



Original Research

Informative censoring in maintenance therapy trials for advanced ovarian cancer: An empirical assessment of its impact on treatment benefit

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ABSTRACT

Introduction: A considerable proportion of patients in ovarian cancer maintenance trials may be censored in progression-free survival (PFS) analyses, the primary study endpoint. Such censoring is often informative, reflecting discontinuation due to toxicity, preference, or early switch to alternative therapies, potentially biasing results toward overestimating PFS benefit. We aimed to quantify the impact of informative censoring on PFS in these trials.

Methods: Double-blind, placebo-controlled maintenance therapy trials were selected, and individual patient data reconstructed from published survival curves. A sensitivity analysis reclassified varying proportions of all censored events as progressions to model scenarios from 0 % to 100 % informative censoring. Hazard ratios (HRs) were re-estimated and compared with the originally reported values. Duration of therapy was compared with PFS.

Results: Twenty-two trial units (N = 8256) were included. Nineteen reported statistically significant results, falling to 14 (74 %) at the upper limit of analysis. HRs diminished progressively, with a 6 % reduction at 10 % censoring and 29 % at 100 %. In nine PARP inhibitor trials, treatment duration was shorter than PFS (mean of medians = 12.5 vs 17.6 months). Results were consistent when limited to PARP inhibitor studies. No correlation was observed between adverse events and censoring.

Conclusions: Informative censoring can substantially distort PFS benefit estimates in ovarian cancer maintenance trials. Transparent reporting of censoring rates and their causes is essential for meaningful clinical interpretation and should be standard in all randomised maintenance therapy trials.

1. Introduction

Ovarian cancer is the most lethal gynecologic malignancy for women in high-income countries and the second most lethal worldwide [1]. Standard first-line treatment for newly diagnosed advanced-stage disease typically includes cytoreductive surgery and platinum-based doublet chemotherapy, with or without concomitant bevacizumab [2]. Yet, despite optimal initial management, up to 70 % of women will still experience cancer recurrence [3].

Maintenance therapy is aimed at delaying disease progression and in the first-line setting may offer the potential for long term survival and

possibly cure in a subset of patients with advanced ovarian cancer. While multiple agents have been evaluated as maintenance therapy in randomized controlled trials (RCTs), poly(ADP-ribose) polymerase (PARP) inhibitors have demonstrated the most substantial benefit. In patients with *BRCA* mutations or homologous recombination deficiency (HRD), PARP inhibitors are associated with a 57–70 % reduction in the risk of disease recurrence and a 12–45 % reduction in the risk of death when used in the first-line maintenance setting [4–9].

The clinical benefit of maintenance therapy in advanced ovarian cancer must be weighed against its potential toxicities. This consideration is particularly important as most women are in response at the

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start of maintenance treatment and do not have cancer-related symptoms, although may have residual symptoms related to prior chemotherapy. Extended maintenance therapy can be associated with cumulative toxicity, treatment fatigue, or other factors including financial burden and initiation of non-protocol therapies, any of which can result in premature treatment discontinuation prior to progression or course completion [10–14]. In this context, patients who discontinue treatment for non-progression reasons and subsequently withdraw from protocol-mandated assessments are censored at their last evaluable tumour assessment, highlighting the increased susceptibility of long-duration maintenance trials to adherence-related informative censoring. This form of potentially informative censoring should be distinguished from administrative censoring, which typically occurs at data-cut or planned end of follow-up.

Censoring is typically assumed to be non-informative or random, where the risk of progression in censored patients is similar to those who remain on study [10,11]. However, this assumption may not hold in many oncology trials. Even when censoring is applied strictly according to protocol-defined rules, the non-informative censoring assumption may be violated when censoring arises from different mechanisms or prognostic profiles across arms. In such cases, estimates of both within-arm survival and the comparative treatment effect may be distorted [11,15]. This is particularly so when progression-free survival (PFS) is the primary endpoint [13,16]. Informative censoring can bias PFS estimates in either direction, with the magnitude and direction determined by the clinical context and the reasons for disengagement.

Informative censoring is especially relevant in maintenance therapy RCTs for advanced ovarian cancer, where treatment discontinuation may occur for multiple reasons unrelated to radiographic progression or death, the defining events for PFS. In such studies, a considerable proportion of patients may be censored at the time of the primary PFS analysis [17]. Given that multiple agents have been approved based on PFS benefits observed in randomized clinical trials, the potential for informative censoring biasing the results is considerable and this risk should be made transparent in the primary publication of trials [18–20]. While estimand frameworks such as the International Council for the Harmonization of Technical Requirements for Pharmaceutical for Human Use (ICH) E9(R1) from the European Medicines Agency (EMA) exist to guide the management of intercurrent events in clinical trials, they do not provide methods to detect, measure or estimate the magnitude of informative censoring [21]. Few studies have attempted to systematically quantify the potential impact of informative censoring on trial outcomes and among maintenance therapy trials in ovarian cancer - including trials of PARP inhibition - explicit reporting of informative censoring or the conduct of formal sensitivity analyses remains uncommon [10,22]. Beyond theoretical discussions of biases associated with informative censoring, most prior investigations have either focused on real-world data or involved limited analyses of clinical trials, which are often confounded by heterogeneous treatment regimens and tumor types [10,16,23–25].

The objective of this study was to evaluate whether informative censoring is plausible and potentially consequential in double-blind, placebo-controlled maintenance therapy RCTs for advanced ovarian cancer, using information available from published trial reports. We selected these double-blinded trials to minimize bias introduced by patient or clinician behaviour in the context of unblinded treatment allocation, to reduce the influence of nocebo-related discontinuation, and to enable a clearer, more balanced assessment of the impact of censoring on both investigational and control arms. We quantified the impact of varying degrees of informative censoring on the relative treatment effect estimated from PFS. We further explored the extent to which treatment-related adverse events (AEs) may contribute to informative censoring. Overall, our aim was to highlight the risk of informative censoring, which can bias estimates of treatment benefit, and to emphasize its consideration in the design, analysis, and reporting of future ovarian cancer maintenance trials.

