Real-World Prognostic Relevance of Residual Disease and Other Clinical Factors on the Progression of Disease and Death in Patients With Advanced Ovarian Cancer in the US

Poster Number. 374

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Background

OC remains the leading cause of death in women when compared with all other gynaecologic cancers[1]

Although most patients with OC respond to 1L treatment of surgical cytoreduction and platinum-based CT, up to 85% of patients experience PD within 3 years[2,3]

Identifying demographic and clinical factors that are prognostic of PD and OC survival may inform clinical decision-making about new OC maintenance therapies after response to 1L treatment

For example, visible residual disease (VRD) was found to be more significantly associated with survival than the extent of metastatic disease seen on imaging prior to surgery[4–7]

Objective

To assess the association between residual disease and other clinical factors (e.g. *BRCA* status), and the risk of PD or death in patients with advanced OC in a real-world setting (including academic and community practices)

Methods

This retrospective, real-world study used data from the Flatiron Health database of patients diagnosed with advanced OC between 1 January 2011 and 29 February 2020 to assess demographic and clinical factors associated with TTNT (a surrogate for PFS) and OS

- Flatiron Health is a longitudinal EHR-derived, de-identified database comprised of patient-level data, curated via technology-enabled abstraction from ~280 cancer clinics in the USA nationwide[8]

Eligibility criteria are depicted in **Table 1**

The index date was defined as the last date of 1L treatment

- TTNT: time from index date until start of 2L treatment, death, last activity, or the end of the data period (whichever occurred first)
- OS: time from index date until death, last activity or the end of the data period (whichever occurred first)

KM analyses were used to assess TTNT and OS outcomes

Multivariate Cox regression models with stepwise selection were used to assess demographic and clinical factors associated with TTNT and OS

Table 1. Inclusion/exclusion criteria

Inclusion criteria*	Exclusion criteria
Diagnosis of advanced OC (ovarian, fallopian tube and/or primary peritoneal cancer)	Missing date of surgery
≥18 years of age	Missing residual disease status
Stage III or IV disease	
1L treatment	
≥12 weeks of follow-up after 1L treatment	

*Included patients with no surgery, based on Flatiron Health definitions, which combined patients with unknown surgery status and no surgery together. The no surgery subgroup was excluded as a sensitivity analysis.

Results

Population

1,920/6,940 patients met study inclusion criteria and were included in this analysis

The majority of patients (88%) included in the study received treatment in the community setting (**Table 2**)

- The median follow-up time was 19.7 months (IQR: 10.2–34.8)
- HRd status could not be assessed as a prognostic factor in this analysis, as only 4% of the total population had a known HRd status

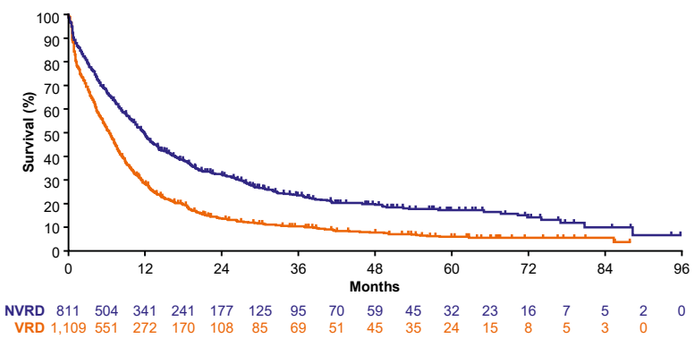
Table 2. Patient demographics and baseline disease characteristics

Characteristic, n (%)		Total population (N=1,920)
Age	18–64 years	808 (42)
	65–79 years	933 (49)
	80+ years	179 (9)
Practice type	Academic*	231 (12)
	Community	1,689 (88)
Race	White	1,426 (74)
	Black	101 (5)
	Asian	40 (2)
	Other	226 (12)
	Missing	127 (7)
ECOG PS	0–1	1,152 (60)
	2–4	162 (8)
	Missing	606 (32)
BRCA status†	*BRCA*m	277 (14)
	*BRCA*wt	994 (52)
	BRCA unknown/missing	649 (34)
Histology‡	BL/CC/E/M/TC§	107 (6)
	Serous	1,484 (77)
	Epithelial NOS/unknown	329 (17)
Disease stage	III	1,293 (67)
	IV	627 (33)
Residual disease‖	NVRD	811 (42)
	VRD	1,109 (58)
Therapy modality	PDS/adjuvant	1,036 (54)
	IDS/neoadjuvant	576 (30)
	No surgery	308 (16)

