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REVIEW

Toripalimab in Esophageal Cancer: A Systematic Review and Meta-Analysis

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Abstract

Background Esophageal cancer (EC) remains a highly aggressive malignancy with a poor prognosis despite advancements in treatment. Toripalimab, a PD-1 inhibitor, has demonstrated the potential to improve clinical outcomes. This systematic review and meta-analysis assess the efficacy and safety of Toripalimab in EC.

Methods Following PRISMA 2020 guidelines, we conducted a systematic review and meta-analysis, searching PubMed, Embase, Scopus, ScienceDirect, and Google Scholar up to January 2025. Eligible studies evaluated Toripalimab in esophageal cancer, including randomized controlled trials and non-randomized controlled trials. Primary outcomes included overall survival (OS), progression-free survival (PFS), and objective response rate (ORR), while safety outcomes assessed treatment-related adverse events. Data were synthesized using random-effects models, with heterogeneity evaluated via Cochrane's Q and I^2 statistics.

Results The pooled analysis included six studies involving 678 patients. Toripalimab demonstrated promising efficacy, with a Complete Response (CR) rate of 33%, Partial Response (PR) rate of 36%, pathological complete response (pCR) rate of 30%, and major pathological response (MPR) rate of 46%. The R0 resection rate was 87%, while OS and PFS rates were reported at 78% and 50%, respectively. Anemia (56%), alopecia (54%), leukopenia (54%), and fatigue (30%) were the most frequently reported adverse effects. Other common adverse effects included nausea (29%), constipation (18%), and vomiting (20%).

Conclusions Toripalimab demonstrates significant potential in treating esophageal cancer, with favorable response rates and survival outcomes. However, the high incidence of adverse effects highlights the need for supportive care and ongoing research. While based on limited sample sizes and single-arm studies that may introduce bias and affect generalizability in this review, we provide valuable preliminary insights into toripalimab's potential, highlighting the need for larger randomized trials to build on these findings.

Keywords Toripalimab · PD-1 inhibitors · Esophageal cancer · Immunotherapy · Clinical outcomes · Adverse effects

Introduction

Esophageal cancer (EC) is a cancer that is aggressive and has a concerning prognosis. In 2022, about 511,054 people were diagnosed with esophageal cancer worldwide, with 445,391 dying from the condition. The age-standardized incidence rates (ASIR) and age-standardized mortality rates (ASMR) for esophageal cancer were 5.00 and 4.30 per 100,000, respectively. In comparison to 2022, it is estimated that by 2050, the prevalence of new esophageal cancer cases will increase by approximately 80.5%, while mortality will rise by 85.4% as a result of aging and population growth [1]. In the United States, the 5-year overall survival rate is around 20% across all stages [2]. EC comprises two primary histological subtypes: esophageal squamous cell carcinoma (ESCC) and esophageal adenocarcinoma (EAC), each with distinct genetic mutations and treatment responses, complicating the development of universal therapies [3].

Treatment for EC has advanced, yet several challenges remain. Traditional approaches, including surgery, chemotherapy, and radiotherapy, continue to be the cornerstone

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of management. However, those therapies cause moderate intensive care-related problems that impact health-related quality of life (HRQoL) [3–6]. A recent review underscores the difficulties in treating ESCC due to its poor prognosis and limited treatment options [7]. Despite progress, current therapies often fall short of providing patients with long-term survival and quality of life.

Recent advancements in immunotherapy have significantly transformed the treatment landscape of esophageal cancer (EC), particularly through the immune checkpoint inhibitors (ICIs) that target PD-1 and PD-L1 pathways. These therapies have shown promising potential in improving patient outcomes and are increasingly being recognized as a key component in both current and future management strategies for EC [8, 9].

Toripalimab is a humanized anti-PD-1 monoclonal antibody developed by Shanghai Junshi Bioscience. Toripalimab was approved by the Food and Drug Administration (FDA) in October 2023 as the first nasopharyngeal carcinoma immunotherapy [10]. It binds to the programmed death protein 1 (PD-1) receptor, blocking its interaction with PD-L1 and PD-L2 ligands, thereby enhancing T-cell activation and immune responses against cancer cells [11, 12]. Toripalimab has shown significant clinical benefit, particularly in multiple cancer types, including ESCC [13]. It has a higher binding affinity to PD-1 than other drugs and induces stronger inflammatory cytokine responses, supporting its potential as a potent immune checkpoint inhibitor [12, 14]. Recent studies show that combining Toripalimab with chemotherapy significantly enhances disease control and survival outcomes, demonstrating its effectiveness in advanced esophageal cancer [14–16].

These findings highlight the significance of Toripalimab as a treatment in oncology. The present study reviews Toripalimab as a potential treatment for EC. It focuses on the safety and efficacy of the drug, therapeutic results, and adverse effects of the treatment.

