Time to Next Treatment (TTNT) of First-Line Maintenance (1Lm) Niraparib Monotherapy in Epithelial Ovarian Cancer (EOC) Patients in the CHAR1ZMA Study

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Background

- The introduction of poly (adenosine diphosphate-ribose) polymerase inhibitor (PARPi) therapies has provided new treatment options for patients with advanced epithelial ovarian cancer, fallopian tube, or primary peritoneal cancer (collectively EOC), who typically have a poor prognosis.[1]
- Niraparib was approved on 29 April 2020 in the United States (US) as a once-daily monotherapy in the first-line maintenance (1Lm) setting for patients with platinum-responsive advanced EOC regardless of breast cancer gene (*BRCA*) mutational and homologous recombination deficiency (HRD) status, based on the findings of the PRIMA clinical trial.[2,3]
- Given the observed benefits of niraparib 1Lm therapy for patients with EOC shown in clinical trials, there is a critical need for clinical outcomes data in the real-world setting.

Aim

- To characterise the real-world time to next treatment (TTNT) of patients with EOC who received niraparib 1Lm monotherapy overall and across key subgroups.

Methods

Study design

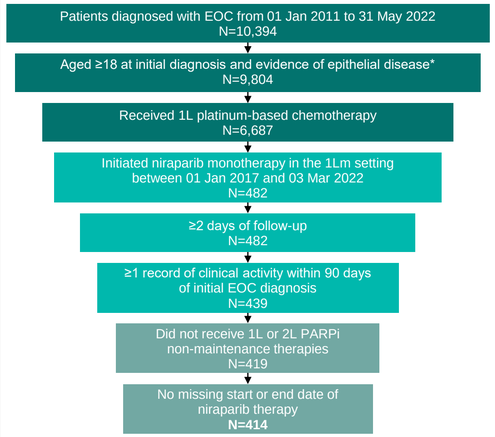
- CHAR1ZMA was a real-world, longitudinal, retrospective cohort study based on the US Flatiron Health electronic health-record derived database, which assessed newly diagnosed patients with EOC who received 1Lm niraparib monotherapy.
  - The Flatiron Health longitudinal database contains de-identified patient-level structured and unstructured data, curated via technology-enabled abstraction.[4,5] Data originated from ~280 cancer clinics (~800 sites of care); of note, the majority (~80%) of patients in the database originate from community oncology practices.
- The index date was defined as the end date of first-line platinum-based chemotherapy.
- Patients were followed from the index date to the earliest occurrence of date of death, end of follow-up, or end of study period (31 May 2022).
- Patients included in the study met the eligibility criteria shown in **Figure 1**.

Data analyses

- Descriptive statistics were used to describe baseline demographic and clinical characteristics, assessed between the initial EOC diagnosis and the index date.
- TTNT, a proxy for real-world progression-free survival (PFS), was defined as the time from index date to the start of the subsequent treatment line (2L) or death.
  - Median TTNT and 95% confidence intervals (CI) were estimated with Kaplan-Meier curves.
  - Patients who did not initiate 2L therapy or did not die before initiating 2L therapy were censored at the end of follow-up.
- TTNT was assessed for patients overall and stratified into four subgroups:
  - Age at index (<75 or ≥75 years of age)
  - *BRCA* status (mutated or wild-type)
  - HRD status (HR-deficient or HR-proficient)
  - Residual disease (RD) status following cytoreductive surgery (no visible RD, visible RD or no surgery)

Results

Figure 1. Patient attrition



*Evidence of epithelial disease included the following histologies: serous, clear cell, mucinous, endometrioid, transitional cell, epithelial NOS, or unknown
1L, first-line; 1Lm, first-line maintenance; 2L, second-line; EOC, epithelial ovarian cancer; NOS not otherwise specified; PARPi, poly (adenosine diphosphate-ribose) polymerase inhibitors.