2. Methods

2.1. Trial identification and data reconstruction

We conducted a systematic search of the MEDLINE, PubMed, and EMBASE databases to identify RCTs of maintenance therapy versus placebo in advanced ovarian cancer for the period between March 2010 and March 2025. Search terms included cancer descriptors (“ovarian cancer”, “epithelial ovarian cancer”), treatment terms (“maintenance treatment”, “placebo control”) and trial descriptors (“randomized control* trial”, “phase 2”, “phase 3”, “blinded”). Eligible RCTs were required to be double-blind superiority studies, with PFS as the primary endpoint. Additionally, trial publications must include high-quality Kaplan–Meier survival curves accompanied by tables of number of patients at risk at different timepoints.

We recorded key trial characteristics, including the study name, design, therapeutic class, discontinuation rates and hazard ratios (HR) for PFS. Kaplan–Meier survival curves were digitized using DigitizeIt software to reconstruct individual patient data (IPD), following the method described by Guyot et al [26].

2.2. Quantification of informative censoring on treatment-effect estimates

To assess whether informative censoring has a plausible and potentially consequential impact of informative censoring on PFS, we employed multiple complementary approaches, selected for their conceptual linkage to censoring mechanisms in maintenance therapy RCTs. Primarily, as an estimand-aligned sensitivity analysis to assess the robustness of treatment-effect estimates under departures from the non-informative censoring assumption, we conducted a case analysis of 10 % informative censoring. In this approach, 10 % of all censored events in each treatment arm were reclassified as progression events, and the hazard ratio (HR) with its 95 % confidence interval (CI) was re-estimated. The analysis was conducted separately for the investigational and placebo arms to assess the differential impact of informative censoring on the relative treatment effect. The modified HR was then compared to the originally published treatment effect and the difference between the logarithmic values of treatment effects were calculated. The procedure was repeated by varying the informative censoring proportion in 10 % increments from 0 % (no informative censoring) to 100 % (upper limit), to span plausible to extreme scenarios and quantify the sensitivity of estimated treatment effects to informative censoring.

For each level, censored cases were randomly selected and re-assigned as progression events, with 1000 replications performed to account for sampling variability. We then summarized results across replications by reporting the percentage change in the estimated treatment effect, either a reduction or improvement, by taking the exponential of the median log-HR difference across replications. Furthermore, for each trial and each percentage-change level, we performed log-rank testing to obtain p-values for the treatment comparison, which were then summarised across trials using the median and inter-quartile range. These data were plotted against the proportion of censored events reclassified as progression, providing a graphical representation of the sensitivity of the estimated treatment effect to varying degrees of informative censoring.

2.3. Subgroup and temporal sensitivity analyses

Among the included studies, PARP inhibitor trials represented the largest and most consistently designed studies. This treatment is also widely used in contemporary clinical practice. We therefore undertook a dedicated PARP inhibitor subgroup analysis. Additionally, we performed a sensitivity analysis in which censored events were reclassified as progression events but limited to those occurring within the first 90- and 180-days following randomization, respectively. This approach aimed to assess the potential influence of early informative censoring on

the estimated treatment effect.

2.4. Identification of trial-related features suggestive of informative censoring

To complement our primary analyses, we additionally examined the relationship between treatment duration and PFS, as well as the associations between changes in estimated treatment effects under informative censoring assumptions and rates of treatment discontinuation, dose reduction, and grade 3–5 adverse events. To identify patterns suggestive of patients discontinuing therapy well before radiographic progression, we compared treatment duration with PFS. Such discrepancies - particularly in maintenance settings where tolerability-related discontinuation is common and follow-up may lapse - can signal an increased potential for informative censoring. Summary data on median duration of therapy were extracted and correlated with published median PFS values.

Given the potential association between cumulative toxicity and treatment discontinuation, we examined correlations between the percentage change in treatment effect, based on upper bound of 100 % informative censoring, and rates of treatment discontinuation, dose reduction, and grade 3–5 AEs. Pearson correlation coefficients (r) were calculated to quantify the strength of these associations. Additionally, we repeated the analyses across a range of censoring-to-progression conversion rates to evaluate the consistency of these correlations across different percentage change in treatment effect and AE measures. The same analysis was also performed for the placebo control arm.

All analyses were performed in R version 4.3.3.

3. Results

A total of 20 eligible RCTs were identified (Figure S1). The key characteristics of these trials are summarized in Table 1. Thirteen RCTs (65 %) assessed PARP inhibitors, while the remaining RCTs investigated other therapeutic agents. Two RCTs (10 %) assessed and reported endpoints in BRCA wild type and mutation positive subgroups as the primary outcome and were therefore treated as separate trial units in our analysis. In total, 22 trial units were analyzed. Median follow-up across these trial units was 18.2 months (range 4.1–41.0), with PFS censoring rates ranging from 8.0 % to 58.4 %.

3.1. Quantification of informative censoring on treatment-effect estimates

In 19 trial units, PFS comparisons between the maintenance agent and blinded placebo met the nominal threshold for statistical significance ($P < .05$). At the upper limit of analysis, where all censored observations in the investigational arm were reclassified as progression events, 14 trial units (74 %) continued to meet this threshold. Across the range of informative censoring, the treatment effect favoring the investigational agent progressively diminished. A 10 % rate of informative censoring resulted in a median 6 % reduction in estimated treatment benefit, increasing to a 29 % reduction at a 100 % rate of informative censoring (Fig. 1A). Fig. 1B presents the variation in P values of the difference in the relative treatment effect across a range of informative censoring rates. A 10 % rate of informative censoring resulted in a median P value of $< .001$ (IQR 0.00–0.09), with a median P value of .03 (IQR 0.001–0.25) at 100 % censoring.