Methodology

Data Sources & Search Strategy

This systematic review and meta-analysis was conducted following the 2020 PRISMA guidelines. A comprehensive search was performed across several databases, including PubMed, Embase, Scopus, ScienceDirect, and Google Scholar, up to January 2025. The search strategy included a combination of keywords such as"Toripalimab,""esophageal cancer,""PD-1 inhibitors,""immunotherapy,"and"clinical trial."to ensure covering many studies relevant to Toripalimab in treating esophageal cancer.

Eligibility Criteria

The studies included in this review were required to meet specific criteria. Eligible studies involved using Toripalimab as a treatment for esophageal cancer and included clinical trials, cohort studies, case–control studies, and other relevant observational studies. The studies were required to provide safety results, including side effects and efficacy outcomes, as well as overall survival and progression-free survival. Observational research and randomized controlled trials were also taken into account. Ineligible studies did not involve Toripalimab or esophageal cancer, non-peer-reviewed articles, editorials, case reports lacking substantial data, and animal or in vitro studies. Additionally, studies not published in English were excluded unless translations were available.

Study Selection

Study selection was performed using a two-step approach. Titles and abstracts were first evaluated to find the relevant studies. Subsequently, full-text publications were obtained, and the inclusion and exclusion criteria were used to determine their eligibility. The senior author was consulted when there was a disagreement between the other authors.

Data Extraction

The data was extracted from the included studies using a standardized form. The extracted information included study characteristics such as authors, year of publication, study design, participants'demographics, and sample size. Intervention details, including dosage and administration schedule, were also recorded, along with efficacy outcomes (overall survival, progression-free survival) and safety outcomes (adverse effects). Data was organized into digital spreadsheets, and discrepancies were discussed with the senior author to ensure accuracy.

Data Synthesis and Outcome Measures

Overall survival (OS) was the main measure used to assess how effective Toripalimab is in treating esophageal cancer. Additional metrics of clinical activity were also assessed, including objective response rate (ORR) and progression-free survival (PFS) to assess Toripalimab's effectiveness in treating esophageal cancer. The safety characteristics of Toripalimab were established by evaluating its side effects, which included nausea, exhaustion, and other toxicities

connected to treatment. Examining the investment and duration of the adverse events.

Risk of Bias Assessment

The listed studies'methodological quality was evaluated using appropriate tools for the study design. The ROBINS-I Risk of Bias Tool for Non randomized controlled trials (NRCTs) and the Cochrane Risk of Bias Tool for the Randomized controlled trials (RCT). Various domains, including randomization, blinding, and outcome reporting, were used to assess the risk of bias. A risk-of-bias visualization was provided to improve transparency in evaluating study quality.

Certainty Assessment

A sensitivity analysis was performed for each outcome in the meta-analysis to evaluate the reliability of the findings. This approach strengthened the results by preventing over-reliance on the outcome of any single study.

Statistical Analysis

The meta-analysis was conducted using RStudio. For the single-arm analysis, the Inverse Variance method was applied through the meta package. The overall summary is presented as a proportion with its 95% confidence interval (CI).Subgroup analysis considered for Overall response rate according to Complete response, Partial response, Stable response, and Progressive response, and considered for all adverse effects according to Any Grades, Grades 1–2 and ≥ Grade 3.

Statistical heterogeneity was assessed via I^2 and Cochrane Q test values, where an I^2 value of < 25% is low, 25–50% is moderate, and > 75% is a high degree of heterogeneity. Cochrane Q test with a p-value of < 0.05 was considered significant for heterogeneity. The random effects model was used in all analyses regardless of heterogeneity to provide more robust outcomes.

Results

Search Results and Study Selection

A total of 203 studies were identified through database searches. After removing duplicates, 190 articles were screened by title and abstract. From this initial screening, 173 articles were excluded as they did not meet the inclusion criteria, leaving 17 studies for full-text evaluation. Of these, 12 were excluded due to insufficient data on Toripalimab use in esophageal cancer, resulting in the inclusion of six studies in this systematic review and meta-analysis. The PRISMA flowchart detailing the selection process is shown in (Fig. 1).

Baseline Characteristics of the Included Studies

The included studies consisted of five non-randomized controlled trials (NRCT) and one randomized controlled trial (RCT), with a total of 167 patients. The median age across studies was 60.9 years, with an age range of 24–96 years. The majority of the participants were males (135 males, 32 females). Most tumors were located in the middle esophagus (57%), with fewer cases in the upper and lower esophagus. The average treatment duration was 10.7 months (range: 1–20 months), and the mean follow-up period was 22.4 months (range: 12–28 months). A detailed summary of the baseline characteristics is presented in (Table 1).