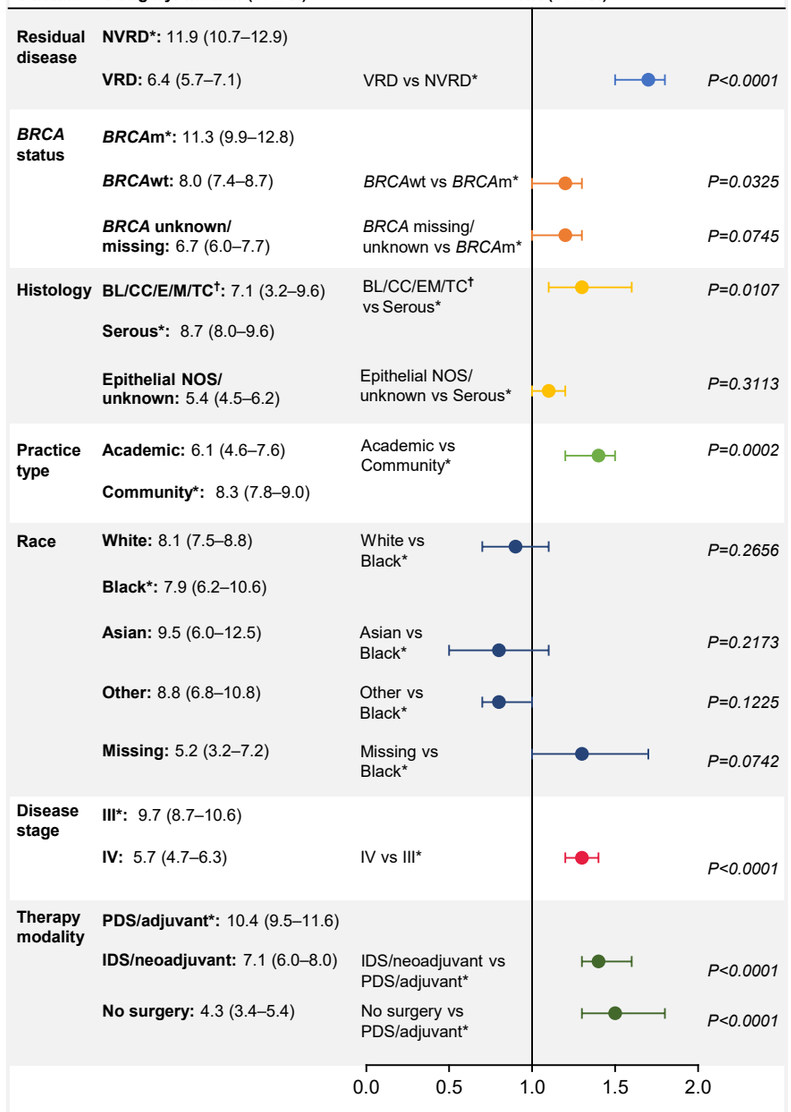
*Academic practices represent NCI-designated cancer centres; †*BRCA* status was based on germline or somatic results. Unknown category included patients with unknown sample types (1%) and untested patients; ‡Data on tumour grade were not available; §Represents borderline (BL), clear cell (CC), endometrioid (E), mucinous (M) or transitional cell (TC) histologies; ‖Patients with no remaining gross RD following surgery were grouped as NVRD. Patients with remaining gross RD following surgery were defined as VRD. Additionally, patients with no/unknown surgery were included in the VRD group.

