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Review Article

Safety and Efficacy of Atezolizumab in Ovarian Cancer

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Abstract

Introduction

Although the efficacy of PD-L1 blockade has been evaluated in analyses that combine pharmacologically distinct antibodies, the specific efficacy and safety of atezolizumab remain unclear. This review aimed to evaluate the efficacy and safety profile of atezolizumab specifically.

Methods

PubMed/MEDLINE and CENTRAL were searched (June 2026) for phase I to III trials of atezolizumab in ovarian cancer, reported in full-text English with at least 10 evaluable patients. Randomized and single-arm designs qualified. Randomized comparisons were pooled under random-effects models with Knapp-Hartung adjustment as hazard ratios for survival and risk ratios for response and safety; single-arm rates were pooled as proportions using generalized linear mixed models. Heterogeneity was assessed with I^2, Cochran Q, and prediction intervals, with leave-one-out sensitivity analysis. Analyses used R 4.6.0.

Results

Twelve studies (13 reports) enrolled 3,179 patients. Atezolizumab reduced the hazard of progression (HR 0.88, 95% CI 0.83 to 0.93) and death (HR 0.86, 95% CI 0.78 to 0.96), without heterogeneity ($I^2 = 0\%$), whereas objective response was unchanged (RR 0.88, 95% CI 0.52 to 1.49). Excess toxicity was immune-mediated, raising serious adverse events (RR 1.32, 95% CI 1.05 to 1.67), any-grade immune-related events (RR 1.57, 95% CI 1.12 to 2.20), and grade ≥3 immune-related events (RR 2.23, 95% CI 1.05 to 4.74).

Conclusion

Atezolizumab adds a small survival benefit to a chemotherapy or bevacizumab backbone, driven by delayed progression rather than tumor regression. Offset by doubled immune toxicity and inseparable from its backbone, the effect may not justify routine use.

1. Introduction

Ovarian cancer (OC) is the most lethal gynecologic malignancy, marked by late-stage presentation and a high propensity for recurrence [1]. An estimated 313,959 new cases and 207,252 deaths occurred worldwide in 2020 [2], and 5-year survival for advanced disease remains near 17% [3]. Ovarian carcinoma comprises five histological subtypes, of which high-grade serous carcinoma predominates at 70%, followed by endometrioid and clear cell carcinoma at 10% each; most tumors are high-grade lesions that behave aggressively and present at an advanced stage [4].

Programmed cell death protein 1 (PD-1) is a key immune checkpoint receptor that regulates the immune response and maintains self-tolerance, and cancer cells co-opt this pathway to escape immune surveillance [5]. On activated T cells, PD-1 engages the ligands PD-L1 (programmed death-ligand 1) and PD-L2 (programmed death-ligand 2); tumors upregulate PD-L1 to suppress T-cell function and avoid destruction [6]. In OC, PD-L1 is expressed on tumor cells and tumor-infiltrating lymphocytes in more than half of patients, and higher CD8-positive lymphocyte density correlates with longer overall survival, providing a mechanistic rationale for blockade of this axis [3]. Atezolizumab, also designated MPDL3280A, is a monoclonal immunoglobulin G antibody that binds and inhibits PD-L1 [7]. Blockade of PD-L1 operates within a broader landscape of immunotherapeutic and molecularly targeted strategies, which includes T-cell-engaging agents and tyrosine kinase inhibitors [8,9].

Evidence for PD-1/PD-L1 blockade in OC derives largely from studies that combine antibodies with distinct molecular targets and pharmacologic profiles [10]. Atezolizumab enters such pooled estimates through only a limited number of studies [2], and its efficacy and safety in this setting remain poorly characterized relative to agents examined on their own [11]. This systematic review and meta-analysis study addresses that gap by focusing on the safety and efficacy of the addition of atezolizumab to standard therapy.

2. Methods

2.1 Study design

This systematic review and meta-analysis evaluated the safety and efficacy of atezolizumab in OC. The review was designed, conducted, and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement.

2.2 Data sources and search strategy

PubMed/MEDLINE and the Cochrane Central Register of Controlled Trials (CENTRAL) were searched to identify studies evaluating atezolizumab in ovarian cancer. PubMed was searched on June 28, 2026, using the following string: ("Ovarian Neoplasms"[MeSH] OR "ovarian cancer"[tiab] OR "ovarian carcinoma"[tiab] OR "ovarian tumor"[tiab] OR "ovarian tumour"[tiab] OR "ovarian malignancy"[tiab] OR "epithelial ovarian"[tiab] OR "EOC"[tiab] OR "high-grade serous"[tiab] OR "HGSOC"[tiab] OR "primary peritoneal carcinoma"[tiab] OR "fallopian tube neoplasm"[tiab]) AND ("Atezolizumab"[MeSH] OR "atezolizumab"[tiab] OR "MPDL3280A"[tiab] OR "Tecentriq"[tiab] OR "anti-PD-L1"[tiab] OR "PD-L1 inhibitor"[tiab] OR "PD-L1 blockade"[tiab] OR "PD-L1 antibody"[tiab] OR "CD274"[tiab] OR "B7-H1"[tiab] OR "immune checkpoint inhibitor"[tiab] OR "Immune Checkpoint Inhibitors"[MeSH]). The CENTRAL search was conducted on June 29, 2026, restricted to title and abstract: (atezolizumab) AND ("ovarian cancer" OR ovary OR ovaries). No date, language, publication type, or other limits were applied to either search.

2.3 Eligibility criteria

Eligibility followed a pre-specified PICOS (Population, Intervention, Comparator, Outcomes, Study design) framework, with inclusion and exclusion criteria specified for each element.

Population. Eligible studies enrolled patients with OC of any histological subtype (epithelial, high-grade serous, clear cell, endometrioid, primary peritoneal, or fallopian tube carcinoma), with no restriction on age, performance status, BRCA (breast cancer susceptibility gene) status, or line of therapy. Studies were excluded when OC patients could not be separated from a mixed-tumor population, when fewer than 10 evaluable OC patients were reported, or when populations overlapped, in which case the most complete report was retained.

Intervention. The intervention was atezolizumab-based therapy at any dose or route, given as monotherapy or in combination with any other agent. Studies without an atezolizumab-containing arm extractable separately were excluded.

Comparator. Any comparator was eligible, whether placebo, standard of care, or an active agent, as were single-arm studies with no comparator.

Outcomes. Eligible studies reported at least one efficacy outcome (progression-free survival (PFS), overall survival (OS), or objective response rate (ORR)) or one safety outcome (adverse events (AE)s, serious AEs, treatment-related AEs, immune-related AEs (irAE)s, AE-related treatment discontinuation, or treatment-related deaths). Studies without extractable data for any pre-specified outcome were excluded.

Study design. Eligible designs were Phase II and III trials (randomized or single-arm) and Phase I/Ib trials reporting

efficacy or safety data from an expansion cohort, limited to full-text original articles published in English with no date restriction. Preclinical studies, case reports, editorials, commentaries, narrative reviews, and conference abstracts were excluded, as were non-English or non–full-text publications and publications in non-recommended journals, in line with published guidance for identifying such venues [12].

2.4 Study selection process

Titles and abstracts were first screened in bulk for OC relevance, presence of an atezolizumab arm, clinical study design, and eligible publication type, with the remaining criteria applied at full-text review. Two researchers independently screened the titles and abstracts of all identified records against the predefined inclusion and exclusion criteria. Studies passing this stage underwent full-text assessment by the same reviewers. Disagreements over eligibility were resolved by a third researcher.

2.5 Data items and data extraction

For each eligible study, data were extracted per treatment arm, covering study identification, population characteristics, intervention and comparator, and efficacy and safety outcomes. Efficacy outcomes comprised PFS, OS, and objective response and its components, together with disease control rate; safety outcomes comprised any-grade and grade 3 or higher (grade ≥3) AEs, irAEs, treatment discontinuation, and treatment-related deaths. Proportions were recorded as raw event counts and denominators, and hazard ratios (HRs) with 95% confidence intervals (CIs) were taken only from randomized comparisons. The full list of extracted variables is provided in **Table S1**.

2.6 Data analysis and synthesis

Analyses were performed in R version 4.6.0 using the metafor and glmmTMB packages, and an outcome was pooled only when at least three studies contributed data. Comparative outcomes were drawn from randomized comparisons of atezolizumab added to a backbone regimen versus the same backbone with placebo, and all were pooled with the same random-effects model, using inverse-variance weighting with restricted maximum likelihood estimation of the between-study variance and the Knapp-Hartung adjustment to the confidence interval. Hazard ratios for PFS and OS were entered as log HRs with standard errors, whereas for objective response and the comparative safety outcomes (any-grade AEs, serious adverse events (SAEs), and irAEs, both any grade and grade ≥3) risk ratios (RRs) were computed from event counts, with a 0.5 continuity correction applied to studies with zero-event cells. Single-arm event frequencies in the atezolizumab arm were pooled as proportions for grade ≥3 AEs, treatment-related grade ≥3 AEs, SAEs, adverse-event-related treatment discontinuation, and grade 5 or treatment-related deaths, using a binomial generalized linear mixed model with multiple arms within a study modeled hierarchically where applicable. Heterogeneity was assessed with the I-squared statistic, tau-squared, the Cochran Q test, and prediction intervals, and leave-one-out omission was used as a sensitivity analysis across pooled outcomes if the number of contributing studies was more than 3.

2.7 Methodological quality assessment

Randomized trials were assessed with the Cochrane Risk of Bias 2 (RoB 2) tool across its five domains, with an overall judgment of low risk, some concerns, or high risk. Data sets analyzed as single arms, comprising the single-arm trials and the randomized trials that contributed single-arm data only, were assessed with the non-comparative Methodological Index for Non-Randomized Studies (MINORS), scoring eight items from 0 to 2 for a maximum of 16.

