The Efficacy and Safety of PD-1/PD-L1 Inhibitors for Advanced Refractory Esophageal and GE Junction Cancer: A Meta-Analysis

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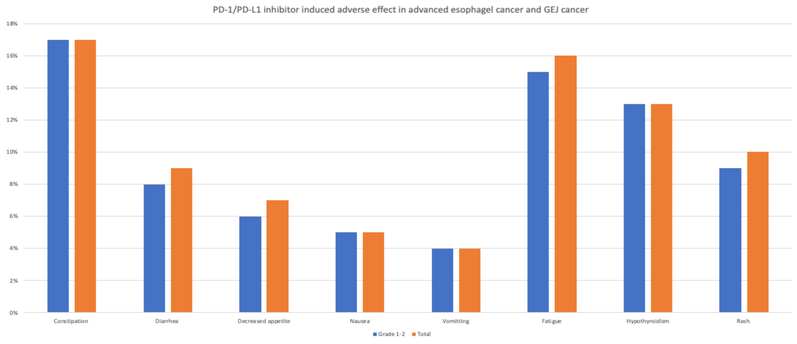
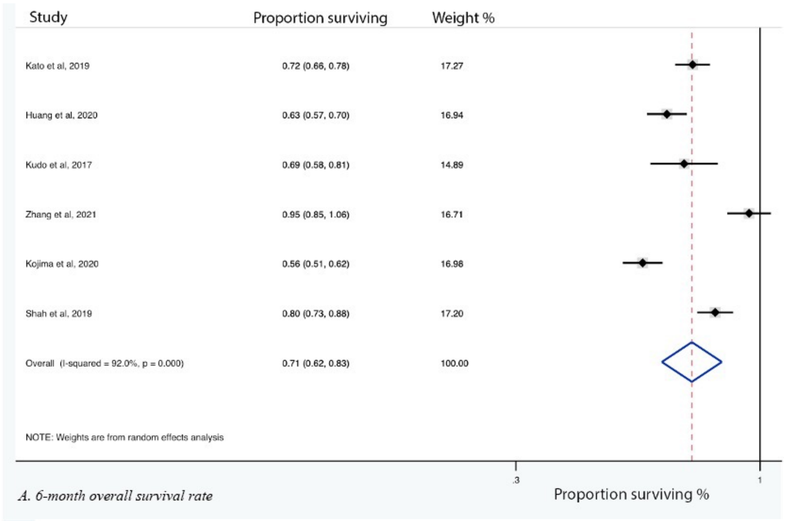
Introduction

- Anti-programmed death-1 (PD-1) and programmed death-ligand (PD-L1) immunotherapy have been studied as adjuvant and neoadjuvant treatment for patients with advanced esophageal or gastro-esophageal junction (GEJ) cancer.
- Our aim was to use the highest quality data available to perform a meta-analysis evaluating their efficacy and safety.

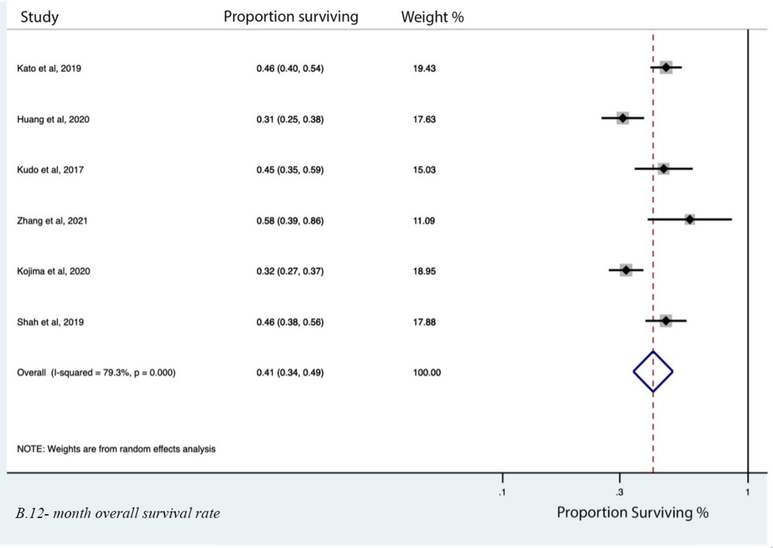
Methods

- We reviewed PubMed, MEDLINE, Embase, and Web of Science Core Collection databases from inception to Aug 1st, 2021, to identify studies evaluating the efficacy and safety profile of PD-1 and PD-L1 inhibitor immunotherapy in the management of advanced refractory esophageal or GEJ cancer.
- Our primary outcome was overall survival. Secondary outcomes were progression-free survival, and objective response including complete response, partial response, stable disease, and progressive disease.
- Adverse effects were characterized according to Common Terminology Criteria for Adverse Events v 4.0.
- Pooled rates with 95% confidence intervals (CI) for all outcomes were calculated using a random-effect model.





A. 6-month overall survival rate



B.12- month overall survival rate

Results

- Literature review identified 12 randomized clinical trial articles and one retrospective chart review study suitable for meta-analysis.
- Most studies were performed in East Asia.
- The median age of participants from all studies ranged from 60 to 65 years.
- The majority of patients included in the studies had stage III or stage IV disease.
- Pooled 6- and 12- month overall survival rates were 71% (95% CI 62%-83%) and 41% (95% CI 34%-49%), respectively (Figure 1). Pooled 6- and 12- month progression-free survival rates were 30% (18%-52%) and 15% (7%-35%), respectively (Figure 1).
- Response rates were as follows: complete response 4% (1%-14%); partial response 30% (17%-52%); stable disease 23% (19%-27%,) and progressive disease 48% (39%-59%).
- The most common side effect was constipation. It occurred in 17% (7%-41%) and was graded 1-2 (mild) in all cases.
- Other common adverse effects were diarrhea, anorexia, nausea, and vomiting (Figure 2).
- The most common non-GI adverse effect was fatigue, with an overall rate of 16% (9%-28%). Fatigue was graded as 1-2 in 94% of cases. The other common non-GI side effects included hypothyroidism and rash.

Conclusions

In summary, use of PD-1/PD-L1 inhibitors provides clinically meaningful rates of survival and response. They demonstrate a well-tolerated safety profile thus supporting their current role as adjuvant or neoadjuvant therapy for advanced esophageal and GEJ cancer.

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