Risk of Bias Assessment

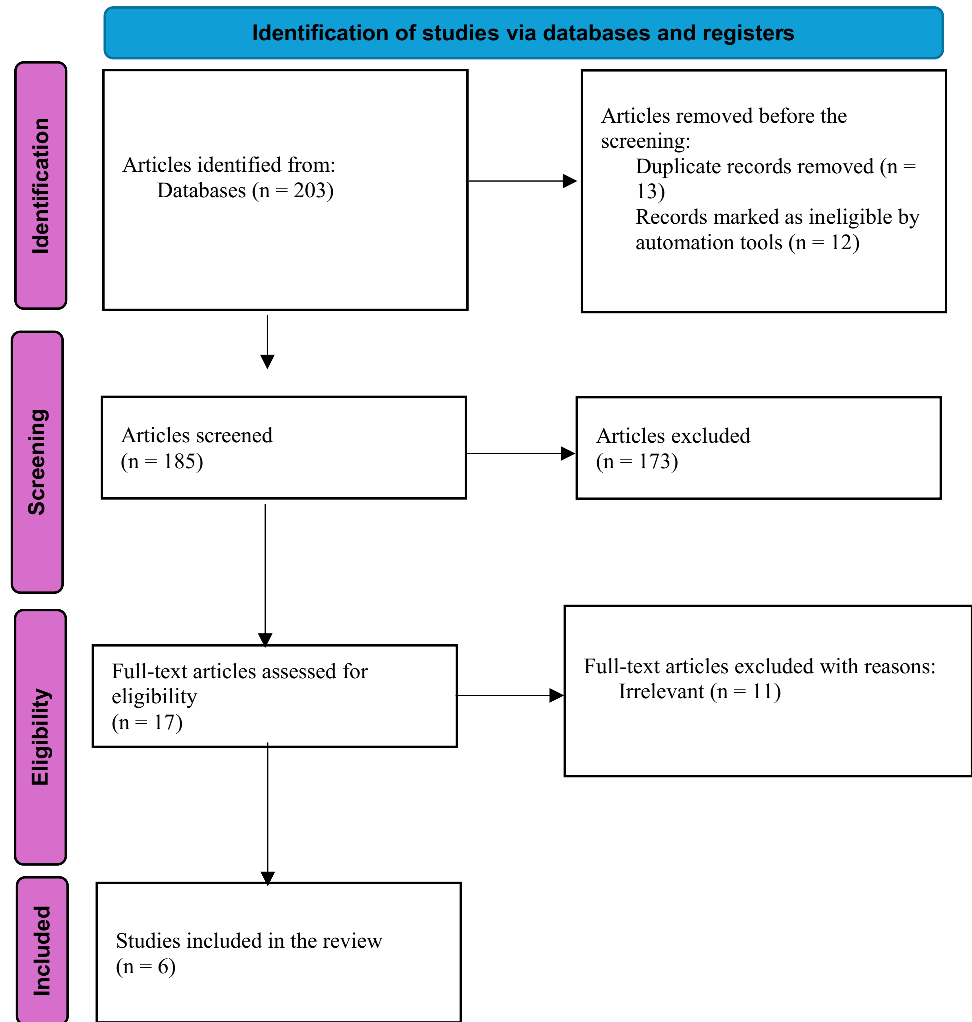
The risk of bias was assessed using the ROBINS-I Risk of Bias Tool for NRCTs and the Cochrane Risk of Bias Tool for the RCT. The results are summarized in (Figure S1-S4). Common issues included a high risk of bias due to confounding factors, incomplete data, and selection of participants in some studies. While the majority of studies had low bias in intervention classification and outcome measurement, concerns were raised regarding randomization processes. Five studies were classified as having an overall high risk of bias, emphasizing the need for caution in interpreting the findings.

Outcomes

Treatment Efficacy and Surgical Outcomes:

The overall complete response rate assessed by six studies [17–22], showed that 405 of 678 patients who underwent neoadjuvant therapy with Toripalimab have expressed a complete response with an overall proportion of 0.33, 95% CI [0.05; 0.82], the heterogeneity of this outcome was considered high ($Chi^2 = 44.28$, $I^2 = 88.7\%$). The overall partial response rate assessed by five studies [17–21], showed that 67 of 164 patients expressed partial response with an overall proportion of 0.36, 95%, CI [0.15; 0.65], the heterogeneity of this outcome is considered high ($Chi^2 = 26.72$, $I^2 = 85\%$). The overall stable response rate assessed by three studies [17, 19, 20], showed that 33 of 100 patients expressed a stable response with a proportion of 0.33, 95% CI [0.25; 0.43], the heterogeneity of this outcome was considered low ($Chi^2 = 0.72$, $I^2 = 0\%$). While the overall progression response rate assessed by three studies [17, 19, 20], showed 3 of 100 patients expressed the progression response with an overall proportion was 0.04, 95% CI [0.01; 0.10], the heterogeneity of this outcome was

Fig. 1 Prisma Flowchart



considered low ($Chi^2 = 0.21$, $I^2 = 0\%$), (Fig. 2). The objective response rate assessed by two studies [19, 20], showed an overall proportion of 0.58, 95% CI [0.33; 0.79], and the heterogeneity of this outcome was considered moderate ($Chi^2 = 2.5$, $I^2 = 59.9\%$). The major pathological response (MPR) assessed by four studies [17, 19–21], showed 55 of 120 patients have an MPR with an overall proportion of 0.46, 95% CI [0.24; 0.69], and the heterogeneity of this outcome is considered moderate ($Chi^2 = 11.88$, $I^2 = 74.7\%$). pCR assessed by five studies [17–21], showed 53 of 164 patients have a pathological complete response with an overall proportion of 0.30, 95% CI [0.16; 0.50], the heterogeneity of this outcome is considered moderate ($Chi^2 = 15.85$, $I^2 = 74.8\%$). R0 resection assessed by three studies [17, 18, 20], showed 110 of 120 patients achieved R0 resection with an overall proportion of 0.87, 95% CI [0.70; 0.95], the heterogeneity of this outcome is considered moderate ($Chi^2 = 7.22$, $I^2 = 72.3\%$). (Figures S5- S9).