Figure 1. Predictors of TTNT in patients with OC

A. NVRD vs VRD



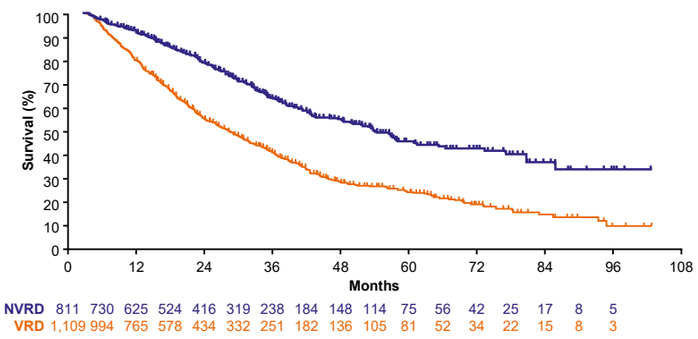
B. Medians and HRs for clinical factors associated with TTNT (months)



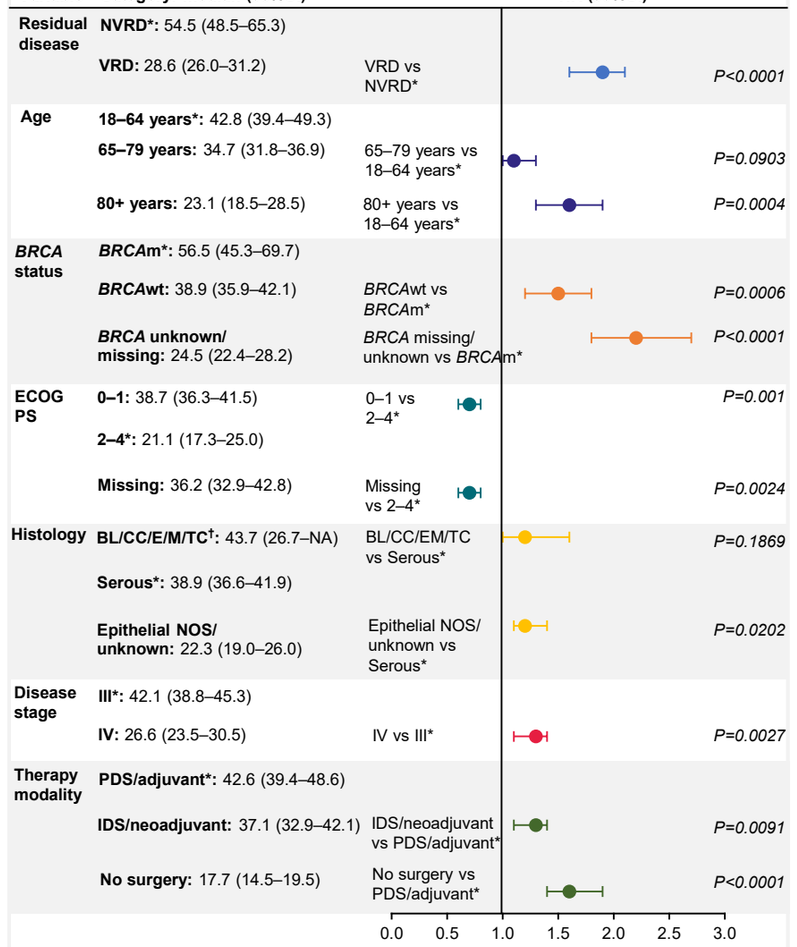
*Reference group; †Represents borderline (BL), clear cell (CC), endometrioid (E), mucinous (M) or transitional cell (TC) histologies. Other covariates input into the stepwise model, which did not remain in the final model were age, body weight, ECOG PS, ethnicity, geographic region, HRd status and laboratories (haemoglobin, neutrophils, platelets).

Figure 2. Predictors of OS in patients with OC

A. NVRD vs VRD



B. Medians and HRs for clinical factors associated with OS (months)



*Reference group; †Represents borderline (BL), clear cell (CC), endometrioid (E), mucinous (M) or transitional cell (TC) histologies. Other covariates input into the stepwise model, which did not remain in the final model were body weight, ethnicity, geographic region, HRd status, practice type, race and laboratories (haemoglobin, neutrophils, platelets).

