#P302

ESGO HYBRID MEETING Oct 23-25, 2021

22nd European Congress on Gynaecological Oncology
Prague, Czech Republic + Online

Niraparib Maintenance Treatment with Individualised Starting Dose was Efficacious with Dose Modification in Chinese Patients with Platinum-sensitive Recurrent Ovarian Cancer : a *Post Hoc* Analysis

Ziling Liu[1], Xiaohua Wu[2], Jianqing Zhu[3], Rutie Yin[4], Jiaxin Yang[5], Jihong Liu[6], Jing Wang[7], Lingying Wu[8], Charlie Zhang[9], and Juan Dong[9]

[1]Department of Oncology, The First Hospital of Jilin University, Changchun, China; [2]Department of Gynecologic Oncology, Fudan University Shanghai Cancer Center, Shanghai, China; [3]Department of Gynecologic Oncology, Cancer Hospital of the University of Chinese Academy of Sciences (Zhejiang Cancer Hospital), Hangzhou, China; [4]Department of Obstetrics and Gynecology, Key Laboratory of Birth Defects and Related Diseases of Women and Children, Ministry of Education, West China Second University Hospital, Sichuan University, Chengdu, China; [5]Department of Gynecologic Oncology, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China; [6]Department of Gynecologic Oncology, Sun Yat-sen University Cancer Center, Guangzhou, China; [7]Department of Gynecologic Oncology, Hunan Cancer Hospital, The Affiliated Cancer Hospital of Xiangya School of Medicine, Central South University, Changsha, China; [8]Department of Gynecologic Oncology, National Cancer Center/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China; [9]R&D Department, Zai Lab (Shanghai) Co., LTD, Shanghai, China

INTRODUCTION

- In the global phase 3 NOVA study of niraparib maintenance therapy (MT) in platinum-sensitive recurrent ovarian cancer (PSROC), niraparib was initiated at 300 mg.[1] *Post hoc* analysis then showed that for patients with baseline bodyweight <77 kg or platelet count <150×10^3/μl, the actual average daily dose received was ~200 mg due to dose interruption and reduction for managing treatment-emergent adverse events (TEAEs), especially haematologic TEAEs.[2]
- In Chinese PSROC patients, the pivotal NORA study (NCT03705156) adopted an **individualised starting dose (ISD)**: patients with baseline bodyweight **<77 kg** or baseline platelet count **<150×10^3/μl** initiated niraparib at **200 mg** and all other patients, at 300 mg.[3]
- Compared to NOVA, ISD in NORA **improved safety** in niraparib-treated patients (e.g., markedly lower frequency of grade ≥3 platelet count decreased [11.3% vs 33.8%] or anaemia [14.7% vs 25.3%] and of TEAEs leading to niraparib discontinuation [4.0% vs 14.7%]), while achieving **comparable efficacy** (risk reduction for disease progression or death: 78% vs 73% for patients with germline *BRCA* mutations, 60% vs 55% for patients without).[1,3]
- NORA protocol also stipulated stringent **dose modification** procedures for managing specific TEAEs during treatment.[3] As such, incidence of niraparib dose modification in NORA was similar to that in NOVA (dose reduction: 59.9% vs 66.5%),[1,3] with majority of patients' niraparib dose stabilising by 4 months after treatment initiation.

AIM

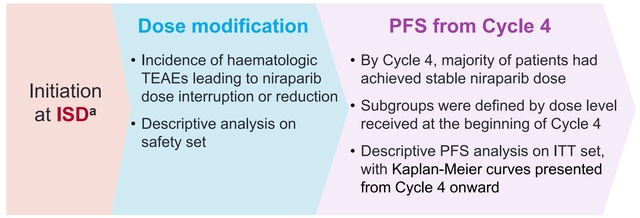
This *post hoc* analysis of NORA aims to further inform the management of Chinese patients receiving niraparib with ISD, specifically by understanding:

- The major haematologic TEAEs necessitating niraparib dose modification, and the temporal pattern of their occurrence
- The efficacy of niraparib at individualised, optimised stable doses

METHOD

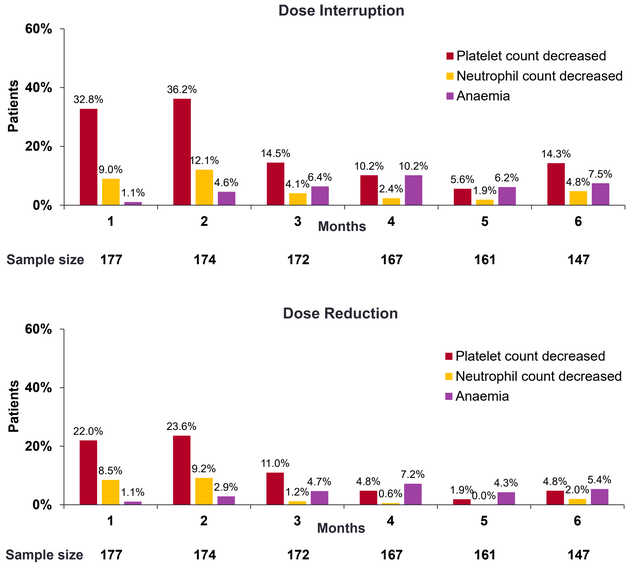
- Key eligibility criteria: 1) ≥18 years old; 2) having received ≥2 prior lines of platinum-based chemotherapy; 3) having complete/partial response to most recent platinum-containing chemotherapy.
- In NORA, patients were randomised 2:1 to niraparib or placebo MT of 28-day cycles. Dose modification (i.e., dose interruption ≤28 days or dose reduction) were allowed (**Figure 1**).
- Safety and efficacy parameters examined in this *post hoc* analysis are shown in **Figure 1.**