Table 1. Baseline patient demographics

	N=414
Age at index (years), median (Q1, Q3)	67 (61, 75)
<75 years, n (%)	310 (74.9)
≥75 years, n (%)	104 (25.1)
Race, n (%)	
Black or African American	32 (7.7)
White	267 (64.5)
Other	83 (20.0)
Unknown	32 (7.7)
Ethnicity, n (%)	
Hispanic or Latino	21 (5.1)
Not Hispanic or Latino	99 (23.9)
Unknown	294 (71.0)
Region,* n (%)	
Midwest	49 (11.8)
Northeast	38 (9.2)
South	203 (49.0)
West	52 (12.6)
Other/Unknown	72 (17.4)
Practice type,† n (%)	
Academic	68 (16.4)
Community	365 (88.2)

*Patients from academic practices had unknown geographic regions. †Patients with records in academic and community practices were counted in both categories; therefore, patient counts and percentages may sum to more than 100%.
Q1/Q3, quartile 1/3.

Study population

- Patient attrition is shown in **Figure 1**.

Baseline characteristics

- A total of 414 patients met the eligibility criteria; baseline demographics are shown in **Table 1.**
  - Most patients were White (64.5%), and were <75 years (74.9%) with a median age of 67 years.
- Clinical characteristics are shown in **Table 2**; most patients had an Eastern Cooperative Oncology Group (ECOG) performance status score of 0–1 (80.7%) and either Stage III or Stage IV EOC at initial diagnosis (49.3% and 34.1% respectively).
- Median patient follow-up from index was 13.8 (quartile 1, quartile 3: 8.4, 20.8) months.
- Of note, patients with *BRCA* mutations were added to the HR-deficient subgroup to improve the completeness of HRD status information in the study population

TTNT

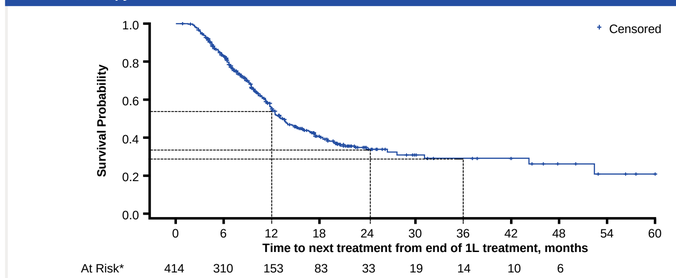
- The Kaplan-Meier curve for observed TTNT is shown in **Figure 2**.
  - Survival rates (95% CI) at 12-, 24-, and 36 months were 55.1% (49.6%, 60.3%), 33.9% (27.9%, 40.0%) and 29.2% (22.2%, 36.6%), respectively.

Table 2. Baseline patient clinical characteristics

	N=414
Median duration of 1L platinum-based chemotherapy, days (Q1, Q3)	141 (112, 169)
ECOG performance status score, n (%)	
0–1	334 (80.7)
2–4	38 (9.2)
Unknown/missing	42 (10.1)
Stage at initial diagnosis,* n (%)	
Stage I	6 (1.4)
Stage II	20 (4.8)
Stage III	204 (49.3)
Stage IV	141 (34.1)
Unknown	43 (10.4)
***BRCA* mutation status,† n (%)**	
Mutated	48 (11.6)
Wild-type	346 (83.6)
Unknown	20 (4.8)
HRD/*BRCA* mutation status, n (%)	
HR-deficient‡	106 (25.6)
HR-proficient or *BRCA* wild-type/HRD status unknown	288 (69.6)
Unknown *BRCA*/HRD status	20 (4.8)
Cytoreductive surgery, n (%)	
Yes	355 (85.7)
No/unknown	59 (14.3)
RD status following cytoreductive surgery, n (%)	
No surgery or unknown surgery status	59 (14.3)
No visible RD	176 (42.5)
Visible RD	92 (22.2)
Unknown RD status	87 (21.0)

*FIGO or AJCC stage; if both stages were reported, abstractors captured the FIGO stage; †Includes somatic and germline mutations; ‡Includes patients with *BRCA* mutation or *BRCA* wild-type/HR-deficient.
1L, first-line; *BRCA*, breast cancer gene; ECOG, Eastern Cooperative Oncology Group; HR, homologous recombination; HRD, homologous recombination deficiency; Q1/Q3, quartile 1/3; RD, residual disease.