Certainty of evidence was rated with the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) framework for each of the fourteen outcomes. The nine comparative outcomes (PFS, PFS [PD-L1-Positive], OS, OS [PD-L1-Positive], ORR, and the any-grade, SAEs, and irAE risk ratios) were graded as effect estimates versus control and, being derived from randomized trials, began at high certainty; the five single-arm outcomes were graded as certainty in a pooled proportion and began at low certainty. Ratings considered risk of bias, inconsistency, indirectness, imprecision, and other considerations, with the risk-of-bias domain drawn from the RoB 2 and MINORS assessments. Evidence was classified as high, moderate, low, or very low certainty.

3. Results

3.1 Study selection

A total of 613 records were identified, comprising 550 from PubMed/MEDLINE and 63 from CENTRAL (Cochrane Central Register of Controlled Trials). After removal of 17 duplicates, 596 records underwent title and abstract screening, of which 565 were excluded. Thirty-one reports were sought for retrieval; one could not be obtained, leaving 30 for full-text assessment. Of these, 17 were excluded: eight lacked an atezolizumab arm, seven were duplicate reports of an already-included study, one had fewer than 10 patients in the atezolizumab arm, and one had fewer than 10 evaluable OC patients separable from a mixed population. Twelve studies, described in 13 reports, met all eligibility criteria and entered the review [13–25] (Figure 1).

3.2 Study and patient characteristics

The 12 included studies enrolled 3,179 patients and were published between 2019 and 2026. By design, 4 (33.3%) were randomized, double-blind, placebo-controlled, 3 (25.0%) randomized, open-label, and 5 (41.7%) single-arm. Four studies (33.3%) were phase III and accounted for 2,906 patients; the remaining eight (66.7%) were phase I to II, comprising 1 (8.3%) phase II, 6 (50.0%) phase Ib or I, and 1 (8.3%) phase I/II. Seven studies were randomized, and five were single-arm (Table 1 & Table 2).

Enrollment was largely restricted to good functional status. Pooled across studies, 1,848 (58.3%) patients had an Eastern Cooperative Oncology Group (ECOG) performance status of 0, 1,240 (39.1%) a status of 1, and 71 (2.2%) a status of 2. Prior treatment exposure spanned the full disease course: 1,320 patients (41.7%) were treatment-naive, 1,033 (32.6%) had received one prior line, 455 (14.4%) two lines, and 213 (6.7%) three lines. High-grade serous carcinoma predominated, at 2,335 (74.9%) patients of those with reported histology. Among patients with staging data, disease was predominantly advanced, 988 (68.8%) stage III and 442 (30.8%) stage IV. Expression of PD-L1 was positive in 1,314 (44.7%) and negative in 1,362 (46.4%), with 262 (8.9%) noninformative or unknown (Table 2 & Table 3).

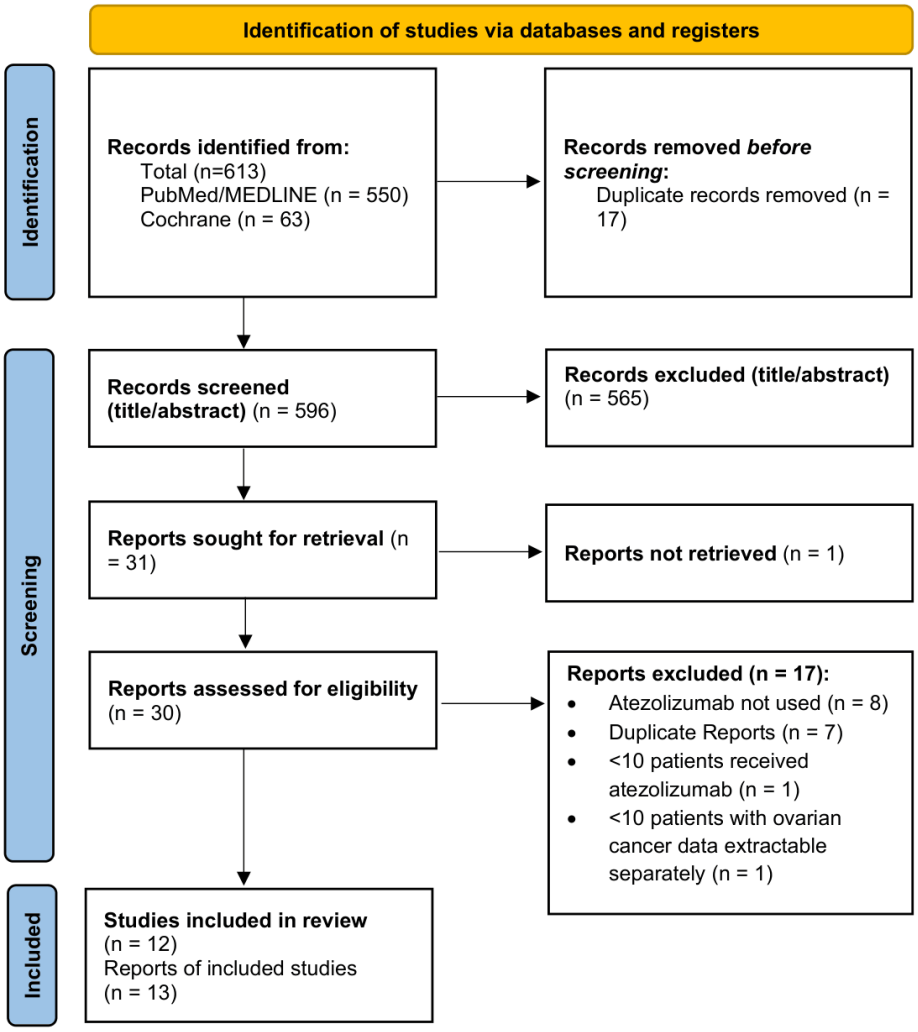

Figure 1. *PRISMA 2020 flow diagram.*

Table 1. Individual Study Characteristics.

	Study Information							Population					Time-to-event					Response										
Study (author, year)	**Trial / acronym**	**Population/line**	**Study Arm(s)**	**Phase**	**Design**	**Analysis pool**	**NCT no.**	**N enrolled (ITT)**	**N treated (safety)**	**N evaluable (response)**	**Median PFS (mo)**	**PFS events n**	**PFS HR (95% CI)**	**PFS population**	**Median OS (mo)**	**OS events n**	**OS HR (95% CI)**	**1-yr PFS %**	**1-yr OS %**	**ORR n**	**ORR N**	**CR n**	**PR n**	**SD n**	**PD n**	**DCR n**	**DCR N**	**DCR definition**	**Response criteria**
			Arm 4: Bev + atezo + placebo	II	Randomized, open-label	Both (proportion + HR vs Arm 1)	NCT02659384	32	31	32	4.1	28	0.84 (0.50–1.38)	ITT (vs Arm 1)	12.1	22	0.89 (0.49–1.59)	NR	NR	6	32	1	5	NR	22	21	32	NR	RECIST 1.1
Banerjee et al. 2025 [13]	EORTC 1508-GCG	Recurrent, platinum-resistant	Arm 1: Bev monotherapy (COMPARATOR)	II	Randomized, open-label	HR comparator	NCT02659384	33	31	33	2.3	32	NR	ITT (reference)	10.4	23	NR	NR	NR	3	33	0	3	NR	27	21	33	NR	RECIST 1.1
			Arm 5: Bev + atezo + ASA	II	Randomized, open-label	Proportion (HR shares Arm 1 control; excl. from HR pool)	NCT02659384	33	33	33	4	29	0.81 (0.49–1.34)	ITT (vs Arm 1)	11.6	22	0.71 (0.39–1.28)	NR	NR	6	33	1	5	NR	26	22	33	NR	RECIST 1.1
Gaillard et al. 2026 [14]	AdORN	First-line, neoadjuvant + interval surgery	Atezolizumab + NACT (wkly pac/carbo) -> maint atezo +/- bev	Ib	Single-arm / non-randomized	Proportion	NCT03394885	18	18	15	23.6	8	NR	ITT	NR	NR	NR	NR	NR	9	15	0	9	6	0	15	15	Sum of partial response and stable disease.	RECIST 1.1
Gonzalez-Martin et al. 2025 [15]	ANITA / ENGOT-OV41 / GEICO 69-O	Recurrent (platinum-based) + maintenance niraparib	Atezolizumab + platinum CT → Atezolizumab + Niraparib	III	Randomized, double-blind, placebo-controlled	Both (HR + proportion)	NCT03598270	208	207	208	11.2	170	0.89 (0.71–1.10)	ITT	NR	NR	NR	44	NR	93	207	14	79	91	NR	NR	NR	NR	RECIST 1.1
			Placebo + platinum CT → Placebo + Niraparib	III	Randomized, double-blind, placebo-controlled	HR comparator	NCT03598270	209	209	209	10.1	174	NR	ITT	NR	NR	NR	35	NR	90	209	13	79	96	NR	NR	NR	NR	RECIST 1.1
Harter et al. 2026 [16]	AGO-OVAR 2.29 / ENGOT-ov34	Recurrent, non-platinum CT	Atezolizumab + bev + non-plat CT	III	Randomized, double-blind, placebo-controlled	Both (HR + proportion)	NCT03353831	285	281	255	6.4	243	0.87 (0.73–1.04)	ITT	14.2	197	0.83 (0.68–1.01)	28	58	101	255	11	90	91	NR	NR	NR	NR	NR
			Placebo + bev + non-plat CT	III	Randomized, double-blind, placebo-controlled	HR comparator	NCT03353831	289	286	248	6.7	261	NR	ITT	13	221	NR	23	56	108	248	6	102	87	NR	NR	NR	NR	NR
Kristeleit et al. 2024 [17]	COUPLET	Platinum-sensitive recurrent, tBRCAmut	Part 2 Arm A: rucaparib + atezo, tBRCAmut ovarian	Ib	Single-arm / non-randomized	Proportion	NCT03101280	10	10	10	NR	NR	NR	ITT	NR	NR	NR	NR	NR	6	10	1	5	NR	NR	NR	10	NR	RECIST 1.1