Applying the same analysis to the placebo arm resulted in one additional trial unit meeting the nominal significance threshold at the upper limit, increasing from 19 units at baseline to 20 units. Across varying informative censoring rates, the relative treatment effect remained largely stable, with only a minor increase in favor of the investigational agent (0.3 % at a 10 % censoring rate to 11 % at 100 %) (Fig. 1C).

Table 1
Characteristics of included trials.

Characteristic	Subgroup	Number (%)
Total†		20 (100)
Phase	II	5 (25)
	III	15 (75)
Agent	PARP inhibitor	13 (65)
	Tyrosine kinase inhibitor	3 (15)
	Other	4 (20)
Line of maintenance treatment	First	9 (45)
	Recurrent	11 (55)
Outcome	Positive	16 (80)
	Negative	4 (20)
Discontinuation rate in investigational arm	0–10 %	7 (35)
	11–20 %	9 (45)
	> 20 %	4 (20)
Discontinuation in the control arm	0–10 %	18 (90)
	11–20 %	2 (10)
	> 20 %	0 (0)
Dose reduction rates in the investigational arm	0–20 %	3 (13.6)
	21–40 %	7 (31.8)
	> 40 %	9 (40.9)
	Unknown	3 (13.6)
Dose reduction rates in the control arm	0–20 %	17 (77.3)
	21–40 %	1 (4.5)
	> 40 %	3 (13.6)
Grade 3–5 adverse events	Unknown	3 (13.6)
	Investigational (median [range])	48.5 [3.4–88]
	Control (median [range])	18.5 [0–77]

Table 1 Summarized characteristics of included trials in our analysis. † Twenty trials were included overall. Two trials reported outcomes separately by BRCA positive/negative status and were considered as separate analysis units, comprising 22 total analysis units. PARP = poly(ADP-ribose) polymerase. Positive or negative outcome according to reported 95 % confidence intervals and p -value < 0.05 .

3.2. Subgroup and temporal sensitivity analyses

Among the 15 trial units evaluating maintenance PARP inhibitors versus placebo, 10 (67 %) retained nominal statistical significance at the upper limit (Fig. 2). Across the full spectrum of informative censoring rates applied to both arms, the relative treatment effect remained consistent with the overall analysis. In the investigational arm, a 10 % informative censoring rate was associated with a median 7 % reduction in estimated treatment benefit, increasing to 31 % at a 100 % informative censoring rate.

At the upper limit of analysis, 17 (89 %) of the 19 trial units in the investigational arm retained nominal statistical significance at 90 days, and 16 (84 %) at 180 days. In the placebo arm, the treatment effect remained robust, with 17 (90 %) and 18 (95 %) trial units meeting the threshold at 90 and 180 days, respectively. We assessed the proportional hazards assumption for these HR-based sensitivity analyses using Schoenfeld residuals and found no evidence of violation. Consistent with the untimed analysis, the estimated treatment effect favoring the investigational agent progressively diminished across increasing informative censoring rates. Earlier timing of informative censoring was associated with a smaller impact on treatment effect, with median reductions in estimated benefit ranging from 3 % at 10 % conversion to 7 % at 100 % informative censoring at 90 days, and from 3 % to 10 % at 180 days (Fig. 3).

