Prognostic value of the modeled CA-125 kinetics parameter KELIM-PARP in patients with advanced ovarian cancer (AOC): analysis of the phase II BOLD study

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#Abstract 10342

Background & Objectives

- In patients with recurrent High Grade Ovarian Cancer (HGOC), the combination of durvalumab (anti-PL1 monoclonal antibody), olaparib (PARP inhibitor) and bevacizumab (anti-VEGF monoclonal antibody) was associated with promising efficacy and safety in MEDIOLA and BOLD trials [1].
- The CA-125 modeled ELIMination rate contant K (KELIM^{TM}) is a reproducible indicator of the tumor chemosensitivity [2]. In recurrent HGOC patients treated by rucaparib (another PARP inhibitor), the modeled KELIM-PARP score was associated with radiological response and Progression-Free Survival (PFS) [3].
- The objective of the present study was to assess the **prognostic value of KELIM-PARP**, adjusted to **BOLD trial** data, in terms of **PFS** and Overall Survival (**OS**), in patients with recurrent HGOC treated with this chemotherapy-free regimen.

Methods

- *Data:*

Phase II clinical trial BOLD (NCT04015739) [1], evaluating safety and efficacy of olaparib, bevacizumab and durvalumab combinaison in 74 patients with recurrent high-grade AOC.

- *Model (NONMEM 7.5.0):*

K-PD model, was previously described [3]. Model validation criteria:

- Relative Standard Errors (RSE) Basic Goodness-Of-Fits (GOF) plots
- Visual Predictive Checks (VPC)

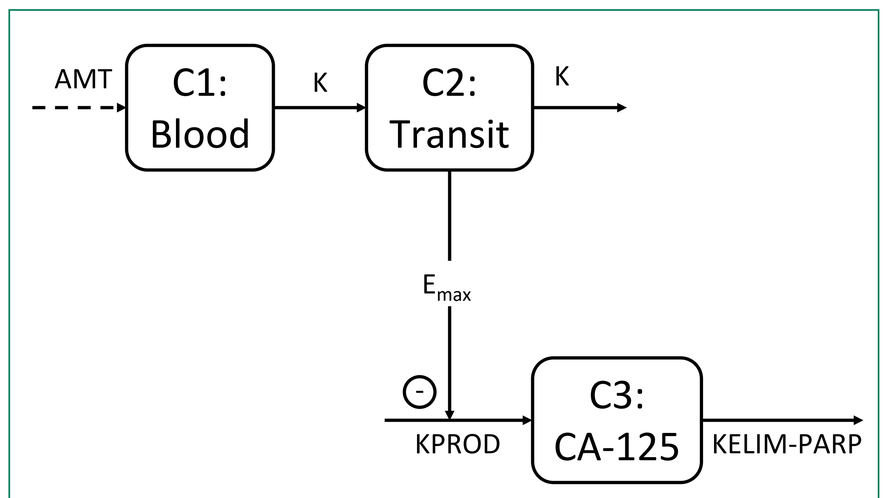
- *Survival analyses:*

Estimation of Individual values of the **modeled KELIM-PARP** parameter.

➢ Categorize patients with **KELIM-PARP score**:

- **Unfavorable**: KELIM-PARP < median KELIM-PARP
- **Favorable:** KELIM-PARP ≥ median KELIM-PARP

100-day landmark time point analysis to avoid bias between KELIM-PARP estimations and PFS/OS status