Table 1. Continued…

Kurtz et al. 2023 [18]	ATALANTE / ENGOT-ov29	Platinum-sensitive recurrent	Atezolizumab + bev + platinum CT	III	Randomized, double-blind, placebo-controlled	Both (HR + proportion)	NCT02891824	410	408	410	13.5	348	0.83 (0.69–0.99)	ITT	35.5	NR	0.81 (0.65–1.01)	56	89	62	410	NR	NR	NR	NR	NR	NR	NR	RECIST 1.1
			Placebo + bev + platinum CT	III	Randomized, double-blind, placebo-controlled	HR comparator	NCT02891824	204	201	204	11.3	187	NR	ITT	30.6	NR	NR	46	87	66	204	NR	NR	NR	NR	NR	NR	NR	RECIST 1.1
Liu et al. 2019 [19]	PCD4989g	Advanced, monotherapy	Atezolizumab monotherapy (ovarian cohort)	Ia/I	Single-arm / non-randomized	Proportion	NCT01375842	12	12	9	2.9	NR	NR	Efficacy evaluable (n=10)	11.3	NR	NR	20	41.7	2	9	1	1	0	5	2	9	Percentage of patients with best response of CR, PR or SD for ≥24 weeks	RECIST 1.1
Moore et al. 2021 & Pignata et al. 2023 [20, 21]	IMagyn050 / GOG-3015 / ENGOT-OV39	First-line, newly diagnosed stage III/IV	Atezolizumab + carboplatin/paclitaxel + bevacizumab	III	Randomized, double-blind, placebo-controlled	Both (HR + proportion)	NCT03038100	651	642	251	19.5	323	0.92 (0.79–1.07)	ITT	50.5	254	0.92 (0.78–1.09)	NR	NR	233	251	NR	NR	NR	NR	NR	NR	NR	RECIST 1.1
			Placebo + carboplatin/paclitaxel + bevacizumab	III	Randomized, double-blind, placebo-controlled	HR comparator	NCT03038100	650	644	239	18.4	341	NR	ITT	46.6	278	NR	NR	NR	212	239	NR	NR	NR	NR	NR	NR	NR	RECIST 1.1
Moroney et al. 2020 [22]	GP28328	Recurrent ovarian	Atezolizumab + bevacizumab	Ib	Single-arm / non-randomized	Proportion	NCT01633970	20	20	20	4.9	NR	NR	Safety evaluable	10.2	NR	NR	NR	48.75	3	20	0	3	8	5	11	20	≥12 weeks	RECIST 1.1
Mutch et al. 2024 [23]	YO40482	Platinum-sensitive recurrent, BRCA-wt	Triplet: PARPi + MEKi + atezolizumab	Ib	Randomized, open-label	Both (HR + proportion)	NCT03695380	37	37	37	7.4	28	NR	ITT	NR	NR	NR	NR	73	NR	37	NR	NR	NR	NR	NR	NR	NR	RECIST 1.1
			Doublet: PARPi + MEKi (no atezo)	Ib	Randomized, open-label	HR comparator	NCT03695380	39	39	39	6	28	NR	ITT	NR	NR	NR	NR	82	NR	39	NR	NR	NR	NR	NR	NR	NR	RECIST 1.1
Rocconi et al. 2022 [24]	—	Relapsed ovarian	Atezo-1st	I	Randomized, open-label	Proportion	NCT03073526	10	10	10	2.8	NR	NR	ITT	10.8	NR	NR	NR	NR	NR	10	NR	NR	NR	NR	NR	NR	NR	RECIST 1.1
			Vigil-1st	I	Randomized, open-label	Proportion	NCT03073526	11	11	11	3.4	NR	0.76 (0.28–2.00)	ITT	NR	NR	0.33 (0.06–1.70)	NR	NR	NR	11	NR	NR	NR	NR	NR	NR	NR	RECIST 1.1
Simonelli et al. 2022 [25]	ACT15377	Advanced solid tumors (ovarian cohort)	Isatuximab + atezolizumab (OVARIAN subset only)	I/II	Single-arm / non-randomized	Proportion	NCT03637764	18	18	18	2.04	NR	NR	all treated	NR	NR	NR	NR	NR	1	18	0	1	6	10	7	18	Not Defined	RECIST 1.1

***Abbreviations**: AGO-OVAR, Arbeitsgemeinschaft Gynäkologische Onkologie–Ovarian Cancer Study Group; ASA, acetylsalicylic acid (aspirin); atezo, atezolizumab; bev, bevacizumab; BRCA-wt, BRCA wild-type; carbo, carboplatin; CI, confidence interval; CR, complete response; CT, chemotherapy; DCR, disease control rate; ENGOT, European Network of Gynaecological Oncological Trial groups; EORTC, European Organisation for Research and Treatment of Cancer; GCG, Gynaecological Cancer Group; GEICO, Grupo Español de Investigación en Cáncer de Ovario; GOG, Gynecologic Oncology Group; HR, hazard ratio; ITT, intention-to-treat; maint, maintenance; MEKi, MEK inhibitor; mo, months; NACT, neoadjuvant chemotherapy; NCT, ClinicalTrials.gov registration number; NR, not reported; ORR, objective response rate; OS, overall survival; pac, paclitaxel; PARPi, poly(ADP-ribose) polymerase inhibitor; PD, progressive disease; PFS, progression-free survival; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumors; SD, stable disease; tBRCAmut, tumor BRCA-mutated; wkly, weekly.*

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Table 2. Summary of Study and Patient Characteristics.

Characteristic	n (%)
Study & Trial Characteristics	
Study Design (N=12)	
Randomized, double-blind, placebo-controlled	4 (33.3%)
Randomized, open-label	3 (25.0%)
Single-arm / non-randomized	5 (41.7%)
Trial Phase (N=12)	
Phase III	4 (33.3%)
Phase II	1 (8.3%)
Phase Ib	4 (33.3%)
Phase I	1 (8.3%)
Phase Ia/I	1 (8.3%)
Phase I/II	1 (8.3%)
Patient Baseline Characteristics	
Histology (N=3118)	
High-grade serous	2335 (74.9%)
Low-grade serous	183 (5.9%)
Serous (grade unspecified)	180 (5.8%)
Endometrioid	99 (3.2%)
Clear cell	109 (3.5%)
Seromucinous	32 (1.0%)
Mucinous	17 (0.5%)
Other	163 (5.2%)
FIGO Tumor Stage (N=1437)	
Stage I	2 (0.1%)
Stage II	4 (0.3%)
Stage III	988 (68.8%)
Stage IV	442 (30.8%)
Unknown / Missing	1 (0.1%)
ECOG Performance Status (N=3169)	
0	1848 (58.3%)
1	1240 (39.1%)
2	71 (2.2%)
Missing	10 (0.3%)
PD-L1 Status (N=2938)	
PD-L1 Positive	1314(44.7%)
PD-L1 Negative	1362 (46.4%)
Other (noninformative / missing / unknown)	262 (8.9%)
Prior Therapy Lines (N=3168)	
No prior therapy (treatment-naive)	1320 (41.7%)
1 prior line/regimen	1033 (32.6%)
2 prior lines/regimens	455 (14.4%)
3 prior lines/regimens	213 (6.7%)
Missing	3 (0.1%)
Other (≥3 / range-reported)	144 (4.5%)
Efficacy and Safety Outcomes	
Response	
ORR (objective response) (N=2193)	1001 (45.7%)
Complete response (CR) (N=1089)	48 (4.4%)
Partial response (PR) (N=1089)	382 (35.1%)
Stable disease (SD) (N=981)	385 (39.3%)
Progressive disease (PD) (N=160)	95 (59.4%)
DCR (disease control) (N=160)	99 (61.9%)
Worst AE Grade (N=2296)	
Grade 1–2 (mild–moderate)	562 (24.5%)
Grade 3–4 (severe, non-fatal)	1700 (74.0%)
Grade 5 (fatal)	22 (1.0%)
Not separable (any-grade only)	12 (0.5%)

Abbreviations: *AE, adverse event; CR, complete response; DCR, disease control rate; ECOG, Eastern Cooperative Oncology Group; FIGO, International Federation of Gynecology and Obstetrics; ORR, objective response rate; PD, progressive disease; PD-L1, programmed death ligand 1; PR, partial response; SD, stable disease.*

3.3 Efficacy

Progression-free survival was pooled from five randomized comparisons of atezolizumab added to a backbone regimen versus the backbone with placebo. The pooled HR was 0.88 (95% CI 0.83 to 0.93, p = 0.003), favoring atezolizumab, with no detectable heterogeneity (I^2 = 0.0%, Q p = 0.94) and a stable estimate across leave-one-out analysis (HR 0.86 to 0.89). In the PD-L1–positive subgroup, progression-free survival was pooled from four randomized comparisons (1297 patients; 686 atezolizumab, 611 control), giving a pooled HR of 0.82 (95% CI 0.76 to 0.89, p = 0.004), likewise favoring atezolizumab, again without heterogeneity (I^2 = 0.0%, Q p = 0.95) and stable on leave-one-out analysis (HR 0.81 to 0.84) (Figure 2).