3.3. Identification of trial-related features suggestive of informative censoring

Data on treatment duration were available for nine trial units (41 %),

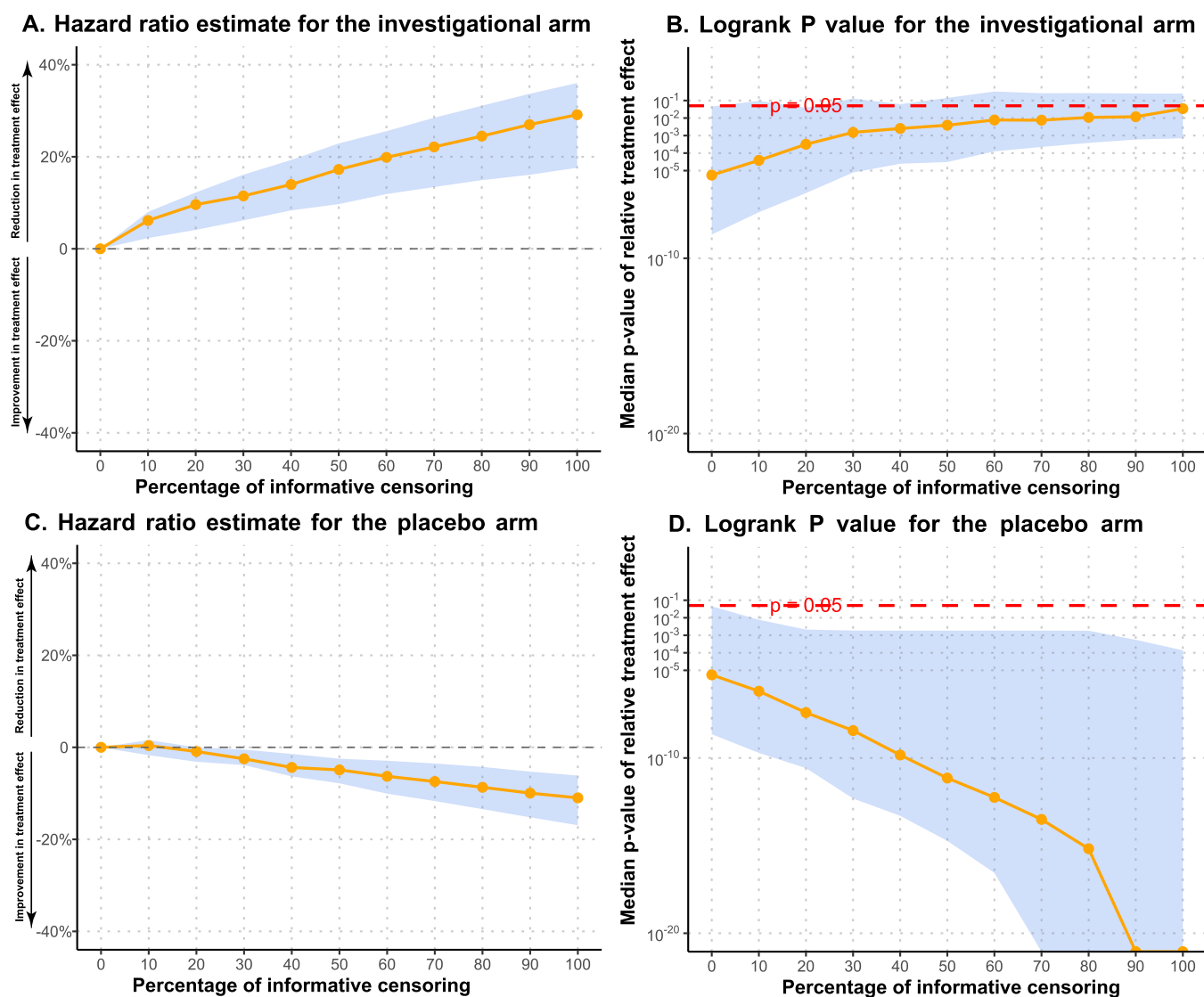


Fig. 1. Relative difference in HR and median p-value when proportion of informative censoring varied from 0% to 100% in the investigational arm (A,B) and placebo arm (C,D).

all evaluating PARP inhibitors. In the placebo arm, the mean of the median treatment duration was 7.7 months (IQR 5.5–10.2). The mean of the median PFS was 8.1 months (IQR 5.1–10.9). Median treatment duration correlated strongly with median PFS ($r=0.91$). In contrast, in the investigational arm, there was only moderate correlation between median treatment duration and median PFS ($r=0.65$). The mean of the median treatment duration was 12.5 months (IQR 7.8–18.7). The mean of the median PFS was 17.6 months (IQR 12.9–21.9) (Fig. 4).

Information on dose discontinuation was available for all trial units. In the investigational arm, a median of 12% of patients (range 2–39%) discontinued treatment for reasons other than disease progression, compared to 2% (range 0–18%) in the placebo arm. Data on dose reductions and grade 3–5 AEs were available for 19 (86%) and 18 (82%) trial units, respectively. The median rate of dose reductions was 28% (range 12–71%) in the investigational arm and 6% (range 0–63%) in the placebo arm. Grade 3–5 AEs occurred in a median of 49% of patients (range 3–88%) in the investigational arm, versus 19% (range 0–77%) in the placebo arm.

Correlation analyses between AE metrics (including grade 3–5 AEs, dose reductions and treatment discontinuation) and changes in treatment effect at the upper limit yielded variable results. A modest

correlation ($r = 0.60$) was observed between grade 3–5 AE incidence and change in treatment effect in the investigational arm, though this weakened ($r = 0.41$) after excluding three outlier trial units ([27–29]). There were poor associations between change in treatment effect with dose reductions ($r = 0.34$) and treatment discontinuation ($r = 0.01$) (Fig. 5). Similar patterns were observed across varying rates of informative censoring, with reduced informative censoring percentages associated with attenuated correlations (data not shown). In the placebo arm, correlations between AE metrics and treatment effect changes were generally weak. Findings were consistent in the subset of trials evaluating maintenance PARP inhibitors (Figure S2).

4. Discussion

Our analysis highlights the role of informative censoring as a source of bias in maintenance therapy trials for advanced ovarian cancer, where early treatment discontinuation may result from cumulative toxicity, patient preference, or physician judgment. At the upper limit of analysis, reclassifying all censored events as progressions reduced the relative PFS treatment effect by almost 30% and led to loss of nominal significance in over 20% of trials. While this upper-bound estimate

