Impact of Residual Disease on Outcomes in Patients With Ovarian Cancer: A Meta-Analysis

Dana Chase,[1] Anadi Mahajan,[2] David Alexander Scott,[2] Neil Hawkins,[2] Tatia Woodward,[3],* Linda Kalilani[4]

[1]Arizona Oncology (US Oncology Network), University of Arizona College of Medicine, Phoenix, AZ, USA; [2]Bridge Medical, London, UK; [3]GlaxoSmithKline, Philadelphia, PA, USA; [4]GlaxoSmithKline, Durham, NC, USA
*Employed by GlaxoSmithKline when the research was conducted

Background

- OC is the fifth leading cause of cancer death among women in the USA.[1]
- Most cases of OC are diagnosed at an advanced stage where prognosis is poor, and >50% of patients with advanced disease die within 5 years of diagnosis.[2]
- Currently, the main treatment options for OC are a) PDS + adjuvant platinum-based chemotherapy, and b) NACT + IDS + postoperative chemotherapy.[3]
- RD after debulking surgery for advanced-stage OC is based on the diameter of the residual tumour (defined as no RD [0 cm], optimal cytoreduction RD [≤1 cm] or suboptimal cytoreduction RD [>1 cm]) and is one of the important prognostic factors for disease progression.[4]
- This systematic literature review and meta-analysis assesses the impact of RD status on PFS and OS in adults with OC who had undergone PDS or IDS.

Methods

Table 1. Data sources

	Structured search	Supplementary search
Databases	MEDLINE®, Embase® and Cochrane Central databases	Gray literature, bibliographic searches and conference proceedings (2019–2020)
Search timeframe	1 January 2011–7 July 2020	14–20 August 2020
Eligible articles	**Clinical trials** (RCTs, non-RCTs, single-arm trials) or **observational studies** (prospective/retrospective cohort, case-control and cross-sectional)	

- The PICOS framework was used to identify relevant publications; eligibility criteria included:

  Population: Adults (≥18 years) with OC

  Country: US, EU, China, Japan

  Intervention: Evaluating patient outcomes after PDS or IDS

- Data were extracted by one reviewer and independently checked by another. Discrepancies were resolved by a third reviewer.
- Study quality was assessed against the National Institute of Clinical Excellence checklist, Agency for Healthcare Research and Quality checklist, or the Newcastle-Ottawa Scale, depending on study design.
- Both fixed and random effects meta-analysis were conducted to compare progression and survival been RD levels across studies. Random effects model was preferred when I^2 was ≥50%.
- The PFS and OS definitions were based on individual study definitions and varied across studies.

Results

50 primary studies were included (Figure 1):

- 43 observational studies (41 retrospective and 2 prospective); 4 retrospective analyses of randomised controlled trials (RCT) and 3 RCTs.

Figure 1. PRISMA flow chart of included studies

Table 2. Baseline characteristics across studies
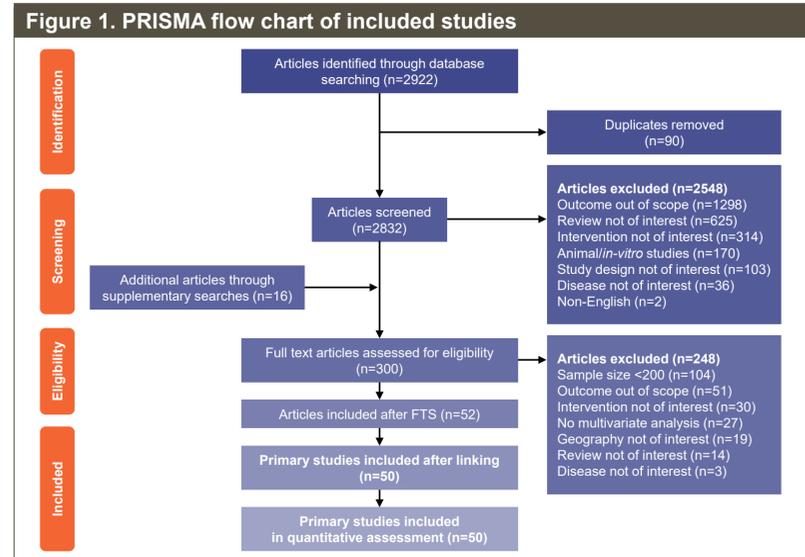
| Characteristics	Total
Sample size, range (no. of patients)	203–8652
Median age, range (years)	46–75
Type of surgery, no. of studies (%)*	
PDS only	15 (30)
Tumour histology, no. of studies (%)*	
Epithelial OC	24 (48)
Ovarian FIGO stage, no. of studies*	
Mixed, stage I–IV	45
Stage III	3
Stage IV	2

*Of the 50 included studies.

Study outcomes

- Median PFS ranged between 9 months and 50.2 months, and median OS ranged between 6 months and 110 months (**Figure 2**).