Overall survival, pooled from four randomized comparisons, gave an HR of 0.86 (95% CI 0.78 to 0.96, p = 0.021), again favoring atezolizumab, without heterogeneity (I^2 = 0.0%, Q p = 0.79) and consistent on leave-one-out analysis (HR 0.82 to 0.88). In the PD-L1–positive subgroup, overall survival was pooled from three randomized comparisons (1148 patients; 610 atezolizumab, 538 control), giving an HR of 0.83 (95% CI 0.71 to 0.98, p = 0.040), also favoring atezolizumab and without heterogeneity (I^2 = 0.0%, Q p = 0.85). Leave-one-out analysis was not performed for this outcome, as omitting any single trial would have left fewer than three studies (Figure 3).

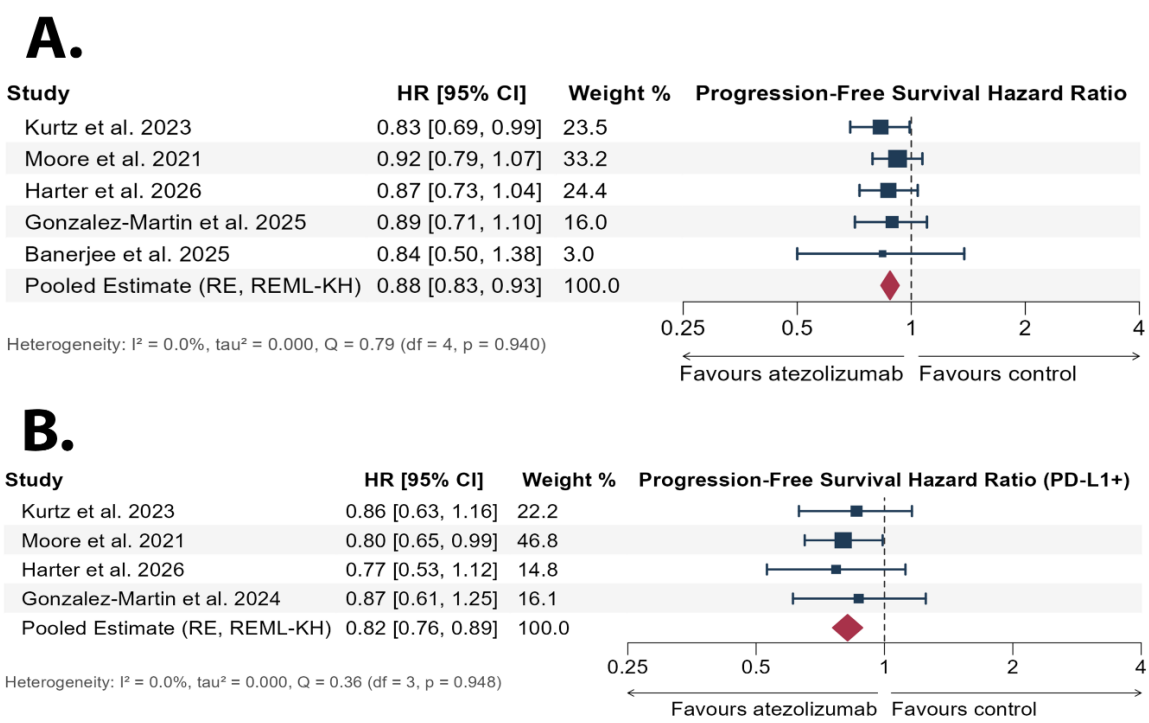

Figure 2. (A) *Random-effects meta-analysis of progression-free survival for atezolizumab versus control across 5 randomized comparisons. Squares represent study HRs (area proportional to weight), lines the 95% CIs, and the diamond the pooled estimate; an HR below 1 favors atezolizumab.* ***(B)*** *Random-effects meta-analysis of progression-free survival for atezolizumab versus control for the PD-L1-positive subgroup across 4 randomized comparisons. Squares represent study HRs (area proportional to weight), lines the 95% CIs, and the diamond the pooled estimate; an HR below 1 favors atezolizumab. Abbreviations: CI, confidence interval; HR, hazard ratio; RE, random effects; REML-KH, restricted maximum likelihood with Knapp-Hartung adjustment.*

Objective response, pooled from five randomized comparisons, gave an RR of 0.88 (95% CI 0.52 to 1.49, p = 0.55), showing no significant difference between atezolizumab and control. Unlike the survival endpoints, heterogeneity was substantial ($I^2 = 92.3\%$, Q $p < 0.001$), with per-study risk ratios spanning both directions (0.47 to 2.06) and a wide prediction interval (0.25 to 3.15); the pooled estimate ranged from 0.84 to 1.04 on leave-one-out analysis (Figure 4).

3.4 Safety

3.4.1 Adverse event profile

The overall AE profile was dominated by events attributable to the chemotherapy and anti-angiogenic backbone, which occurred at similar frequencies in both arms. Common all-grade events included fatigue (42% with atezolizumab vs 41% with control), nausea (52% vs 55%), anemia (43% vs 42%), neutropenia (35% vs 35%), and alopecia (47% vs 51%). Grade ≥3 AEs were predominantly hematologic and comparable between arms, including neutropenia (23% vs 23%), anemia (13% vs 11%), thrombocytopenia (12% vs 12%), and hypertension (14% vs 14%).

The excess toxicity associated with atezolizumab was concentrated in immune-related, cutaneous, and endocrine categories. Relative to control arms, atezolizumab-containing arms showed higher rates of rash (23% vs 15%), maculopapular rash (9% vs 3%), pruritus (14% vs 9%), pyrexia (20% vs 10%), hypothyroidism (12% vs 5%), and colitis (3% vs 1%), together with a higher rate of composite immune mediated events (27% vs 21%), including at grade ≥3 AEs (11% vs 6%) (Table 4).

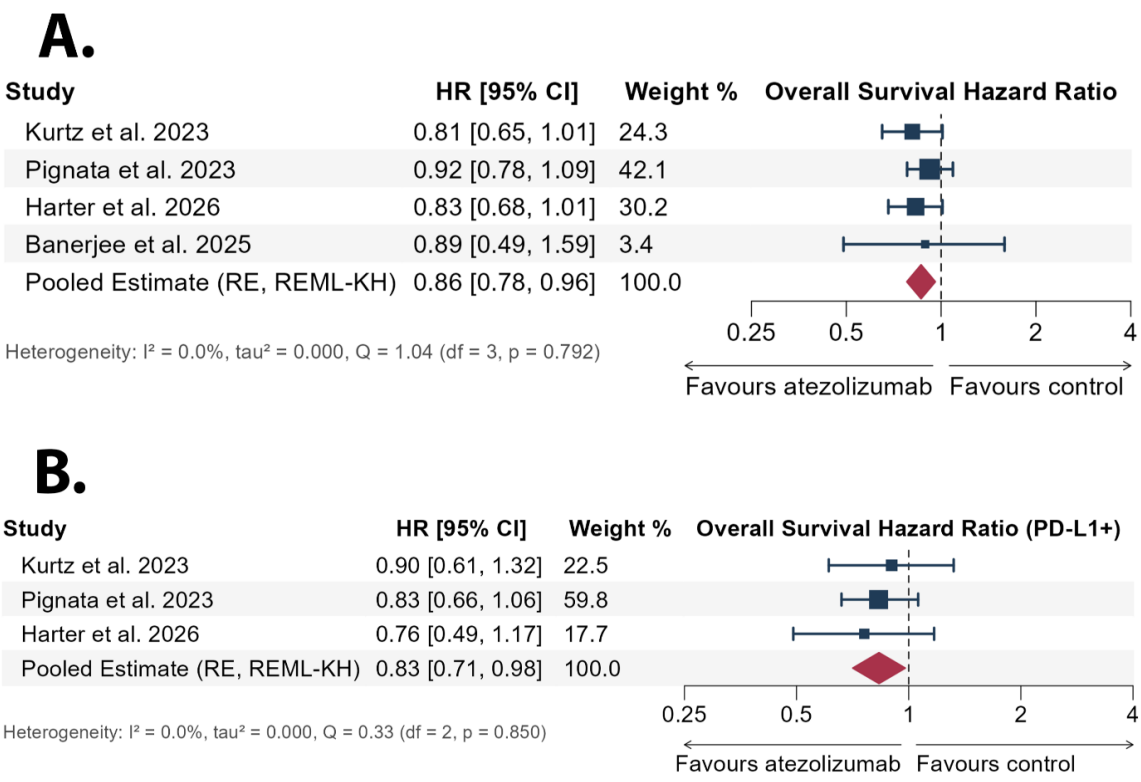

Figure 3. (A) *Random-effects meta-analysis of overall survival across 4 randomized comparisons; an HR below 1 favors atezolizumab. Symbols as in Figure 2. Abbreviations: CI, confidence interval; HR, hazard ratio; RE, random effects; REML-KH, restricted maximum likelihood with Knapp-Hartung adjustment.* ***(B)*** *Random-effects meta-analysis of overall survival for the PD-L1-positive subgroup across 3 randomized comparisons; an HR below 1 favors atezolizumab. Symbols as in Figure 2. Abbreviations: CI, confidence interval; HR, hazard ratio; RE, random effects; REML-KH, restricted maximum likelihood with Knapp-Hartung adjustment.*

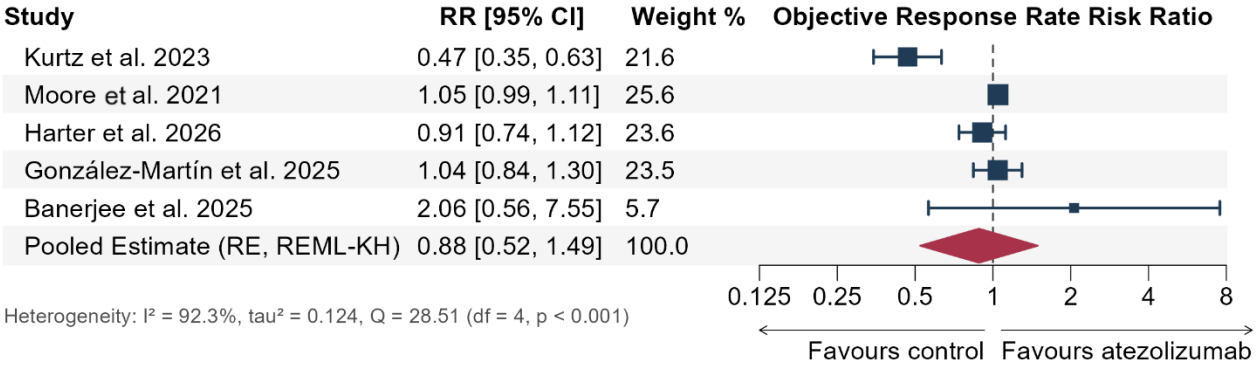

Figure 4. *Random-effects meta-analysis of objective response rate across 5 randomized comparisons, as risk ratios; an RR above 1 favors atezolizumab. Symbols as in Figure 2. Abbreviations: CI, confidence interval; RE, random effects; REML-KH, restricted maximum likelihood with Knapp-Hartung adjustment; RR, risk ratio.*

Barw Medical Journal | 2026;4(2) | https://doi.org/10.58742/bmj.v4i2.238

Table 3. Baseline Demographic and Disease Characteristics of Patients.