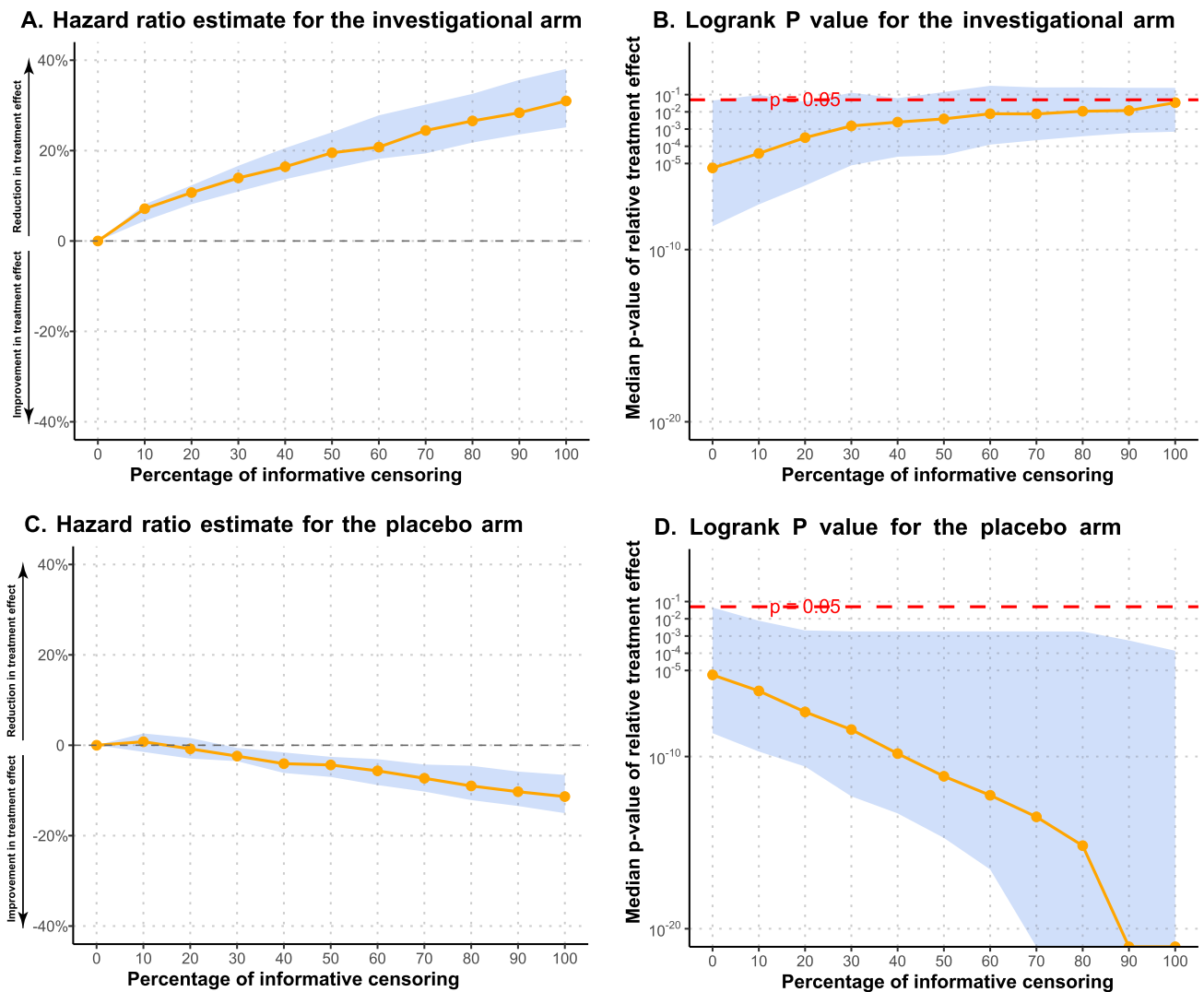


Fig. 2. Magnitude of difference of HR and median p-value change over levels of censoring from 0 % to 100 % for the investigational arm (A,B) and placebo arm (C,D) for trials of PARP inhibition versus placebo.

aligns with prior methodological work using worst-case assumptions when detailed patient-level data and censoring reasons are unavailable, we additionally evaluated a range of more modest and clinically plausible scenarios [13,25]. Even a limited reclassification of 10 % produced a 6 % decline and a reclassification of 20 % of censored cases produced a 10 % reduction in benefit, reflecting a graded decline in relative treatment effect with increasing levels of informative censoring in the investigational arm. As many historical and emerging strategies - including antibody-drug conjugates - share toxicity profiles that may lead to early discontinuation and censoring, the broader maintenance-therapy cohort remains relevant for evaluating mechanisms of informative censoring. Nevertheless, we also examined a subgroup restricted to PARP-inhibitor trials, a contemporaneous therapy in advanced ovarian cancer, and observed similar patterns. Importantly, reclassifying censoring times as progression events had minimal impact on PFS estimates in the placebo arm, an effect that is most plausibly explained by the lower absolute number of censoring events in placebo groups rather than by any arm-specific differences in the mechanism of informative censoring.

Our work is novel, representing the first analysis of its kind in maintenance therapy trials for ovarian cancer. Our analytical approaches are aligned with estimand frameworks that guide the interpretation of outcome data in the presence of intercurrent events [21].

However, our methods extend beyond these frameworks by explicitly quantifying the potential impact of informative censoring on estimated treatment effects under a range of clinically plausible and extreme assumptions, rather than relying solely on estimand specification. Together, these findings highlight the importance of interpreting PFS outcomes within the specific context of maintenance therapy, where patient adherence is critical and continued follow-up until disease progression is required to preserve the validity of treatment effect estimates.

Non-informative or random censoring is a standard assumption of the analysis of time-to-event endpoints such as PFS and OS, requiring that the reasons for censoring are unrelated to the endpoint. Informative censoring occurs when this assumption is violated, such as where the censored patients differ systematically in prognosis from those remaining under observation. This may occur either within or between treatment arms, e.g. systematically removing sicker patients and thereby biasing treatment comparisons. While censoring is often unavoidable, trials should, at a minimum, transparently report the reasons for censoring - particularly those related to treatment discontinuation due to AEs. For example, the PRIMA trial reported a median PFS of 21.9 months with 12 % of patients discontinuing maintenance niraparib due to AEs [30]. In contrast, a large real-world study (N = 560) observed a substantially higher discontinuation rate of 29 % within the first 90 days of treatment initiation, with a median treatment duration of only 7.2