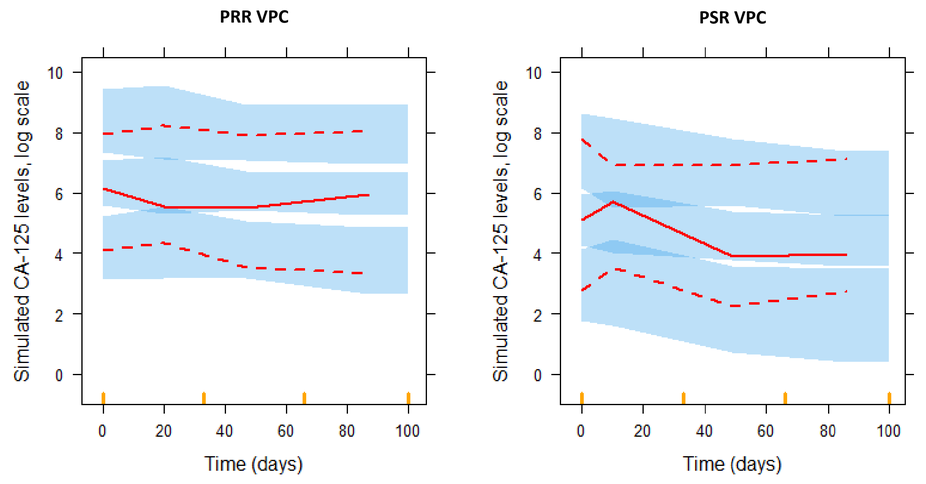


K-PD MODEL

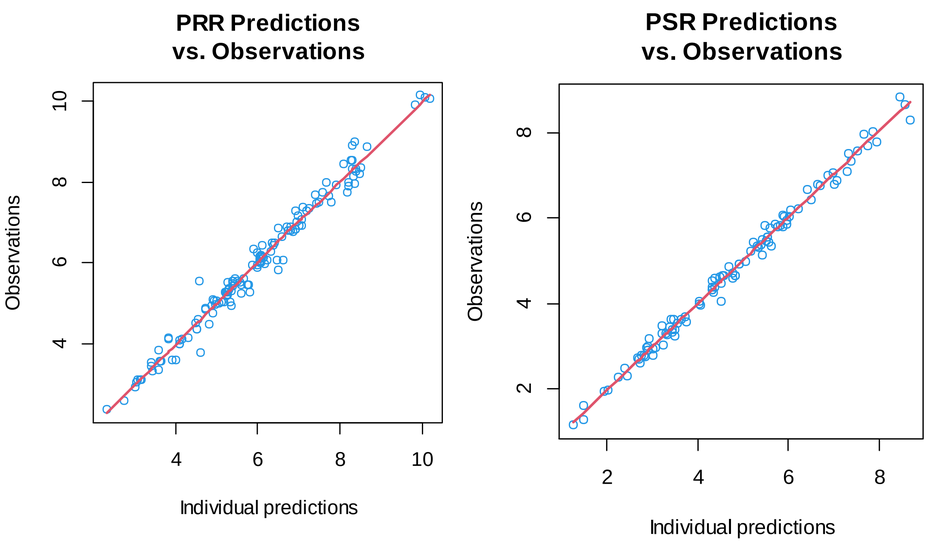
Results

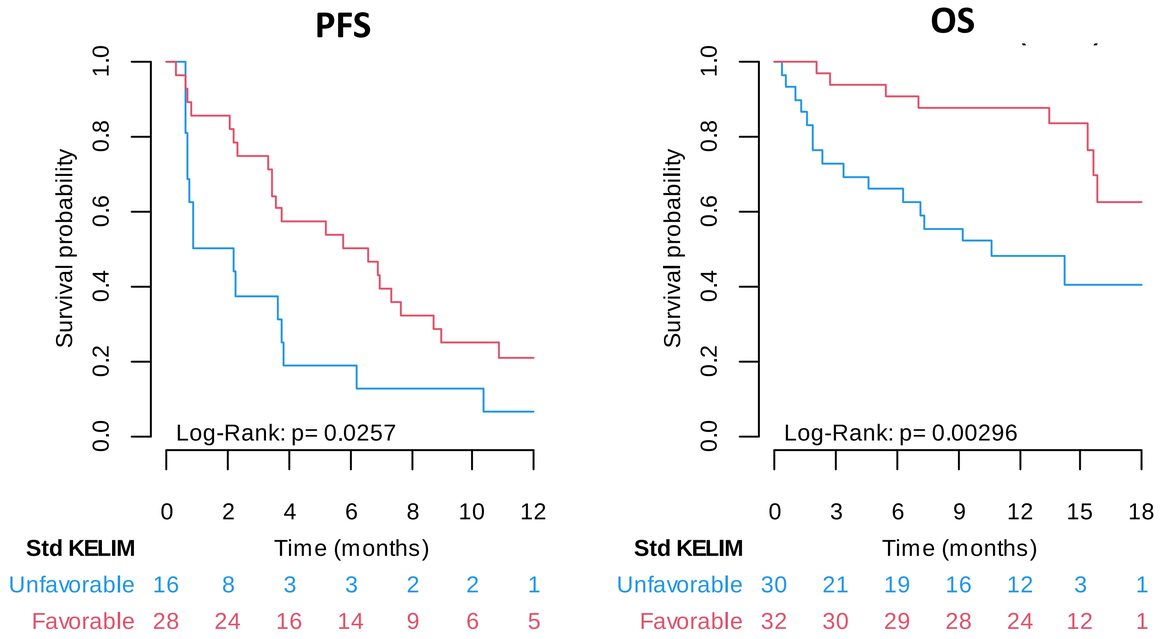
- 62 over 74 enrolled patients were assessable.
- The platinum-sensitivity status (platinum–sensitive relapse (PSR) or platinum-resistant relapse (PRR)) was used as a baseline covariate [3].
- GOF plots and VPC suggested good predictions of CA-125 kinetics.
- KELIM-PARP score exhibited prognostic value regarding PFS and OS.

VPC



Individual Predictions vs. Observations





	Median (months) [95% CI]	p-value (logRank)	Hazard Ratio [95% CI]	Concordance index [95% CI]	p-value (Cox)
PFS (RECIST)					
Unf. KELIM-PARP 1.54 [0.70; 6.19] *Fav. KELIM-PARP* 6.20 [3.48; 9.00]		0.03	0.47 [0.24; 0.92]	0.61 [0.53; 0.68]	0.027
OS					
Unf. KELIM-PARP 10.6 [6.33; NR] *Fav. KELIM-PARP* NR [15.80; NR]		0.003	0.29 [0.12; 0.69]	0.68 [0.59; 0.76]	0.005

Conclusion

- The model developed for rucaparib in patients with recurrent ovarian cancer was effective to characterize individually CA-125 kinetics in AOC patients during the first 100 days of treatment with durvalumab, olaparib and bevacizumab.
- Like for patients treated with chemotherapy, KELIM-PARP score exhibited a strong prognostic value regarding PFS and OS in patients treated with this chemotherapy-free regimen.

References

[1] Freyer, G., et al., 733P Bevacizumab (Bev), olaparib (Ola) and durvalumab (Durva) in patients with recurrent advanced ovarian cancer (AOC): The GINECO BOLD study. Annals of Oncology, 2021.
[2] Lauby, A., et al., The Increasing Prognostic and Predictive Roles of the Tumor Primary Chemosensitivity Assessed by CA-125 Elimination Rate Constant K (KELIM) in Ovarian Cancer: A Narrative Review. Cancers, 2022
[3] Colomban, O., et al., Mathematical modeling of the early modeled CA-125 longitudinal kinetics (KELIM-PARP) as a pragmatic indicator of rucaparib efficacy in patients with recurrent ovarian carcinoma in ARIEL2 & STUDY 10. eBioMedicine