Study & arm characteristics			Histology, n (%)						Tumor Stage, n (%)					Performance status, n (%)				Prior therapy lines, n (%)				
Study (year) / trial	**Arm**	**N**	**High-grade serous**	**Low-grade serous**	**Serous, NOS**	**Endometrioid**	**Clear cell**	**Other / mixed**	**Stage 1**	**Stage 2**	**Stage 3**	**Stage 4**	**Unknown**	**PS 0**	**PS 1**	**PS 2**	**Missing / other**	**Treatment-naïve**	**1 line**	**2 lines**	**≥3 lines**	**Grouped (as reported)**	**Missing**
Banerjee et al. 2025 [13]	Bev monotherapy (Arm 1)	33	—	—	25 (75.8)	0 (0)	3 (9.1)	5 (15.2)*	1 (3.0%)	1 (3.0%)	22 (66.7%)	9 (27.3%)	0	14 (42.4)	19 (57.6)	0 (0)	—	—	—	—	28 (84.8)	≤2: 5 (15.2)	—
	Bev + atezo + placebo (Arm 4)	32	—	—	28 (87.5)	1 (3.1)	2 (6.3)	1 (3.1)	1 (3.1%)	2 (6.3%)	21 (65.6%)	7 (21.9%)	1 (3.1%)	13 (40.6)	19 (59.4)	0 (0)	—	—	—	—	27 (84.4)	≤2: 5 (15.6)	—
	Bev + atezo + ASA (Arm 5)	33	—	—	33 (100)	0 (0)	0 (0)	0 (0)	0 (0.0%)	1 (3.0%)	19 (57.6%)	13 (39.4%)	0	23 (69.7)	10 (30.3)	0 (0)	—	—	—	—	27 (81.8)	≤2: 6 (18.2)	—
Gaillard et al. 2026 [14]	Atezo + neoadjuvant CT → maint. atezo ± bev	18	18 (100)	—	—	—	—	—	0	0	13 (72.2%)	5 (27.8%)	0	2 (11.1)	11 (61.1)	5 (27.8)	—	18 (100)	—	—	—	—	—
González-Martín et al. 2025 [15]	Atezo → atezo + niraparib	208	187 (90)	—	—	11 (5)	—	10 (4.8)*	NR	NR	NR	NR	NR	132 (63)	73 (35)	—	Missing 3 (1)	—	181 (87)	26 (13)	—	—	1 (<1)
	Placebo → placebo + niraparib	209	196 (94)	—	—	5 (2)	—	8 (3.8)*	NR	NR	NR	NR	NR	123 (59)	82 (39)	—	Missing 4 (2)	—	179 (86)	28 (13)	—	—	2 (1)
Harter et al. 2026 [16]	Atezo + bev + non-platinum CT	285	214 (75)	8 (2.8)	—	12 (4.2)	17 (6.0)	34 (11.9)*	NR	NR	NR	NR	NR	163 (57)	120 (42)	—	Missing 2 (0.7)	—	70 (25)	112 (39)	103 (36)	—	—
	Placebo + bev + non-platinum CT	289	230 (80)	10 (3.5)	—	8 (2.8)	16 (5.5)	25 (8.7)*	NR	NR	NR	NR	NR	152 (53)	136 (47)	—	Missing 1 (0.3)	—	70 (24)	115 (40)	104 (36)	—	—
Kristeleit et al. 2024 [17]	Rucaparib + atezo (Arm A)‡	10	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Kurtz et al. 2023 [18]	Atezo + bev + platinum CT	410	346 (84)	32 (8)	—	12 (3)	8 (2)	12 (3)	NR	NR	NR	NR	NR	277 (68)	131 (32)	2 (<1)	—	—	307 (75)	103 (25)	—	—	—
	Placebo + bev + platinum CT	204	169 (83)	8 (4)	—	11 (5)	9 (4)	7 (3)	NR	NR	NR	NR	NR	147 (72)	57 (28)	0 (0)	—	—	159 (78)	45 (22)	—	—	—
Liu et al. 2019 [19]	Atezo monotherapy	12	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	6 (50.0)	6 (50.0)	—	—	1 (8.3)‖	0 (0)	—	—	≥2: 11 (91.7)	—
Moore et al. 2021 [20,21]¶	Atezo + carbo/pac + bev	651	504 (77)	67 (10)	—	14 (2)	29 (4)	37 (6)	0	0	448 (69%)	203 (31%)	0	355 (55)	263 (40)*	33 (5)*	—	651 (100)	—	—	—	—	—
	Placebo + carbo/pac + bev	650	489 (75)	58 (9)	—	21 (3)	22 (3)	60 (9)	0	0	448 (69%)	201 (31%)	0	353 (54)	266 (41)*	31 (5)*	—	650 (100)	—	—	—	—	—
Moroney et al. 2020 [22]	Atezo + bev	20	—	—	12 (60)	3 (15)	2 (10)	3 (15)	NR	NR	NR	NR	NR	11 (55)	9 (45)	—	—	—	—	—	13 (65)*	1–2: 7 (35)§	—
Mutch et al. 2024 [23]	Cobi + nira + atezo (triplet)	37	—	—	31 (84)	—	—	6 (16)	NR	NR	NR	NR	NR	25 (78)†	12 (22)†	—	—	—	29 (68)	8 (32)	—	—	—
	Cobi + nira (doublet)	39	—	—	35 (90)	—	—	4 (10)	NR	NR	NR	NR	NR	31 (79)	8 (21)	—	—	—	27 (69)	11 (28)	—	—	1 (3)
Rocconi et al. 2022 [24]	Atezo first (then Vigil)	10	NR	NR	NR	NR	NR	NR	0	0	9 (90.0%)	1 (10.0%)	0	2 (20.0)	8 (80.0)	—	—	—	2 (20)§	3 (30)	5 (50)*	—	—
	Vigil first (then atezo)	11	NR	NR	NR	NR	NR	NR	0	0	8 (72.7%)	3 (27.3%)	0	7 (63.6)	4 (36.4)	—	—	—	5 (45.5)§	4 (36.4)	2 (18.2)*	—	—
Simonelli et al. 2022 [25]	Isatuximab + atezo	18	—	—	16 (88.9)	1 (5.6)	1 (5.6)	—	NR	NR	NR	NR	NR	12 (66.7)	6 (33.3)	—	—	—	4 (22.2)	—	—	≥2: 14 (77.8)§	—

Abbreviations: *ASA, acetylsalicylic acid; atezo, atezolizumab; bev, bevacizumab; carbo, carboplatin; cobi, cobimetinib; CT, chemotherapy; maint., maintenance; nira, niraparib; NOS, not otherwise specified; NR, not reported; pac, paclitaxel; PS, performance status.*

Notes affecting how a value reads.

* *Percentage recomputed from N (not printed by the trial); all other percentages are as reported.*

† *Mutch triplet: printed performance-status percentages (78 / 22) do not reconcile with n = 37 (25/37 ≈ 68 %, 12/37 ≈ 32 %); shown as printed.*

‡ *Kristeleit: Arm A not reported separately; values are pooled Part 2 ovarian Arms A + B (n = 14) — e.g., PS 0 = 11 (79), PS 1 = 3 (21); eligibility was 1–2 prior platinum-containing regimens.*

§ *Counted by the trial as prior regimens rather than lines (Rocconi, Moroney, Simonelli).*

‖ *Liu: "treatment-naïve" = 0 prior lines (advanced-disease phase Ia setting).*

¶ *Moore (IMagyn050) baseline is shared with Pignata 2023 (OS/PRO update of the same randomized population) and is listed once.*

Table 4. Adverse Events in Atezolizumab-containing Versus Non-atezolizumab Arms.