TTNT outcomes

Patients with VRD showed a statistically significant decrease in TTNT compared with patients with NVRD (**Figure 1A**)

BRCA status, histology, practice type, race, disease stage and therapy modality were also statistically significant predictors (**Figure 1B**)

OS outcomes

Patients with NVRD had an OS that was statistically significantly longer compared to patients with VRD (**Figure 2A**)

Age, *BRCA* status, ECOG PS, histology, disease stage and therapy modality were also statistically significant predictors of OS (**Figure 2B**)

Study Limitations

- HRd could not be assessed as a predictor of TTNT or OS outcomes due to a limited number of patients with an HRd status
- PFS could not be measured directly and was instead measured by proxy using TTNT
- The impact of RD volume on TTNT and OS outcomes could not be assessed because of limited data on disease volume

Conclusions

- In this retrospective database analysis, VRD after surgery was a key predictor of TTNT and mortality in patients with advanced OC
- *BRCA* status, histology, disease stage and therapy modality were also predictors of TTNT and OS in this analysis
- A key strength of this study is that it evaluated real-world data of patients with OC with the majority treated in community oncology centres

Implications for the Field of OC

Factors such as VRD and *BRCA* status are prognostic for worse TTNT and OS in this real-world OC patient population; consideration of these highest risk clinical characteristics in treatment decision-making for 1L OC therapy may impact outcomes

Disclosures

DC declares advisory/consultancy for AstraZeneca, GlaxoSmithKline (GSK), Clovis Oncology; speaker bureaus for AstraZeneca, GSK; and travel/accommodation/expenses from AstraZeneca, GSK. **JP, DG, LK, LS** and **TW** are employees of GSK. **AG-M** declares advisory/consultancy for Amgen, AstraZeneca, Clovis Oncology, Genmab, GSK, ImmunoGen, Merck Sharp & Dohme, Novartis, Oncoinvent, Pfizer/Merck, PharmaMar, Roche, Sotio; speaker bureaus for AstraZeneca, PharmaMar, Roche, GSK; research grants/funding from Roche, GSK; and travel/accommodation/expenses from AstraZeneca, Pharmamar Roche, GSK

Acknowledgements

Editorial assistance was provided by Sarah Hauze and Jo Mehat at Fishawack Indicia Ltd, UK, part of Fishawack Health, and funded by GSK. This study (213807) was funded by GSK.
The authors would like to acknowledge Johanna Bruneau, publications manager, for her contributions to this publication.

Abbreviations

1L/2L, first/second line of therapy; BL/CC/E/TC, borderline, clear cell, endometrioid, mucinous, or transitional cell; *BRCA*, BReast CAncer gene; *BRCA*m/wt, *BRCA* mutant/wild type; CI, confidence interval; CT, chemotherapy; ECOG PS, Eastern Cooperative Oncology Group Performance Status; EHR, electronic health record; HR, hazard ratio; HRd, homologous recombination deficiency; IDS, interval debulking surgery; IQR, interquartile range; KM, Kaplan–Meier; NA, not applicable; NCI, National Cancer Institute; NOS, not otherwise specified; NVRD, no visible residual disease; OC, ovarian cancer; OS, overall survival; PD, disease progression; PDS, primary debulking surgery; PFS, progression-free survival; RD, residual disease; TTNT, time to next treatment; VRD, visible residual disease

References

1. Ovary: Globocan 2018. Lyon, France: International Agency for Research on Cancer, 2018 Available at: https://gco.iarc.fr/today/data/factsheets/cancers/25-Ovary-fact-sheet.pdf [last accessed Nov 2020].
2. González-Martín B, et al. *N Engl J Med* 2019;381:2391–402.
3. Wang Q, et al. *Signal Transduct Target Ther* 2020; 5:137.
4. Makar AP, et al. *Gynecol Oncol* 1995;56:175.
5. Winter WE, et al. *J Clin Oncol* 2007;25:3621.
6. Winter WE, et al. *J Clin Oncol* 2008;26:83.
7. Aletti GD, et al. *Am J Obstet Gynecol* 2007;197:676.
8. Flatiron Health. Quick Facts. Available at: https://flatiron.com/about-us/ [last accessed Nov 2020].

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Presented at European Society of Gynaecological Oncology State of the Art (ESGO-SOA) Conference 2020 (Virtual Meeting); 14–16 December 2020.