Survival Metrics

Overall survival assessed by six studies [17–22], showed that 476 of 678 patients survived after neoadjuvant treatment, with an overall proportion of 0.78, 95% CI [0.67; 0.86]. The heterogeneity of this outcome is considered moderate (Chi2 = 15.78, I2 = 68.3%) (Fig. 3). Pathological regression-free survival assessed by three studies [17, 21, 22], showed an overall proportion of 0.50, 95% CI [0.26; 0.74]. The heterogeneity of this outcome is considered high ($Chi^2 = 36.13$, $I^2 = 94.5\%$).

Adverse Events

The safety profile of Toripalimab was evaluated by pooling data on treatment-related adverse events from the included studies. Treatment-related AEs of any grade, as well as those classified as Grade 1–2 and ≥ Grade 3 during the

Table 1 The baseline characteristics of the included studies

Study characteristics	Author, Year		Zhang, 2023	Chen, 2023	Gao, 2022	He, 2022	Ning jiang, 2024	Zi-Xian Wang, 2024
	Country		China	China	China	China	China	China
	Intervention model		Single arm	Single arm	Single arm	Single arm	Single arm	multi-center, randomize
	Sample size		60	44	20	20	20	514
	Follow-up duration sub-group		20 months	28 months	12 months	N/A	24.5 months	22 months and 2 days
	Treatment Setting		Neoadjuvant	Neoadjuvant	Neoadjuvant	Neoadjuvant	Neoadjuvant	Palliative
Population criteria	Age	Median	60.9	60	58.3	61.4	65	63 arm 1 and arm 2
		Range	(45–75)	(24–96)	(49–69)	(51.5–72.3)	(37–72)	(20–75)
	Sex	Male	51 (85%)	34 (%77)	17 (85.0%)	15(75%)	18(78%)	217(84.4%)
		Female	49(81.67)	10 (%23)	3 (15.0%)	5(25%)	5(22%)	40(15.6%)
Clinical stage	I		1 (1.67%)	1 (%2)	4 (33.3%)	N/A	N/A	3(1.2%)
	II		9 (15%)	4 (9%)	1 (8.3%)	N/A	5(22%)	3(1.2%)
	III		28 (46.67%)	30 (68%)	7 (58.3%)	16(80%)	9(39%)	22(8.6%)
	IV		22 (36.66%)	9 (20%)	0 (0.0)	4(20%)	9(39%)	231(89.9%)
Tumor location	Upper		N/A	2 (4%)	2 (10%)	N/A	4(17%)	27(10.5%)
	Middle		41(68.3)	21 (48%)	13 (65%)	14(70%)	13(57%)	80(31.1%)
	Lower		19(31.67%)	21 (48%)	6(26)	6(30%)	6(26%)	83(32.3%)

neoadjuvant treatment period, are shown in (Table 2). Treatment-related AEs were common, and most being graded 1–2 in severity. The most common AEs were Anemia, with an overall proportion of 95% CI 0.60 [0.42; 0.75], Among the 296 patients who experienced anemia, 266 cases were Grade 1–2.

Alopecia was also frequently reported, with 424 patients affected. Of these, all 188 recorded cases were classified as Grade 1–2, with an overall proportion of 0.51 (95% CI: 0.25–0.76).

The overall proportion (95% CI) of Leukopenia, Neutropenia, and Nausea were 0.58 [0.32; 0.80], 0.49 [0.17; 0.82], and 0.56 [0.29; 0.80], respectively. The most frequent grade 3 AEs was Neutropenia with an overall proportion of 95% CI 0.26 [0.07; 0.60]. (Figures S10- S29).

Discussion

Despite improvements in therapeutic strategies, EC remains a significant global health challenge because of its aggressive nature and poor prognosis. ICIs, such as toripalimab, represent an important milestone in the treatment of EC. This review assesses the efficacy and toxicity profiles of Toripalimab as a treatment option for esophageal cancer. It pays particular attention to response rates, pathological outcomes, surgical outcomes, mortality and complication rates, and other target effects.