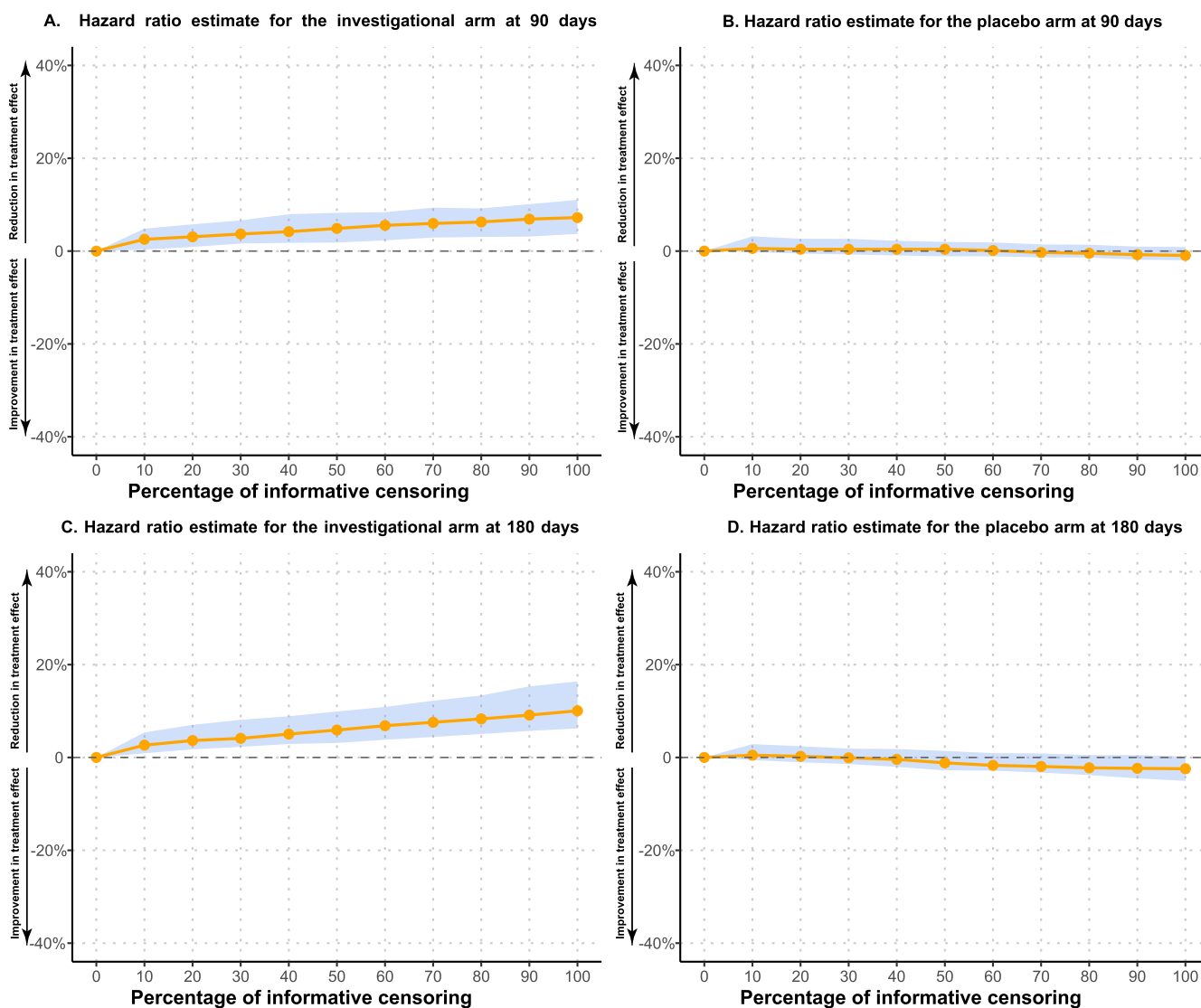


Fig. 3. Magnitude of difference of HR change over levels of censoring from 0 % to 100 % for the investigational arm and placebo arm at 90 days (A,B) and 180 days (C,D).

months [31]. While these differences predominantly reflect the inherent challenges of translating RCT findings into routine practice, substantial informative censoring can additionally distort absolute survival estimates - for example, by inflating PFS if patients with poorer prognosis are preferentially censored. This highlights the importance of transparent reporting of censoring patterns and their causes within RCTs, together with treatment discontinuation data. Ideally this information should be both included in the statistical analysis plan and reported in the primary manuscript.

The most effective strategy to mitigate informative censoring is through robust trial design, particularly in the selection of endpoints [14]. Prioritizing OS over PFS reduces the risk of bias, as deaths, regardless of cause, are events that are less susceptible to informative censoring [11]. However, given the urgency to accelerate drug development for patients with advanced ovarian cancer and limited prognosis, PFS will likely remain the primary endpoint in future maintenance studies. As adherence to protocol-mandated imaging may decline after discontinuation of long-duration maintenance therapy - where patients are generally asymptomatic and discontinuation for tolerability or preference is more common - it is important to continue post-discontinuation tumour assessments wherever feasible.

Complementary endpoints such as time to treatment discontinuation (TTD) and patient-reported outcomes (PROs) help contextualize PFS in this setting by capturing treatment burden, tolerability, and the real-world durability of benefit [11]. In our analysis, while TTD as such was not reported in any of the eligible RCTs, we observed that the mean of the median treatment duration was shorter as compared to mean of the median PFS (12.5 vs 17.6 months) in nine trial units evaluating efficacy of PARP inhibitors. This disparity suggests that early discontinuation may reflect treatment intolerance rather than radiographic progression, raising concerns about potential overestimation of benefit. However, complementary endpoints such as TTD are themselves vulnerable to informative censoring and clinical discretion. Consequently, although TTD may enhance the interpretability of PFS in maintenance settings, its susceptibility to these influences necessitates cautious interpretation.