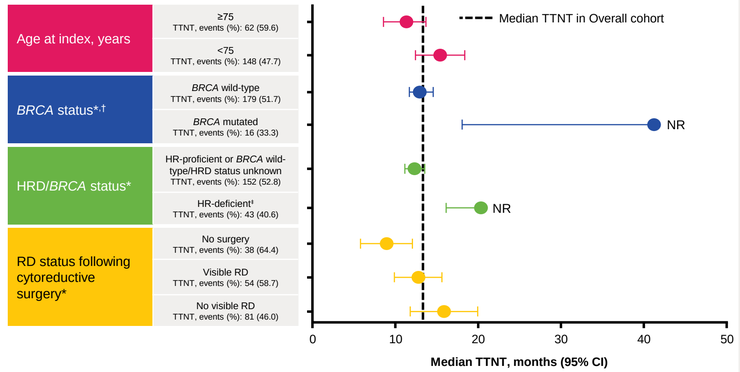
Figure 2. Kaplan-Meier curve for TTNT among patients with advanced EOC who received niraparib 1Lm monotherapy



*n<5 patients at risk at 54 and 60 months, thus not reported to maintain patient confidentiality.
1L, first-line; 1Lm, first-line maintenance; EOC, epithelial ovarian cancer; TTNT, time to next treatment.

- For the 414 patients, the observed median TTNT was 13.3 months (95% CI: 12.0, 15.8).
- Observed TTNT varied by demographic and clinical characteristics (**Figure 3**).
  - The longest median TTNT in each subgroup (excluding patients with unknown data) was for patients who were <75 years of age, patients with *BRCA* mutations, patients who were HR-deficient, and patients with no visible RD following surgery.

Figure 3. TTNT in patients with EOC receiving niraparib 1Lm monotherapy by subgroups



*Unknown categories excluded in the Kaplan-Meier analyses; †Includes somatic or germline mutations; ‡Includes patients with *BRCA* mutation or *BRCA* wild-type/HR-deficient.
1Lm, first-line maintenance; *BRCA*, breast cancer gene; CI, confidence interval; EOC, epithelial ovarian cancer; HR, homologous recombination; HRD, homologous recombination deficiency; NR, not reached; RD, residual disease; TTNT, time to next treatment.

Conclusions

- The CHAR1ZMA study is the first to describe the TTNT of a demographically diverse cohort of patients with advanced EOC who received niraparib 1Lm therapy in a real-world setting.
  - Notably, more than one quarter of patients had an electronic health record value for race as other than White and were aged 75 years or older; these patients are not typically well-represented in US gynaecological cancer clinical trials.[6]
- The real-world trend in PFS observed in this study was demonstrated across all biomarkers, with longer observed TTNT for patients who were HR-deficient (than HR-proficient) and had *BRCA* mutations (than no mutations), supporting findings shown in the PRIMA clinical trial.[3]
  - Whilst patients with no visible RD were not included in the PRIMA clinical trial, results from the current study suggest these patients have a longer median TTNT than patients with no surgery or visible RD.
- The results shown here also suggest that patient characteristics can impact clinical outcomes for patients with EOC who receive niraparib as 1Lm therapy and highlight the importance of biomarker testing; the lack of HRD status testing in the real-world was also evident.
- Given the relatively small size of some subgroups, these results should be interpreted with caution. Future research should aim to contextualise these results to further inform clinical management of patients with EOC.

Disclosures

RLC reports advisory role fees (Abbvie, Arrivive, AstraZeneca, Clovis Oncology, Eisai, Genentech/Roche, GSK, Janssen, Merck, Novocure, Oncomed/Mateo, OncoQuest, OncoSec) and research funding (Abbvie, Genmab, V-foundation). **RS** reports advisory role fees (Merck, Mersana, Seagen), speaker bureau fees (Merck), writing engagement fees (UpToDate) and has been a principal investigator (non-funded) for Genentech. **FB** reports advisory role fees (Agenus, AstraZeneca, Clovis, Eisai, GSK, Immunogen, Merck, Myriad) and has been a principal investigator (funded) for BeiGene, Clovis, Eisai, Immunogen, Merck and Natera. **JP** is an employee of GSK and holds stock/shares in GSK and Boston Scientific. **TACB**, **JL**, **LK**, **JS**, **JAH,** and **AG** are employees of GSK.

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