This analysis shows that Toripalimab has a significant clinical and pathological response in patients diagnosed with EC. The overall response rate (ORR) was 0.58 (95% CI [0.33; 0.79]), which includes a 0.33 complete response (CR) and a 0.36 partial response (PR) [17–22], underscores the potential of Toripalimab to induce meaningful tumor regression. Importantly, the majority of the studies included in this analysis evaluated toripalimab in the neoadjuvant setting, aiming to improve resectability and pathological response prior to surgery. One exception is Wang et al. [22], which investigated toripalimab in the palliative setting for metastatic or unresectable disease.

These findings are particularly significant from the perspective of EC, where response rates to conventional therapies such as chemotherapy and radiation remain suboptimal. For instance, studies examining the impact of various preoperative radiation doses in esophageal cancer patients found that even with higher doses, many patients did not achieve a complete pathologic response, and outcomes remained unsatisfactory [23, 24]. Furthermore, the major pathological response (MPR) was seen in 0.46 of cases (95% CI [0.24; 0.69]), with a pathological complete response (pCR) achieved in 0.30 of patients (95% CI [0.16; 0.50]). Such findings suggest that Toripalimab is a promising therapeutic agent and increases the chance of optimal surgical outcomes.

Pathological complete response (pCR) refers to the total absence of residual tumor in both the esophagus and the resected lymph nodes. In contrast, MPR has no more than