Adverse event	Atezolizumab arms		Non-atezolizumab arms	
	All grade	Grade ≥3	All grade	Grade ≥3
General / constitutional				
Fatigue	531/1261 (42%)	40/1261 (3%)*	495/1209 (41%)	31/1209 (3%)*
Asthenia	222/898 (25%)	22/898 (2%)*	217/892 (24%)	19/892 (2%)*
Pyrexia / fever	188/925 (20%)	7/945 (1%)*	85/884 (10%)	8/884 (1%)*
Decreased appetite / anorexia	132/962 (14%)	34/962 (4%)*	120/923 (13%)	34/923 (4%)*
Weight loss	22/82 (27%)	0/82 (0%)*	5/31 (16%)	0/31 (0%)
Mucositis / mucosal inflammation	55/308 (18%)	3/308 (1%)*	54/279 (19%)	3/279 (1%)*
Peripheral edema	9/64 (14%)	0/64 (0%)	2/31 (6%)	0/31 (0%)
Gastrointestinal				
Nausea	505/980 (52%)	24/1000 (2%)*	510/923 (55%)	8/923 (1%)*
Vomiting	252/980 (26%)	29/1000 (3%)*	254/923 (28%)	13/923 (1%)*
Diarrhea	441/1249 (35%)	38/1249 (3%)*	379/1209 (31%)	32/1209 (3%)*
Constipation	361/950 (38%)	5/950 (1%)*	362/923 (39%)	9/923 (1%)*
Abdominal pain	378/1261 (30%)	37/1281 (3%)*	370/1209 (31%)	27/1209 (2%)*
GI perforation	7/281 (2%)	6/281 (2%)	12/286 (4%)	12/286 (4%)
Ileus	16/673 (2%)	10/673 (1%)*	12/675 (2%)	6/675 (1%)*
Colitis	26/923 (3%)	14/923 (2%)*	13/930 (1%)	8/930 (1%)*
Hematologic				
Anemia	545/1261 (43%)	161/1261 (13%)*	503/1209 (42%)	130/1209 (11%)*
Neutropenia	421/1194 (35%)	272/1194 (23%)*	410/1170 (35%)	266/1170 (23%)*
Febrile neutropenia	64/642 (10%)	64/642 (10%)*	34/644 (5%)	34/644 (5%)*
Thrombocytopenia	283/931 (30%)	114/951 (12%)*	267/853 (31%)	106/853 (12%)*
Leukopenia / WBC decreased	98/913 (11%)	52/913 (6%)*	101/853 (12%)	42/853 (5%)*
Lymphopenia	17/706 (2%)	6/706 (1%)*	7/644 (1%)	3/644 (0%)*
Hepatic / metabolic				
ALT increased	9/82 (11%)	0/82 (0%)*	2/31 (6%)	1/31 (3%)
AST increased	51/326 (16%)	1/326 (0%)*	39/279 (14%)	3/279 (1%)*
Elevated liver enzymes (composite)	43/281 (15%)	10/281 (4%)	33/286 (12%)	9/286 (3%)
Lipase increased	14/101 (14%)	6/101 (6%)	8/70 (11%)	3/70 (4%)
Amylase increased	12/101 (12%)	3/101 (3%)	13/70 (19%)	3/70 (4%)
Hypomagnesemia	69/849 (8%)	27/849 (3%)*	72/853 (8%)	25/853 (3%)*
Hypokalemia	11/55 (20%)	4/55 (7%)*	12/683 (2%)	4/683 (1%)*
Renal / urinary				
Proteinuria	141/706 (20%)	13/726 (2%)*	142/675 (21%)	23/675 (3%)*
Urinary tract infection	159/950 (17%)	17/950 (2%)*	146/923 (16%)	8/923 (1%)*
Cardiovascular / vascular				
Hypertension	349/1231 (28%)	171/1251 (14%)*	379/1209 (31%)	169/1209 (14%)*
Pulmonary embolism	75/679 (11%)	53/679 (8%)*	63/683 (9%)	48/683 (7%)*
Respiratory				
Dyspnea	241/1261 (19%)	105/1281 (8%)*	209/1209 (17%)	93/1209 (8%)*
Cough	35/289 (12%)	0/289 (0%)*	26/240 (11%)	0/240 (0%)*

Table 4. Continued....

Pneumonitis / ILD	3/299 (<1%)	2/319 (<1%)*	0/286 (0%)	0/286 (0%)
	Neurological			
Headache	194/913 (21%)	3/913 (0%)*	215/884 (24%)	4/884 (0%)*
Peripheral sensory neuropathy	291/941 (31%)	25/941 (3%)*	282/930 (30%)	25/930 (3%)*
Dysgeusia	23/207 (11%)	0/207 (0%)*	23/209 (11%)	0/209 (0%)*
	Musculoskeletal			
Arthralgia	315/943 (33%)	3/943 (0%)*	304/884 (34%)	10/884 (1%)*
Myalgia	154/724 (21%)	5/724 (1%)*	168/675 (25%)	3/675 (0%)*
Back pain	40/271 (15%)	1/271 (0%)*	31/240 (13%)	3/240 (1%)*
	Dermatologic			
Rash	206/886 (23%)	22/906 (2%)*	136/892 (15%)	5/892 (1%)*
Rash maculopapular	62/709 (9%)	21/709 (3%)*	18/683 (3%)	2/683 (0%)*
Pruritus	126/879 (14%)	5/879 (1%)*	75/853 (9%)	0/853 (0%)*
Alopecia	401/849 (47%)	0/849 (0%)*	434/853 (51%)	0/853 (0%)*
Palmar-plantar erythrodysesthesia	23/207 (11%)	2/207 (1%)*	14/209 (7%)	0/209 (0%)*
	Endocrine / immune-related			
Hypothyroidism	85/697 (12%)	0/289 (0%)*	21/441 (5%)	0/240 (0%)*
Hyperthyroidism	4/18 (22%)	0/18 (0%)*	—	—
Immune-mediated / autoimmune (composite)	206/753 (27%)	37/345 (11%)	101/487 (21%)	17/286 (6%)
Immune-related hepatitis	36/313 (12%)	9/313 (3%)*	28/286 (10%)	7/286 (2%)
	Infections			
Infection (any)	71/923 (8%)	15/923 (2%)*	76/930 (8%)	14/930 (2%)*
Pneumonia	18/642 (3%)	6/642 (1%)*	12/644 (2%)	4/644 (1%)*
Sepsis	3/642 (<1%)	3/662 (<1%)*	11/644 (2%)	5/644 (1%)*

** **Grade ≥3** value pools one or more studies that reported Grade 3/4 rather than Grade ≥3 (IMagyn050, González-Martín, Moroney; Gaillard reported Grade 3 and Grade 4 separately, summed here). Grade 5 events, where applicable, were tabulated separately in those studies and are not included.* ***Abbreviations:*** *ILD, interstitial lung disease; WBC, white blood cell; ALT, alanine aminotransferase; AST, aspartate aminotransferase; GI, gastrointestinal. Neutrophil / platelet / lymphocyte / WBC "count decreased" terms are pooled with neutropenia / thrombocytopenia / lymphopenia / leukopenia respectively.*

3.4.2 Pooled safety outcomes

Any-grade AEs were near-universal in both arms and did not differ, with a pooled RR of 1.00 (95% CI 1.00 to 1.00; three comparisons) and no heterogeneity (I^2 = 0.0%, Q p = 0.95). Serious adverse events were more frequent with atezolizumab, with a pooled RR of 1.32 (95% CI 1.05 to 1.67, p = 0.036; three comparisons) and low heterogeneity (I^2 = 32.4%, Q p = 0.27). Immune-related adverse events of any grade were increased (RR 1.57, 95% CI 1.12 to 2.20, p = 0.024; four comparisons), with moderate heterogeneity in the magnitude of effect (I^2 = 54.0%, Q p = 0.09) and a stable estimate on leave-one-out analysis (1.42 to 1.75). Grade ≥3 irAEs were approximately doubled (RR 2.23, 95% CI 1.05 to 4.74, p = 0.044; three comparisons), with moderate heterogeneity (I^2 = 42.8%, Q p =

0.18); the wide interval reflects the small number of events (Figure 5).

Pooled single-arm incidence of key safety events in the atezolizumab arm ranged from 1.8% (95% CI 1.1 to 2.9) for grade 5 or treatment-related deaths to 66.5% (95% CI 53.0 to 77.8) for grade ≥3 AEs, with several outcomes showing substantial between-trial heterogeneity (Table 5).

3.5 Risk of bias and certainty of evidence

The five randomized trials contributing comparative data were appraised with RoB 2. Four were rated overall low risk and one some concerns, driven by its open-label design and investigator-assessed outcome. The seven data sets analyzed as single arms (the five single-arm trials and the two randomized trials that contributed single-arm data only) were assessed with MINORS, scoring 11 to 13 of 16, with deductions concentrated on consecutive inclusion, independent endpoint assessment, loss to follow-up, and prospective sample-size calculation (Figure 6).

Certainty of evidence was assessed across 14 outcomes. Of the nine comparative outcomes from randomized controlled trials, five were rated high certainty, three moderate, and one very low. Downgrading was driven solely by inconsistency and imprecision; risk of bias, and indirectness raised no concerns. The five single-arm pooled proportions began at low certainty and, except treatment-related death, were downgraded to very low for inconsistency, and two of these were downgraded for imprecision as well (Table 6).