Our study has several key strengths. We conducted a comprehensive analysis by reconstructing patient-level data from 22 trial units, encompassing over 8000 participants. Using novel and complementary approaches grounded in established methodological principles, we robustly evaluated a range of informative censoring scenarios. All included studies were RCTs with placebo-blinded designs, allowing us to

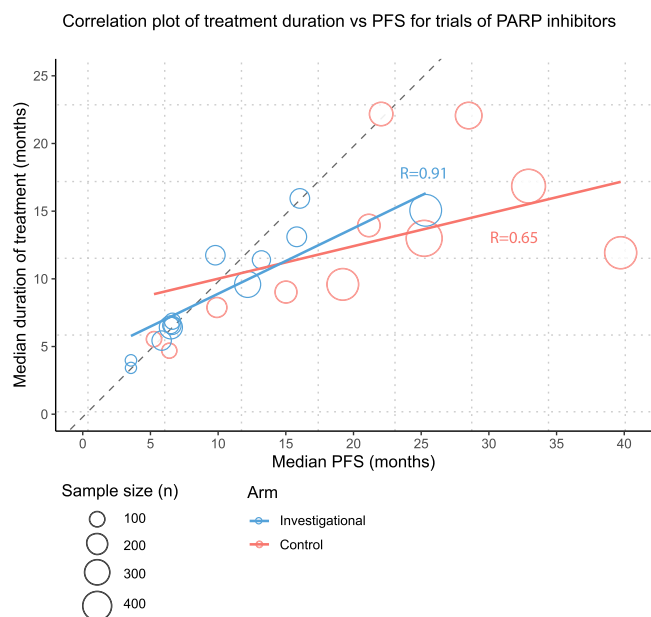


Fig. 4. Linear regression plot of median duration of treatment versus median PFS, weighted by sample size, separated by arm (placebo versus investigational).

mitigate additional sources of bias and separately evaluate the investigational and placebo arms, thereby assessing the differential impact of informative censoring. We examined this effect across a diverse range of therapeutic agents and performed a focused subgroup analysis on trials involving PARP inhibitors - a class of treatments widely used in current clinical practice. Finally, the use of blinded studies mitigates concerns that early placebo discontinuation was driven by access to active treatment.

Our study also has limitations. We did not have access to patient-level data detailing the reasons for censoring at each time point, which constrained our ability to distinguish between toxicological and non-toxicological drivers of treatment discontinuation and limited the possibility of using formal methods to directly adjust for informative censoring. Consistent with ICH E9(R1) guidance, these analyses are intended as conceptual illustrations of how PFS measurement depends on censoring assumptions, rather than as a definitive audit of trial conduct or as an attempt to estimate the relative treatment effect by adding or reassigning events. While a 100 % informative censoring rate might not be clinically plausible, it serves as an upper bound to demonstrate the possible magnitude of bias. Even modest levels of hypothetical informative censoring (10–20 %), whereby censored observations are treated as immediate progression, are likely to overestimate true bias, as this assumption rarely holds in clinical practice. Additionally, our analysis has not shown any definitive correlations between AEs and informative censoring since we were limited by the absence of data on their timing which prevented us from directly linking AE occurrence to censoring events. These gaps highlight the need for access to individual patient data from registration studies to enable more nuanced assessments of censoring-related bias.

The risk of informative censoring in maintenance therapy trials underscores the need for improved study design, transparent reporting, and rigorous analytical approaches. Interpretation of PFS benefit should be cautious and must be supported by OS data, PROs or surrogate endpoints that reflect treatment tolerability and adherence. Regulatory decisions should incorporate sensitivity analyses and statistical adjustments for differential toxicity and dropout. Transparent reporting of censoring rates and causes in treatment arms is essential to ensure meaningful clinical interpretation. This aligns with current guidance, including the Estimands and Sensitivity Analysis framework endorsed by the EMA, which stresses transparent handling of intercurrent events and sensitivity analyses to evaluate assumptions underlying time-to-event outcomes [21]. Finally, further research is needed to evaluate the impact of informative censoring across other tumor types and treatment settings,