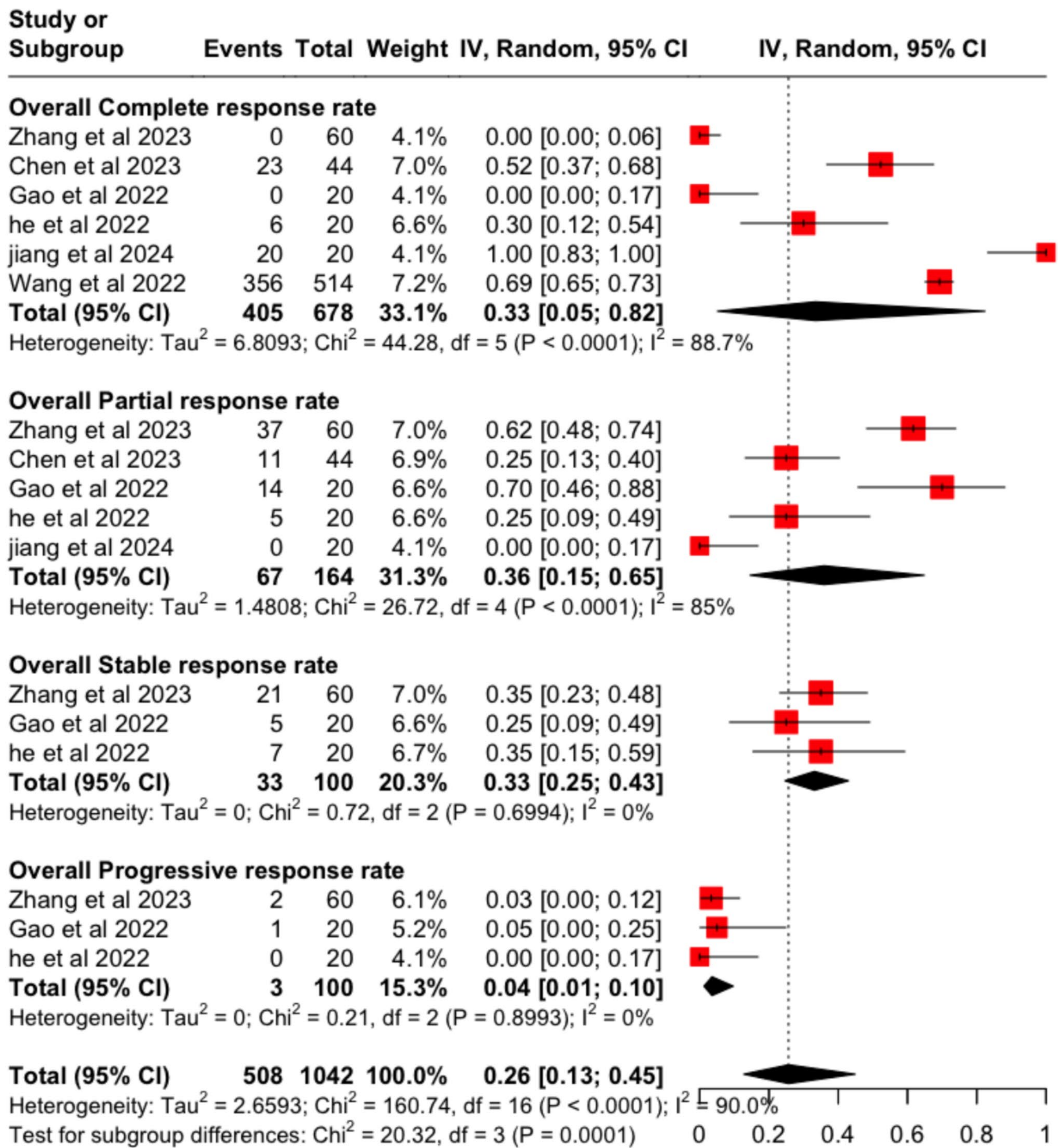


Fig. 2 Overall Response Rate

10% residual viable tumor cells. Zhang et al. (2023) [17] considered PD-L1 high if CPS ≥ 10, with no significant difference in PD-L1 expression regarding overall survival (OS), progression-free survival (PFS), and disease control rate (DFS). About Chen et al. (2023) [18], the exploratory endpoint was the association between PD-L1 expression and treatment efficacy. OS and disease-free survival were not reported in this study due to data immaturity. The pCR rate was slightly higher in patients with PD-L1 CPS ≥ 10 compared to those with PD-L1 CPS < 10, but the difference was not statistically significant (55% vs. 47%, P = 0.88). Similarly, no significant difference in pCR rates was observed between patients with PD-L1 CPS ≥ 1 and those with PD-L1 CPS < 1. Furthermore, this study compared pCR rates and

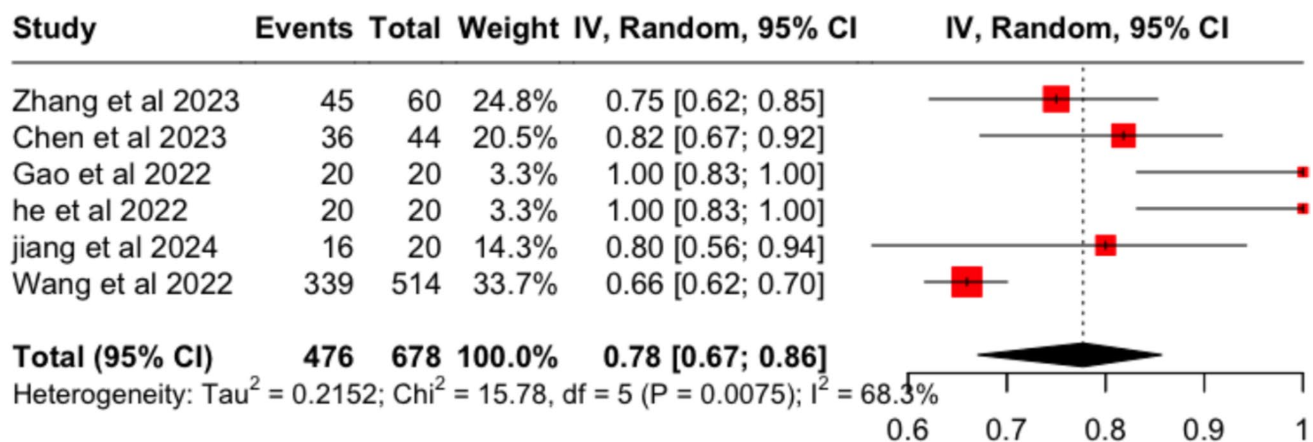


Fig. 3 Overall Survival

TRG scores among patients with different PD-L1 expression levels at cut-offs of 1% and 10%, according to TPS. However, none of the differences were statistically significant. Regarding He et al. (2022) [20], 7 (39%) patients had a CPS of PD-L1 expression greater than 1. The CPS of PD-L1 expression decreased in 3 patients (3/17, 18%) and increased in 6 patients (6/17, 35%), including 5 patients whose CPS changed from 0 to ≥ 1 (5/6, 83%). Both of 2 PD-L1 expression values (TPS and CPS) showed no statistical difference before and after treatment. In the study by Jiang et al. (2024) [21], there was no difference in the pCR rate between patients with CPS $\geq 5\%$ and those with CPS $< 5\%$ ($p = 0.315$).

Notably, the studies by Zhang et al., Chen et al., and He et al. [17, 18, 20] achieved a high R0 resection rate of 0.87 (95% CI [0.70; 0.95]), which suggests that Toripalimab is an effective neoadjuvant therapy. This treatment could potentially increase long-term survival rates by reducing the risk of residual disease. Combined with surgery, this immunotherapeutic approach is an effective strategy for achieving curative outcomes in locally advanced EC, as observed in previous studies that demonstrated the effectiveness of combining neoadjuvant anti-PD-1 therapies with chemotherapy for treating EC. One study showed a primary pathological response in 75% of tumors [25], while another found a pathologic complete response (pCR) rate of 33.3% and an R0 resection rate of 96.3% [26]. Additionally, a phase 3 trial reported higher pCR outcomes than traditional chemotherapy, indicating that PD-1 inhibitors can significantly enhance the effectiveness of neoadjuvant treatment in EC [27].