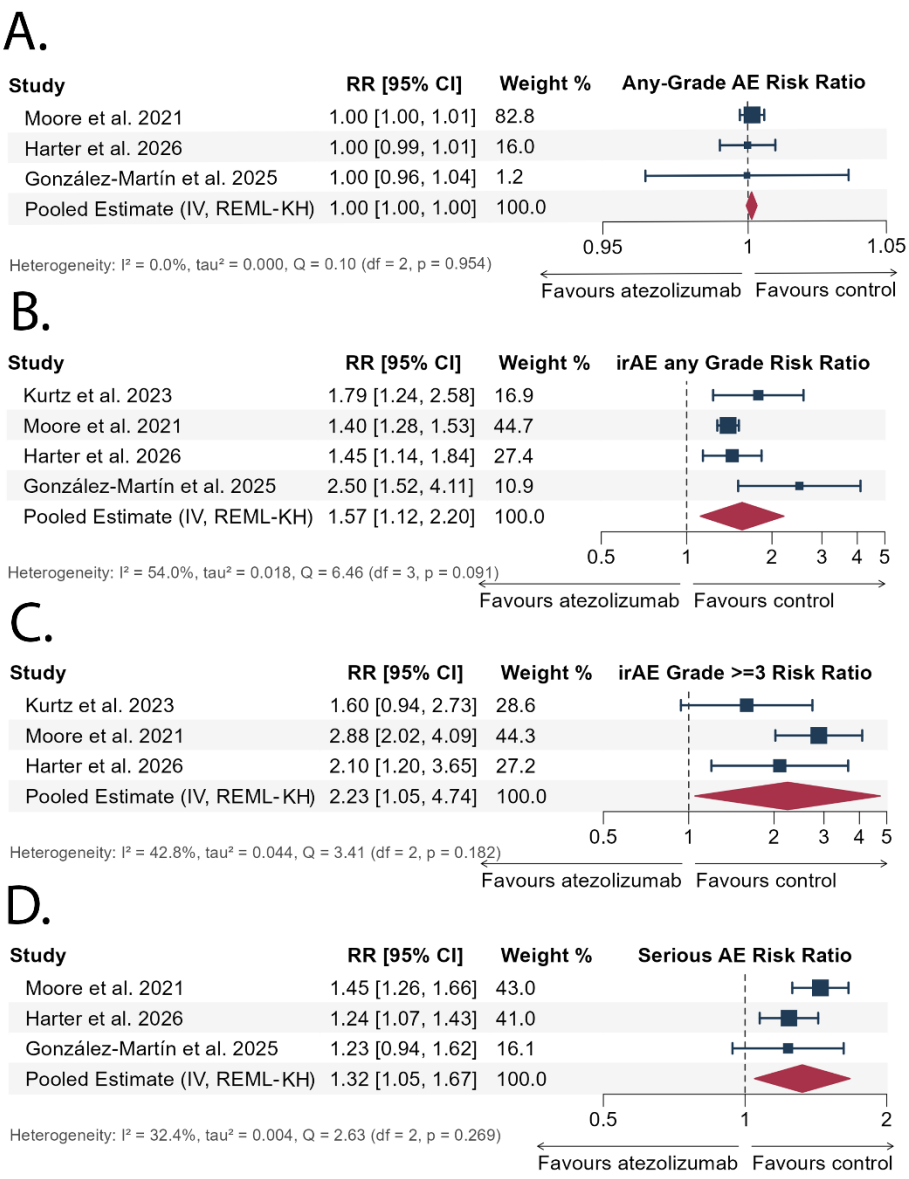

Figure 5. Random-effects meta-analyses of comparative safety, as risk ratios: (A) any-grade AEs, (B) any-grade irAEs, (C) grade ≥3 irAEs, and (D) serious AEs; an RR above 1 favors control. Abbreviations: AE, adverse event; CI,confidence interval; irAE, immune-related adverse event; IV, inverse variance; REML-KH, restricted maximum likelihood with Knapp-Hartung adjustment; RR, risk ratio.

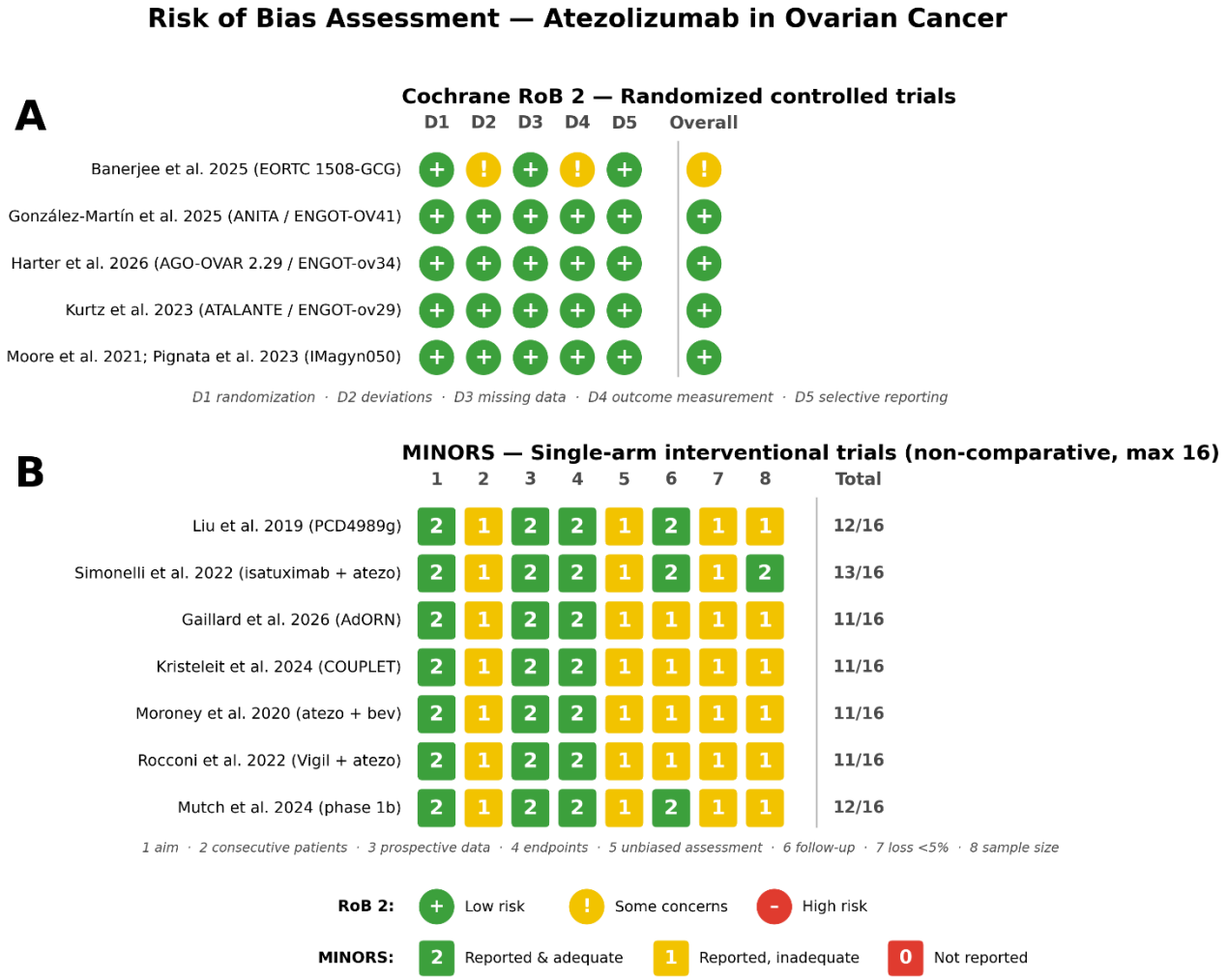

Figure 6. *Methodological quality assessment: (A) Cochrane RoB 2 for the 5 randomized trials across domains D1 to D5; (B) MINORS scores (maximum 16) for the 7 single-arm data sets. Abbreviations: MINORS, Methodological Index for Non-Randomized Studies; RoB 2, Risk of Bias 2 tool.*

Table 5. Pooled Safety Outcomes of Atezolizumab in Ovarian Cancer.

Safety outcome	Studies, k (arms)	Events / total	Primary GLMM, % (95% CI)	Leave-one-out range, %	I^2, %	95% prediction interval, %
Grade ≥3 AE	10 (11)	1312 / 1699	66.5 (53.0–77.8)	62.0–68.8	93.7	21.4–93.6
TRAE, grade ≥3	8 (8)	851 / 1625	39.5 (22.2–59.8)	34.2–46.1	97.7	3.4–92.3
Serious AE (SAE)	6 (6)	572 / 1180	38.5 (24.8–54.3)	34.4–45.6	93.9	7.2–83.4
AE-related discontinuation	9 (10)	295 / 1473	11.6 (6.6–19.7)	10.0–14.5	89.6	1.9–47.5
Grade 5 / treatment-related death	12 (14)	33 / 1738	1.8 (1.1–2.9)	1.4–1.9	18.4	0.7–4.2

Abbreviations: *AE, adverse event; CI, confidence interval; GLMM, generalized linear mixed model; SAE, serious adverse event; TRAE, treatment-related adverse event.*

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Table 6. Summary of Findings with GRADE Domain Assessments.