Figure 1. Study overview



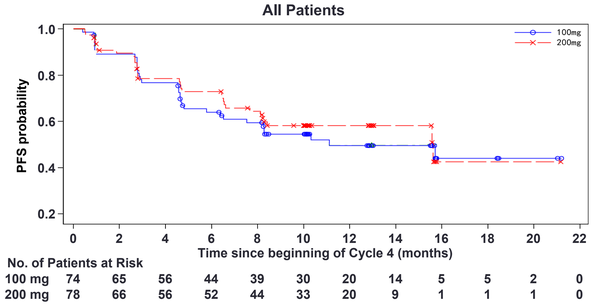
[a]First 16 patients enrolled in NORA followed 300-mg fixed starting dose before protocol amendment to ISD, with 11/16 randomised to niraparib. ISD, individualised starting dose; ITT, intention-to-treat; PFS, progression-free survival; TEAE, treatment-emergent adverse event.

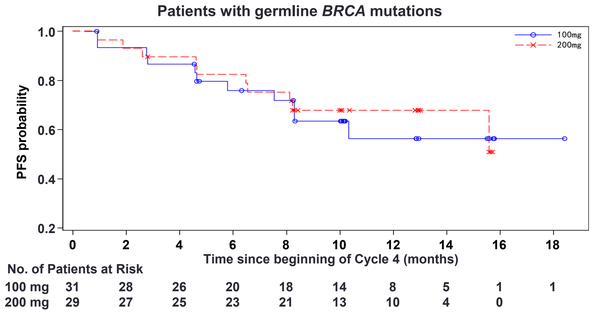
Figure 2. Haematologic TEAEs[a] leading to niraparib dose modification by month (safety set[b])

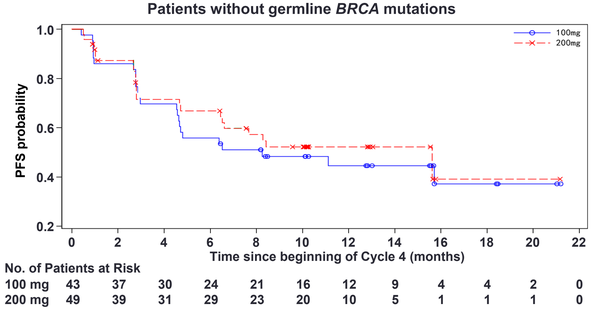


[a]For any month, all evident TEAEs were included, not only those with first start date within the month. Events that continue throughout a month, i.e., with start date prior to the month and stop date (or continuing) after the month, were considered as occurring within the month concerned. Percentages are based on the number of patients starting a given month. [b]Safety set in NORA consisted of all randomised patients who received ≥1 dose of study medication. TEAE, treatment-emergent adverse event.

Figure 3. Kaplan-Meier curves for PFS by niraparib dose level at the beginning of Cycle 4 (ITT set[a])







[a]ITT set in NORA was defined as all randomised patients regardless of exposure to study medication. ITT, intention-to-treat; PFS, progression-free survival.

RESULTS

Niraparib Dose Modification

- Safety set: a total of 177 patients received ≥1 dose of niraparib treatment.
- In Months 1–2, dose modification occurred in **22.0%–36.2%** of patients due to platelet count decrease, and in **8.5%–12.1%** of patients due to neutrophil count decrease (**Figure 2**).
- These percentages decreased from **Month 3** onward and remained low through Months 4–6 (**Figure 2**).

PFS from Cycle 4

- At the beginning of Cycle 4, 158 patients from the ITT set were on niraparib treatment (n=74 on 100 mg; n=78 on 200 mg; n=6 on 300 mg).
- PFS curves were similar between the 100-mg and 200-mg subgroups, regardless of germline *BRCA* mutation status (**Figure 3**).
- The 300-mg subgroup PFS data were not interpretable due to small sample size and are thus not presented here.

CONCLUSIONS

In Chinese patients from the NORA study

- Compared to fixed starting dose in NOVA, niraparib with ISD in NORA showed improved safety and comparable efficacy in the overall study population.[1,3]
- Platelet count decrease and neutrophil count decrease were the major haematologic TEAEs necessitating niraparib dose modification, the frequency of which decreased substantially three months after niraparib initiation.
- Upon achieving stable, optimised doses in majority of patients, the PFS was comparable between subgroups receiving niraparib MT at 200-mg and 100-mg dose levels.

References

1. Mirza *et al.* N Eng J Med 2016; 375(22):2154-2164.
2. Berek *et al.* Ann Oncol 2018; 29(8):1784-1792.
3. Wu *et al.* Ann Oncol 2021; 32(4):512–521.

Acknowledgements

This study was sponsored by Zai Lab and partially supported by the National Major Scientific and Technological Special Project for "Significant New Drugs Development" in 2018 (2018ZX09736019), China. The authors acknowledge Ning-Yu Chan, PhD, Costello Medical, Singapore, for medical writing and editorial assistance. All costs associated with the development of this poster were funded by Zai Lab.

Author Disclosure

CZ, JD: Employee of Zai Lab; ZL, XW, JZ, RY, JY, JL, JW, LW: Nothing to declare.