In support of these findings, two recent network meta-analyses have provided comparative evidence regarding the effectiveness of PD-1 inhibitors in advanced oesophageal cancer. They found that toripalimab, in combination with chemotherapy, demonstrated the largest overall survival benefit (HR: 0.58; 95% CI: 0.43–0.78) compared to chemotherapy alone. Although all PD-1 inhibitors studied, nivolumab, pembrolizumab, sintilimab, camrelizumab, tislelizumab, and serplulimab, improved outcomes, sintilimab and camrelizumab ranked best for progression-free survival, and nivolumab for objective response rate. These findings support growing evidence of toripalimab's relative efficacy and safety within the class of immunotherapies [28, 29].The survival metrics in this review add to the evidence that Toripalimab effectively extends life expectancy in patients with EC. The overall survival (OS) rate of 0.78 (95% CI [0.67; 0.86]) and progression-free survival (PFS) rate of 0.50 (95% CI [0.26; 0.74]) are much higher than historical EC benchmarks. However, it is crucial to interpret these outcomes within the context of the therapeutic setting. In neoadjuvant studies, such as those by Gao et al. and He et al. [19, 20], Toripalimab was used before surgical resection with curative intent. These studies reported favorable outcomes, including extended progression-free intervals and high rates of complete and major pathological responses, suggesting that immunotherapy in the neoadjuvant setting can improve resectability and potentially long-term survival.

In contrast, the JUPITER-06 trial by Wang et al. [22] evaluated Toripalimab in a palliative setting for advanced or metastatic esophageal cancer. This large, randomized phase 3 trial showed a significant overall survival benefit with Toripalimab plus chemotherapy compared to chemotherapy alone (HR: 0.58; 95% CI: 0.43–0.78). These findings underscore its value in prolonging life even in patients with unresectable disease [19, 20].

By enhancing tumor regression and enabling curative surgical interventions, Toripalimab contributes to prolonged disease control and survival. These results align with previous studies on anti-PD-1 therapies, such as pembrolizumab and nivolumab, which enhance tumor regression and facilitate curative surgical interventions, leading to prolonged

Table 2 Treatment related adverse events

AEs	NO. of Study	Total	Any Grades	Proportion, 95% CI	Chi^2, I^2	Grade 1–2	Proportion, 95% CI	Chi^2, I^2	≥ Grade 3	Proportion, 95% CI	Chi^2, I^2
Anemia	6	424	296	0.61 [0.39; 0.79]	34.66, 85.6%	266	0.60 [0.42; 0.75]	19.15, 73.9%	30	0.05 [0.02: 0.12]	8.13, 38.5%
Leukopenia	5	364	233	0.58 [0.32; 0.80]	23.55, 83%	166	0.46 [0.41; 0.51]	7.23, 44.7%	67	0.15 [0.07: 0.30]	12.56, 68.1%
Neutropenia	4	320	201	0.49 [0.17; 0.82]	29.89, 90%	77	0.24 [0.20; 0.29]	2.34, 0%	124	0.26 [0.07; 0.60]	13.78, 78.2%
Thrombocytopenia	5	404	101	0.22 [0.11; 0.39]	20.38, 80.4%	95	0.21 [0.10: 0.38]	20.59, 80.6%	6	0.02 [0.01: 0.04]	0.77, 0%
Diarrhea	5	401	82	0.20 [0.15; 0.26]	6, 33.4%	80	0.20 [0.15; 0.25]	4.98, 19.7%	2	0.02 [0.01: 0.05]	5.28, 24.2%
Constipation	5	364	81	0.20 [0.12; 0.32]	9.04, 55.7%	81	0.20 [0.12; 0.32]	9.04, 55.7%	0	0.01 [0.00; 0.04]	2.31, 0%
Nausea	5	380	178	0.56 [0.29; 0.80]	23.05, 82.6%	176	0.55 [0.28; 0.80]	23.32, 82.8%	2	0.02 [0.01: 0.06]	3.96, 0%
vomiting	5	380	117	0.18 [0.08; 0.36]	27.18, 85.3%	112	0.17 [0.08; 0.35]	24.99, 84%	5	0.02 [0.01: 0.04]	0.46, 0%
Esophagitis	2	67	40	0.48 [0.03; 0.97]	22.94, 95.6%	39	0.46 [0.03; 0.96]	21.58, 95.4%	1	0.03 [0.01; 0.11]	0.09, 0%
Rash	4	382	96	0.27 [0.20; 0.36]	6, 50%	80	0.24 [0.15; 0.35]	11.1, 73%	16	0.05 [0.01; 0.22]	25.37, 88.2%
Dermatitis	3	84	21	0.19 [0.06; 0.45]	8.05, 75.2%	20	0.16 [0.04; 0.47]	8.99, 77.8%	1	0.04 [0.01; 0.13]	1.51, 0%
Alopecia	6	424	188	0.51 [0.25; 0.76]	50.4, 90.1%	188	0.51 [0.25; 0.76]	50.4, 90.1%	0	0.01 [0.00: 0.03]	2.37, 0%
Anorexia	3	127	72	0.70 [0.22; 0.95]	10.34, 80.7%	72	0.70 [0.22: 0.95]	10.34, 80.7%	0	0.01 [0.00: 0.06]	0.23, 0%
Weight loss	2	301	92	0.33 [0.23; 0.45]	2.56, 60.9%	84	0.32 [0.19; 0.48]	4.22, 76.3%	8	0.03 [0.02; 0.06]	0.57, 0%
Hypo/Hyperthyroidism	3	127	11	0.09 [0.03; 0.26]	5.72, 65.1%	11	0.09 [0.03: 0.26]	5.72, 65.1%	0	0.01 [0.00: 0.06]	0.23, 0%
Hyperglycemia	3	340	46	0.15 [0.08; 0.25]	5.88, 66%	44	0.14 [0.08: 0.23]	4.85, 58.8%	2	0.01 [0.00; 0.04]	1.71, 0%
Fatigue	6	424	170	0.33 [0.21; 0.48]	21.3, 76.5%	158	0.31 [0.20; 0.46]	21.2, 76.4%	12	0.04 [0.02: 0.07]	3.17, 0%
Fever	3	340	56	0.19 [0.10; 0.32]	6.17, 67.6%	53	0.18 [0.09: 0.32]	6.64, 69.9%	3	0.01 [0.01; 0.03]	0.22, 0%
Arthralgia/myalgia	3	361	106	0.24 [0.02; 0.81]	53.32, 96.2%	103	0.23 [0.02: 0.80]	55.47, 96.4%	3	0.01 [0.00; 0.03]	0.12, 0%
Respiratory Disorder (Pneumonia or pneumonitis)	5	404	31	0.07 [0.04; 0.12]	4.04, 1.1%	15	0.04 [0.03; 0.07]	0.52, 0%	16	0.04 [0.02: 0.08]	3.21, 0%

