Chemioimmunotherapy versus Immunotherapy for first line treatment of advanced non-small cell lung cancer with a PD-L1 Score of 50-100%

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INTRODUCTION

Anti-PD(L)-1 immunotherapy with or without chemotherapy has shown superior overall survival as first-line treatment for patients with advanced non-small cell lung cancer (aNSCLC) and high tumor expression of PD(L)-1 (PD-L1 score ≥50%). However, evidence on the cross-comparative effectiveness of chemioimmunotherapy versus immunotherapy alone in patients with PD-L1 score ≥50% is limited due to lack of head-to-head efficacy trials making it difficult to decide who can be spared the additional side effects associated with combination therapy.

OBJECTIVE

We sought to compare survival in aNSCLC patients with PD-L1 score ≥50% receiving first-line pembrolizumab with or without chemotherapy.

METHODS

Cohort study of aNSCLC patients with PD-L1 score ≥50% who initiated first-line treatment with pembrolizumab monotherapy or in combination with platinum-based chemotherapy between Oct 24, 2016, and Oct 31, 2021, using the nationwide Flatiron Health electronic health record (EHR) derived de-identified database. Kaplan Meier (KM) curves and Cox regression were used to estimate overall survival and hazard ratios, respectively, for all patients with PD-L1 score ≥50% and in the subgroup of patients with PD-L1 score ≥90%. Multiple imputation was used to impute missing covariates. Propensity score-based inverse probability of weighting (IPW) was used to address confounding by age, race, smoking history, PD-L1 expression, KRAS/BRAF mutation, and EGFR performance status. Because of non-proportionality of hazards, we estimated hazard ratios over the first 6 months and over the entire follow-up period (IPW-adjusted Hazard Ratio [aHR] 0.98, 95% CI 0.86-1.2), but was associated with a survival benefit during the first 6 months (aHR 0.74, 95% CI 0.57-0.97). Similarly, in the subgroup of patients with a PD-L1 score ≥90%, chemioimmunotherapy was associated with no overall survival advantage during the entire follow-up period (aHR 0.99, 95% CI 0.87-1.22), but was associated with a survival benefit during the first 12 months (aHR 0.74, 95% CI 0.57-0.97).

CONCLUSION

Chemioimmunotherapy was associated with no overall survival advantage over immunotherapy alone, although associated with a survival benefit in the first 6 months. Among PD-L1 score ≥90% (subgroup), chemioimmunotherapy was not associated with an overall survival benefit, but associated with a survival benefit in the first 12 months. Providers should carefully weigh the short-term benefits of chemioimmunotherapy over immunotherapy versus their long-term equivalence.

REFERENCES


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RESULTS

3066 subjects met inclusion criteria, of whom 32% received chemioimmunotherapy and 68% received immunotherapy alone. Baseline characteristics well balance post weighting (standardized differences <0.1). Chemioimmunotherapy was associated with no overall survival advantage during the entire follow-up period (IPW-adjusted Hazard Ratio [aHR] 0.98, 95% CI 0.86-1.2), but was associated with a survival benefit during the first 6 months (aHR 0.74, 95% CI 0.57-0.97). Similarly, in the subgroup of patients with a PD-L1 score ≥90%, chemioimmunotherapy was associated with no overall survival advantage during the entire follow-up period (aHR 0.99, 95% CI 0.87-1.22), but was associated with a survival benefit during the first 12 months (aHR 0.74, 95% CI 0.57-0.97).

Figure 1. IPW-adjusted KM Curves of Overall Survival by Pembrolizumab use

Figure 2. IPW-adjusted KM Curves of Overall Survival by Pembrolizumab use among Patients with PD-L1 score ≥90%

*Number of patients remaining in each group at risk at each time point