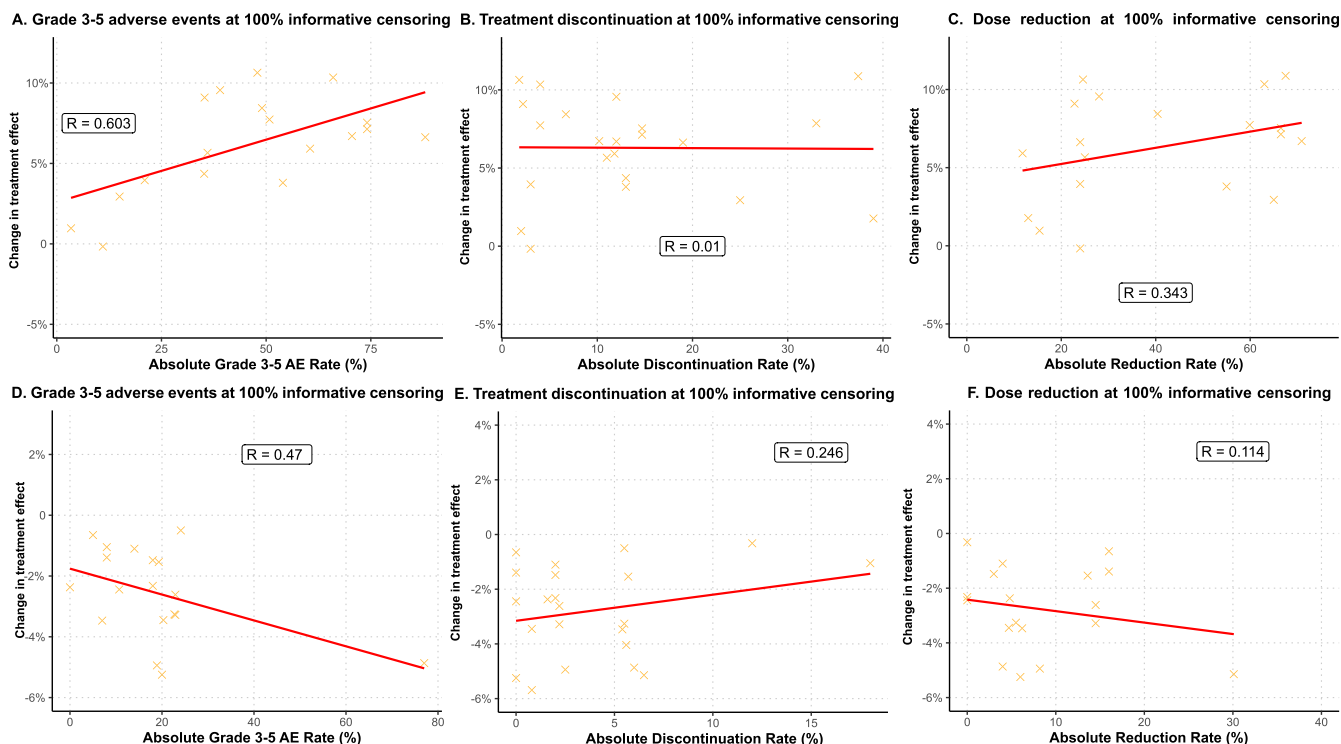


Fig. 5. Correlation plots of linear regression for change in treatment effect and rates of grade 3–5 adverse events, treatment discontinuation and dose reduction in the investigational (A,B,C) and placebo arm (D,E,F).

and to develop or implement advanced statistical strategies such as frailty models and competing risks approaches, that minimize its influence on trial outcomes.

5. Conclusions

Informative censoring, even at low rates, can substantially distort estimates of relative treatment benefit in randomized controlled trials of maintenance therapy. Even a modest reclassification of 20 % of censored cases produced a 10 % reduction in benefit, reflecting a graded decline in relative treatment effect. To ensure accurate interpretation of trial outcomes, strategies to address informative censoring should be integrated prospectively into trial design and endpoint selection. Transparent reporting of censoring rates and their underlying causes in treatment arms is essential to enable meaningful evaluation of relative PFS benefit.

CRedit authorship contribution statement

Chee Khoon Lee: Writing – review & editing, Writing – original draft, Visualization, Supervision, Resources, Methodology, Conceptualization. **Michael Friedlander:** Writing – review & editing, Visualization, Methodology. **Ian C. Marschner:** Writing – review & editing, Visualization, Resources, Methodology, Formal analysis, Conceptualization. **Annelise Decaria:** Formal analysis, Data curation. **John Simes:** Writing – review & editing, Visualization, Conceptualization. **Rachel Woodford:** Writing – review & editing, Writing – original draft, Investigation, Formal analysis, Data curation. **Sally Lord:** Writing – review & editing, Writing – original draft, Supervision.

Declaration of Generative AI and AI-assisted technologies in the writing process

During the preparation of this work the authors used Microsoft Copilot for the purpose of medical editing. After using this tool, the authors reviewed and edited the content as needed and take full responsibility for the content of the publication.

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Declaration of Competing Interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Chee Khoon Lee reports a relationship with AstraZeneca Pharmaceuticals LP that includes: consulting or advisory, funding grants, and travel reimbursement. Chee Khoon Lee reports a relationship with Pfizer that includes: consulting or advisory and travel reimbursement. Chee Khoon Lee reports a relationship with Amgen Inc that includes: consulting or advisory, funding grants, and travel reimbursement. Chee Khoon Lee reports a relationship with Takeda Oncology that includes: consulting or advisory and travel reimbursement. Chee Khoon Lee reports a relationship with Roche that includes: funding grants and travel reimbursement. Chee Khoon Lee reports a relationship with Merck Sharp & Dohme (Australia) Pty Limited that includes: travel reimbursement. Chee Khoon Lee reports a relationship with GlaxoSmithKline LLC that includes: travel reimbursement. Chee Khoon Lee reports a relationship with Novartis that includes: consulting or advisory and travel reimbursement. Chee Khoon Lee reports a relationship with Merck KGaA that includes: consulting or advisory, funding grants, and travel reimbursement. Chee Khoon Lee reports a relationship with Janssen Pharmaceuticals Inc that includes: travel reimbursement. Chee Khoon Lee reports a relationship with Merck & Co Inc that includes: consulting or advisory. Michael Friedlander reports a relationship with AstraZeneca

Pharmaceuticals LP that includes: consulting or advisory, funding grants, speaking and lecture fees, and travel reimbursement. Michael Friedlander reports a relationship with Merck Sharp & Dohme (Australia) Pty Limited that includes: consulting or advisory and travel reimbursement. Michael Friedlander reports a relationship with Novartis that includes: consulting or advisory, funding grants, and travel reimbursement. Michael Friedlander reports a relationship with GSK that includes: consulting or advisory, speaking and lecture fees, and travel reimbursement. Michael Friedlander reports a relationship with AbbVie Inc that includes: consulting or advisory, speaking and lecture fees, and travel reimbursement. Michael Friedlander reports a relationship with Eisai Inc that includes: consulting or advisory. Michael Friedlander reports a relationship with Incyclix that includes: consulting or advisory. Michael Friedlander reports a relationship with Gilead Sciences Inc that includes: consulting or advisory. Michael Friedlander reports a relationship with BeiGene that includes: funding grants. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at [doi:10.1016/j.ejca.2026.116231](https://doi.org/10.1016/j.ejca.2026.116231).

Data availability

All data used is present in the public domain.

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