disease control and improved survival in EC patient's anti-PD-1 treatments, including pembrolizumab and nivolumab, which increase tumor regression and allow curative surgical interventions, leading to longer disease control and improved survival in EC patients [30–33].

Despite the encouraging efficacy results, Toripalimab is associated with side effects that require careful evaluation. Hematological toxicities, such as anemia (0.61), leukopenia (0.58), and neutropenia (0.49), were commonly reported, and these findings are consistent with the known safety profile of PD-1 inhibitors. A recent study also found that anemia and leukopenia are among the most common hematologic immune-related adverse events associated with PD-L1 inhibitors [34]. Non-hematologic adverse events, including Alopecia (0.51) and fatigue (0.33) were also frequent, with the latter having a notable impact on patients'quality of life and treatment adherence. Gastrointestinal toxicities, such as nausea (0.56), constipation (0.20), and vomiting (0.18), highlight the need for supportive care measures to mitigate these side effects [18, 19, 21].

Despite the mild to moderate nature of most adverse events, the cumulative impact of these toxicities cannot be disregarded. PD-L1 inhibitors have been associated with immune-related adverse events (irAEs) that affect multiple organ systems. It could also persist long-term, leading to delay or discontinuation of treatment and even potentially leading to serious complications. Delayed irAEs could also occur, with occasional high-grade severity and leading to fatal outcomes. These toxicities typically lead to decreased energy, emotional distress, and physical impairment, with adverse effects on the quality of life and daily functioning of patients [35, 36]. Effective management of irAEs from PD-1 inhibitors include early detection, accurate grading, and targeted immunosuppressive therapy. Mild irAEs may need monitoring, while moderate to severe cases often require corticosteroids, with resistant cases needing additional immunosuppressants. A multidisciplinary approach is essential for organ-specific toxicities. Early recognition and proactive mitigation strategies are key to maintaining adherence and achieving optimal outcomes [37, 38].

Finally, future studies need to identify predictive biomarkers that can identify people who will benefit the most from Toripalimab with the least severe toxicities.

Limitations

This review has several limitations. The reliance on single-arm studies restricts the capacity to make firm judgments regarding the effectiveness of Toripalimab, as comparisons to control groups were unavailable. This limitation is reflected in the quality assessment of the included studies which were single-arm designs and demonstrated a serious risk of bias due to confounding and incomplete data. Although such limitations are common in non-randomized trials, this requires cautious interpretation and future randomized trials to validate our findings.

Further. The variability in patient epidemiology, treatment protocols, and study designs may also affect the strength and generalizability of the results. Moreover, due to the few included studies, meta-regression or sensitivity analyses might have offered a deeper understanding of the variables affecting results. Nonetheless, these studies provide critical and novel insights into the safety and effectiveness of Toripalimab.

Future Research Recommendations

To better establish the clinical benefit of Toripalimab, subsequent studies should include large multicenter randomized controlled trials with longer follow-ups to assess long-term safety and efficacy more accurately. Comparative trials with other PD-1 inhibitors would help to establish relative therapeutic benefits. Additionally, studies should investigate combination therapies, including Toripalimab with chemotherapy or radiotherapy, to evaluate potential synergistic effects.

Conclusion

This review emphasizes Toripalimab in the treatment of esophageal cancer. Responses were associated with improved survival and a high rate of complete surgical resection, supporting its role as a therapeutic option. Although treatment-related adverse events were frequent, they were manageable with adequate monitoring and supportive care. These results highlight the potential of Toripalimab to improve the outcomes of individuals with EC, and further validation in large randomized clinical trials will help define its place in standard practice.

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