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Correlation between progression-free survival and overall survival in patients with ovarian cancer after debulking surgery

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BACKGROUND

Ovarian cancer (OC)

- Standard treatment: Debulking surgery with platinum-based chemotherapy.[1]
- 85% of patients who achieve complete remission with 1L therapy experience a recurrence of disease.[2]
- Prognosis is based on clinical and biological factors, including tumour stage/grade at diagnosis, size of the mass, and residual disease after debulking surgery.[3]

Endpoints in clinical trials

- OS is regarded as the gold standard primary endpoint in OC clinical trials but requires large trials with a longer duration to demonstrate a difference between treatments than PFS.[3]
- PFS is commonly used as an endpoint, but in some cancers, it is only weakly associated with OS.[4]
- This systematic literature review evaluated the relationship between PFS and OS in adult patients with OC following primary debulking or interval debulking surgery.

METHODS

- A literature search was conducted using the PICOS framework to identify relevant publications (**Table 1**).
- Data were extracted by one reviewer and independently checked by another. Discrepancies were resolved by a third reviewer.
- Study quality was assessed against the NICE checklist, Agency for Healthcare Research and Quality checklist, or the Newcastle-Ottawa Scale, depending on study design.
- A weighted linear regression analysis was used to evaluate the correlation between PFS and OS in patients with OC.
- The study weights were calculated as 1/(4 x N).[5] Residual disease status was entered as a factor in the linear regression.
- The weighted linear regression was conducted using both the median and the log hazard ratio for PFS to predict the median and log hazard ratio for OS, respectively.

Table 1. Data sources and study criteria

Structured searches	Supplementary searches
MEDLINE®, Embase® and Cochrane Central databases	Grey literature, bibliographic searches, conference proceedings (ASCO, ESMO, SGO; 2019–2020)

Category	Details	
Population	Adults ≥18 years with OC	
Intervention	Studies evaluating patient outcomes following debulking surgery irrespective of the type of chemotherapy used as neoadjuvant and adjuvant treatment The following surgery types were considered: • PDS and neoadjuvant chemotherapy followed by IDS	
Outcomes	OS, PFS	
Study design	Inclusion criteria • Clinical trials • Observational studies	Exclusion criteria • Case series • Case reports
Countries	US, EU, China, Japan	
Sample size	Studies with >200 patients	
Statistical criteria	Studies with results for multivariate analysis	

Structured searches were conducted between 1 January 2011 and 7 July 2020, and supplementary searches were conducted between 14 and 20 August 2020. Diagnosis of OC included ovarian, fallopian tube cancer and primary peritoneal cancer. Only English language studies were included.

CONCLUSIONS

- Among patients with OC who had received 1L treatment (primary debulking or interval debulking surgery) and chemotherapy, there was a direct and positive correlation between PFS and OS.
- This analysis expands on the growing body of evidence showing that OC treatments effective in delaying disease progression can meaningfully extend OS.

REFERENCES

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ABBREVIATIONS

1L, first-line; ASCO, American Society of Clinical Oncology; ESMO, European Society for Medical Oncology; FIGO, International Federation of Gynecology and Obstetrics; HR, hazard ratio; IDS, interval debulking surgery; NICE, National Institute of Clinical Excellence; OC, ovarian cancer; OS, overall survival; PDS, primary debulking surgery; PFS, progression-free survival; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; RCT, randomised controlled trial; RD, residual disease; SGO, Society of Gynecologic Oncology.

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RESULTS

- 50 primary studies were included (**Figure 1**):
  - 43 observational studies (41 retrospective and 2 prospective); 4 retrospective analyses of RCTs and 3 RCTs.
- Sample sizes ranged between 203 and 8,652 patients.
- The PFS and OS definitions were based on individual study definitions and varied across studies.
- OS was defined as either the time from surgery, diagnosis or study entry to death or last follow-up.
- PFS was defined as either the time from treatment to disease progression or disease recurrence, the time from initial diagnosis to the time of first recurrence, or the date that recurrence was confirmed on tissue biopsy or imaging.

Baseline characteristics across studies

- The median age of patients in the included studies ranged from 46 to 75 years.
- Most studies (n=45) enrolled patients with mixed FIGO stage (stage I–IV).

Study outcomes

- There was a strong positive association between PFS and OS, irrespective of RD status (**Figure 2**).
- There was a positive association between logHRs for OS and PFS (**Figure 3**).

Figure 1. PRISMA flow chart of included studies

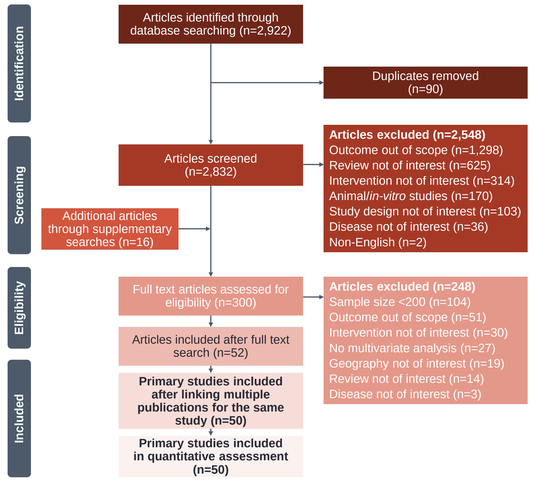
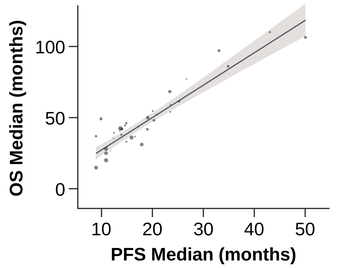


Figure 2. Relationship between median OS and median PFS

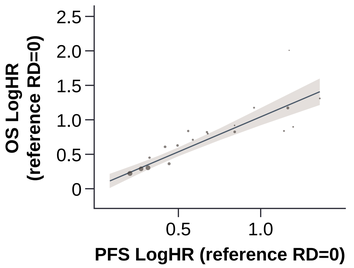


Regression of median OS by PFS

	Coefficients	SE
Intercept	4.49	3.26
Median PFS	2.27	0.17

median OS = 4.49 + [2.27 x median PFS]
adjusted R^2 = 0.84

Figure 3. Relationship between logHR OS and logHR PFS



Regression of logHR OS by logHR PFS irrespective of comparison of RD status

	Coefficients	SE
Intercept (RD <0.5 vs 0)	0.03	0.06
Log PFS HR	1.01	0.10

logHR OS = 0.03 + (1.01 × logHR PFS)
adjusted R^2 = 0.86

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