Outcome	No studies	Certainty assessment							№ patients (intervention / comparator)	Effect (95% CI)	Certainty (GRADE)	Impor-tance
		Study design / Starting certainty	Analysis model	Risk of bias	Incon-sistency	Indirect-ness	Impre-cision	Other consi-derations				
Comparative efficacy — time-to-event (hazard ratios)												
Progression-free survival	5	RCT / High	IV random-effects (REML, Knapp–Hartung)	not serious	not serious	not serious	not serious	none	1,562 / 1,364	HR 0.88 (0.83–0.93)	⊕⊕⊕⊕ **High**	Critical
Progression-free survival (PD-L1-positive)	4	RCT High	IV random-effects (REML, Knapp–Hartung)	not serious	not serious	not serious	not serious	none	686 / 611	HR 0.82 (0.76–0.89)	⊕⊕⊕⊕ **High**	Critical
Overall survival	4	RCT / High	IV random-effects (REML, Knapp–Hartung)	not serious	not serious	not serious	not serious	none	1,355 / 1,155	HR 0.86 (0.78–0.96)	⊕⊕⊕⊕ **High**	Critical
Overall survival (PD-L1-positive)	3	RCT High	IV random-effects (REML, Knapp–Hartung)	not serious	not serious	not serious	serious	none	610 / 538	HR 0.83 (0.71–0.98)	⊕⊕⊕◯ **Moderate**	Critical
Comparative efficacy — response (risk ratio)												
Objective response rate	5	RCT / High	IV random-effects (REML, Knapp–Hartung)	not serious	very serious	not serious	serious	none	1,155 / 933	RR 0.88 (0.52–1.49)	⊕◯◯◯ **Very Low**	Important
Comparative safety (risk ratios)												
Any-grade adverse event	3	RCT / High	IV random-effects (REML, Knapp–Hartung)	not serious	not serious	not serious	not serious	none	1,130 / 1,139	RR 1.00 (1.00–1.00)	⊕⊕⊕⊕ **High**	Important
Serious adverse event (vs comparator)	3	RCT / High	IV random-effects (REML, Knapp–Hartung)	not serious	not serious	not serious	not serious	none	1,130 / 1,139	RR 1.32 (1.05–1.67)	⊕⊕⊕⊕ **High**	Critical
Immune-related AE, any grade	4	RCT / High	IV random-effects (REML, Knapp–Hartung)	not serious	serious	not serious	not serious	none	1,538 / 1,340	RR 1.57 (1.12–2.20)	⊕⊕⊕◯ **Moderate**	Important
Immune-related AE, grade ≥3	3	RCT / High	IV random-effects (REML, Knapp–Hartung)	not serious	not serious	not serious	serious	none	1,331 / 1,131	RR 2.23 (1.05–4.74)	⊕⊕⊕◯ **Moderate**	Critical
Single-arm safety — pooled proportions of the atezolizumab arm												
Grade ≥3 AE (pooled proportion)	10	Single-arm / Low	Binomial GLMM	not serious	Serious	not serious	not serious	none	1,699 / –	66.5% (53.0–77.8)	⊕◯◯◯ **Very Low**	Important
Treatment-related AE, grade ≥3 (pooled proportion)	8	Single-arm / Low	Binomial GLMM	not serious	very serious	not serious	Serious	none	1,625 / –	39.5% (22.2–59.8)	⊕◯◯◯ **Very Low**	Important
Serious AE (pooled proportion)	6	Single-arm / Low	Binomial GLMM	not serious	very serious	not serious	not serious	none	1,180 / –	38.5% (24.8–54.3)	⊕◯◯◯ **Very Low**	Critical
AE-related treatment discontinuation (pooled proportion)	9	Single-arm / Low	Binomial GLMM	not serious	very serious	not serious	Serious	none	1,473 / –	11.6% (6.6–19.7)	⊕◯◯◯ **Very Low**	Important
Grade 5 / treatment-related death (pooled proportion)	12	Single-arm / Low	Binomial GLMM	not serious	not serious	not serious	not serious	none	1,738 / –	1.8% (1.1–2.9)	⊕⊕◯◯ **Low**	Critical

Certainty (GRADE): *⊕⊕⊕⊕ High · ⊕⊕⊕◯ Moderate · ⊕⊕◯◯ Low · ⊕◯◯◯ Very Low. Each domain is rated not serious / serious (−1) / very serious (−2). RCT outcomes start High; single-arm pooled proportions start Low.*

Abbreviations: *AE, adverse event; CI, confidence interval; GLMM, generalized linear mixed model; GRADE, Grading of Recommendations Assessment, Development and Evaluation; HR, hazard ratio; IV, inverse variance; PD-L1, programmed death-ligand 1; RCT, randomized controlled trial; REML, restricted maximum likelihood; RR, risk ratio*

4. Discussion

Standard first-line management of OC pairs primary debulking surgery with paclitaxel and carboplatin, reserving neoadjuvant chemotherapy and interval debulking for patients unfit for upfront resection [4]. Maintenance bevacizumab and PARP inhibitors followed, though their benefit concentrates in BRCA1/2-mutated and homologous recombination-deficient tumors [10]. PD-1/PD-L1 inhibitors occupy a biomarker-selected niche in mismatch repair-deficient, microsatellite instability-high, or high tumor mutational burden disease [2]. Atezolizumab is given with bevacizumab or chemotherapy rather than alone, since monotherapy produces limited activity in this immunologically cold tumor, where low mutational burden and abundant regulatory T cells and tumor-associated macrophages constrain T-cell responses [3]. This carries appreciable toxicity, with treatment-related events in roughly 71% of patients and irAE in 29% in recurrent disease [2], dominated by grade 1-2 thyroid dysfunction, fatigue, nausea, and fever [11], and all-grade hypertension near 31% when bevacizumab is added [7].

The present meta-analysis found that atezolizumab lowered the hazard of progression (HR 0.88, 95% CI 0.83 to 0.93) and death (HR 0.86, 95% CI 0.78 to 0.96), each with zero heterogeneity. The individual phase III trials (IMagyn050, ATALANTE) were sized for larger effects, so their concordant sub-threshold estimates missed significance alone; pooling resolves a survival benefit no single trial could establish. Class-level reviews returned overall nulls because they combined pharmacologically distinct antibodies and mixed monotherapy with combination regimens. Vida et al. pooled ten randomized trials and found no overall effect (PFS HR 0.98, 95% CI 0.85 to 1.12; I^2 = 67%) [10], and Ahmadi et al. reported survival intervals crossing unity (PFS HR 0.82; OS HR 0.85) [3]. Ahmadi's network meta-analysis nonetheless ranked checkpoint inhibitor plus chemotherapy combinations among the highest for survival [3]. The current analysis extends that class-level signal to atezolizumab specifically, converting a ranking of mixed agents into a homogeneous, significant estimate for a single antibody given on a chemotherapy or bevacizumab backbone.

Expression of PD-L1 has been proposed as a predictive biomarker for checkpoint blockade in ovarian cancer. The evidence regarding this matter is mixed: one meta-analysis reported a significant PFS benefit with PD-1/PD-L1 inhibitors plus chemotherapy in PD-L1-positive patients (HR 0.65, 95% CI 0.46-0.92) [3], while a separate pooled analysis of ten randomized trials across multiple anti-PD-1 and anti-PD-L1 agents found no significant PFS benefit in this subgroup (HR 0.91, 95% CI 0.79-1.04, I^2 = 64.2%) [10]. That pooled analysis attributed its null result largely to inconsistent PD-L1 thresholds and scoring platforms across the included trials, most of which relied on an arbitrary 1% cutoff without assay harmonization. The problem went beyond the cutoff value itself; an exploratory 5% PD-L1 threshold suggested possible benefit in IMagyn050 (HR=0.64, 95% CI 0.43-0.96) [4], but this signal was not replicated in the FIRST trial despite using the same 5% cutoff, because the two trials scored PD-L1 differently (tumor area proportion versus immune cell score) [10]. The PD-L1-positive findings in the current analysis (PFS HR 0.82, 95% CI 0.76-0.89; OS HR 0.83, 95% CI 0.71-0.98), both without heterogeneity, are more in line with a differential benefit in PD-L1-positive patients than with the null pooled estimate described above. This remains hypothesis-generating, as no formal interaction testing was performed, and confirmation would require standardized PD-L1 assays.

The survival benefit did not extend to ORR in this review, which showed no difference between arms (RR 0.88, 95% CI 0.52 to 1.49). This dissociation may reflect checkpoint blockade acting on the durability of disease control rather than tumor shrinkage, consistent with the modest single-agent activity reported in prior studies, where pooled monotherapy ORR was only 6.7% versus 36% and 30% for combinations with chemotherapy and anti-angiogenic agents, respectively [2]. Prior studies also report that response varies by treatment line and platinum status: ORR was as low as 11.6% in heavily pretreated recurrent disease, and as high as 44% with select combination regimens in platinum-resistant patients [1,3]. This variability likely contributes to the heterogeneity in the pooled ORR estimate (I^2 = 92.3%).

This review demonstrated identical any-grade AEs between arms (RR 1.00), but atezolizumab raised SAEs (RR 1.32, 95% CI 1.05 to 1.67), any-grade irAE (RR 1.57, 95% CI 1.12 to 2.20), and grade ≥3 irAE (RR 2.23, 95% CI 1.05 to 4.74). The excess is immune-mediated and consistent with a meta-analysis of atezolizumab plus bevacizumab that reported 14.1% grade 3 hypertension [7]. A modest survival gain comes at roughly double the risk of a high-grade immune event.

Grade ≥3 rates are lower for less intensive regimens, at 32% for single-arm pembrolizumab [11], 15% in endometrial cancer [26], and 5.4% for tarlatamab in small-cell lung cancer [8]. Against that range, the atezolizumab arm in the present analysis reached 66.5% for grade ≥3 AEs, with 38.5% for SAEs, 11.6% for treatment discontinuation, and 1.8% for treatment-related death. That ordering places the excess with the chemotherapy and bevacizumab backbone rather than the antibody. Fatal toxicity stayed below 2%, and discontinuation near 12% marks the practical limit on tolerability.

Unlike prior reviews, which appraised study quality but did not grade the certainty of their pooled estimates [1,11], the present analysis paired GRADE with RoB 2 and MINORS assessment, allowing the survival benefit to be reported with an explicit certainty rating

Our meta-analysis has several limitations. First, the survival estimates mainly rest on combination trials, so atezolizumab cannot be separated from its backbone. Second, a few large phase III trials dominate the pooled result, so the low heterogeneity may reflect their weight rather than broad replication. Third, OS was immature in several trials and may attenuate with longer follow-up. Finally, enrollment was largely restricted to good performance status (ECOG 0 to 1, 97.4%), limiting generalizability to frail patients common in recurrent disease.

5. Conclusion

Adding atezolizumab to a chemotherapy or bevacizumab backbone in stage 3 and 4 ovarian cancer was associated with a small survival benefit, driven by delayed progression rather than tumor regression, at the cost of increased immune-related toxicity. As the effect was modest and inseparable from its backbone, current evidence may not support routine use.

Declaration

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