with a high-risk & poorly chemosensitive disease to improve their PFS and OS
- Bevacizumab might be discouraged in patients with a low-risk disease & highly chemosensitive disease
- Patient KELIM score easily calculable on https://www.biomarker-kinetics.org/ … and a smartphone application soon …