Figure 2. Median PFS (A) and OS (B) by RD status
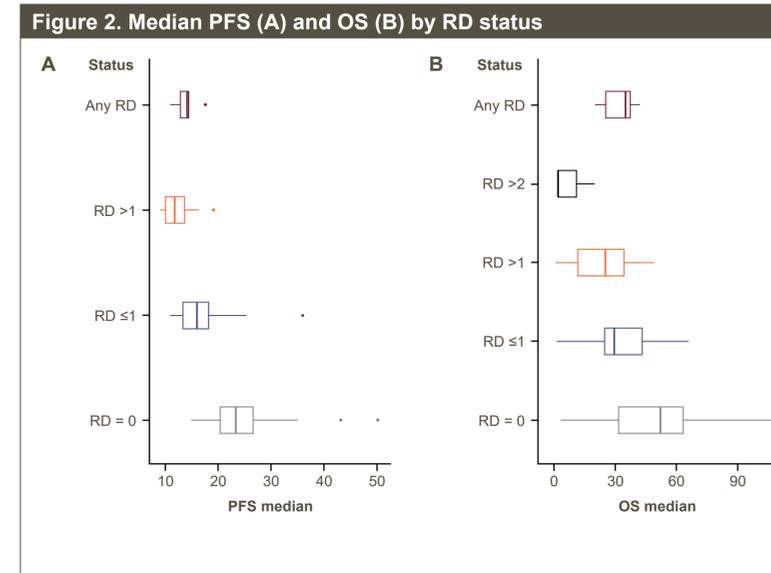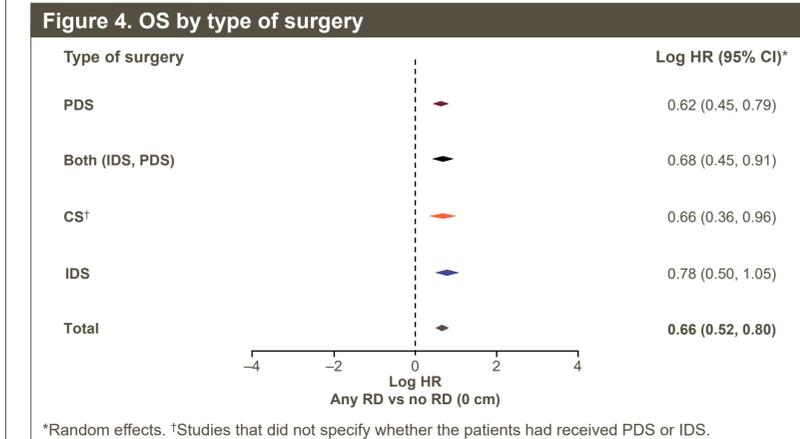

Overall PFS and OS as per RD status

- Lower levels of RD were associated with statistically significantly improved PFS compared with higher levels of RD (**Figure 3A**). Similarly, lower levels of RD were associated with improved OS compared with higher levels of RD (**Figure 3B**).

Figure 3. PFS (A) and OS (B) as per RD status
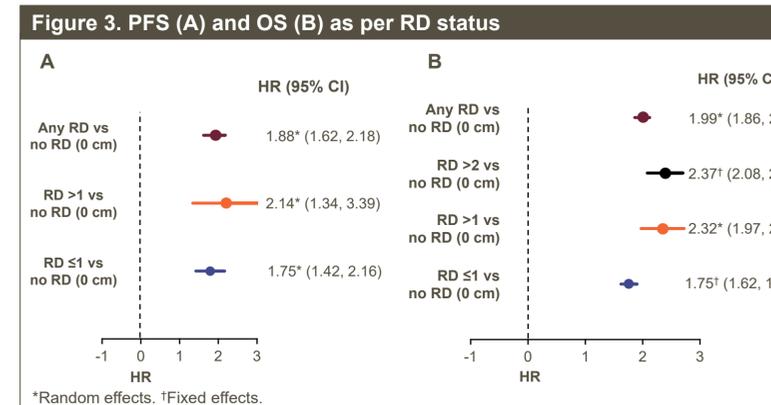
*Random effects. †Fixed effects.

OS by type of surgery

- The results were stratified by type of surgery as indicated in **Figure 4**.

Figure 4. OS by type of surgery

Type of surgery	Log HR (95% CI)*
PDS	0.62 (0.45, 0.79)
Both (IDS, PDS)	0.68 (0.45, 0.91)
CS†	0.66 (0.36, 0.96)
IDS	0.78 (0.50, 1.05)
Total	0.66 (0.52, 0.80)

*Random effects. †Studies that did not specify whether the patients had received PDS or IDS.

Conclusions

- The results of this meta-analysis affirm prior studies[5,6] and further quantify the impact of RD status following PDS or IDS in first-line OC.
- RD was highly predictive of PFS and OS, with improved PFS and OS associated with lower RD status. RD is one of the key factors impacting disease progression.
- RD status could be included in categories such as low- versus high-risk disease and may be associated with tumour biology or other patient-related factors.

Abbreviations

CI, confidence interval; CS, cytoreductive surgery; Embase, excerpta medica database; EU, European Union; FIGO, international federation of gynecology and obstetrics; FTS, full-text search; HR, hazard ratio; IDS, interval debulking surgery; MEDLINE, medical literature analysis and retrieval system online; MRAW, raw mean difference; NACT, neoadjuvant chemotherapy; OC, ovarian cancer; OS, overall survival; PDS, primary debulking surgery; PFS, progression-free survival; PICOS, population, intervention, comparison, outcomes and study; RCT, randomised clinical trial; RD, residual disease; PRISMA, preferred reporting items for systematic reviews and meta-analyses.

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Acknowledgements

Disclosures

DC reports speakers' bureau fees and/or advisory roles from GlaxoSmithKline, AstraZeneca, Takeda, Clovis, Roche and Merck. **AM, DS** and **NH** have no conflict of interest to disclose. **TW** is a former employee of GSK. **LK** is an employee of GSK.