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

Mohsin Shah, MBBS, MSCE, Melina E Marmarelis, MD, MSCE; Rebecca A. Hubbard, PhD; Ronac Mamtani, MD, MSCE; Sean Hennessy Pharm D, PhD

Affiliations: Department of Biostatistics, Epidemiology & Informatics, University of Pennsylvania; Division of Hematology-Oncology, University of Pennsylvania

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%) compared to chemotherapy alone. However, evidence on the cross-comparative effectiveness of chemoimmunotherapy versus immunotherapy alone in patients with PD-L1 score ≥50% and in those with PD-L1 score ≥90% 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

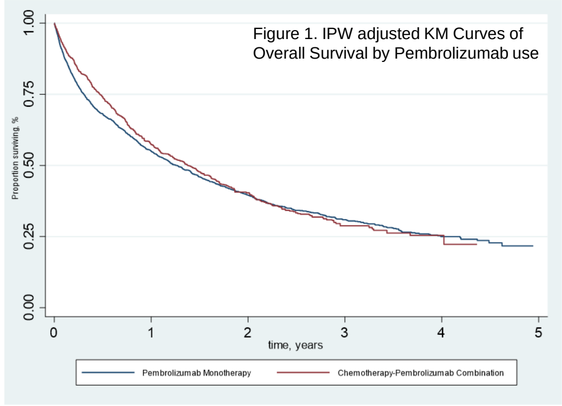
PURPOSE

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

METHODS

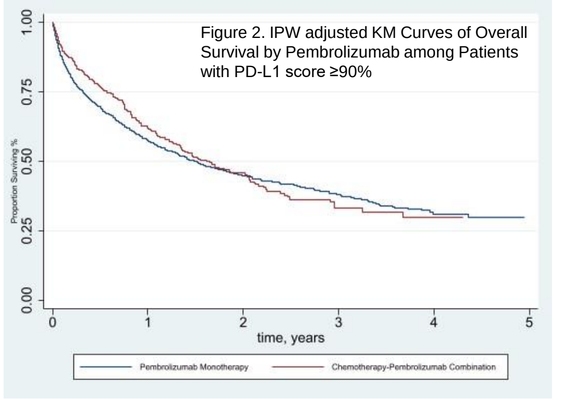
Cohort study of aNSCLC patients with PD-L1 score ≥50% who initiated first-line treatment with pembrolizumab monotherapy or in combination with platinum-based chemotherapy between Oct 24th, 2016, and Oct 29th, 2021, using the nationwide Flatiron Health electronic health record (EHR)-derived de-identified database. Kaplan-Meier (KM) curves and Cox regression were used to estimate 6- and 12-month overall survival and hazard ratios, respectively, for all patients with PD-L1 ≥50% and in the subgroup of patients with PD-L1 ≥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, sex, smoking history, PD-L1 score ≥90%, tumor histology, presence of KRAS/BRAF mutation, practice type, and ECOG performance status. Because of non-proportionality of hazards, we estimated hazard ratios over the first 6 months and after 6 months for the overall cohort, and over the first 12 months and after 12 months for a subgroup of persons with a PD-L1 score of ≥90%

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



	Time, years	0	1	2	3	4	5
Chemoimmunotherapy unadjusted [a]		998	418	189	60	13	0
Chemoimmunotherapy IPW adjusted[a]		3090	1252	551	172	32	0
Immunotherapy alone unadjusted [a]		2088	904	480	243	83	0
Immunotherapy alone IPW adjusted[a]		3055	1359	728	375	130	0

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



	Time, years	0	1	2	3	4	5
Chemoimmunotherapy unadjusted [a]		426	190	91	29	7	0
Chemoimmunotherapy IPW adjusted[a]		1382	593	273	82	16	0
Immunotherapy alone unadjusted [a]		946	424	244	129	39	0
Immunotherapy alone IPW adjusted[a]		1376	624	368	198	59	0

[a] Number of patients remaining in each group at risk at each time point

RESULTS

3086 subjects met inclusion criteria, of whom 32% received chemoimmunotherapy and 68% received immunotherapy alone. Baseline characteristics **well balanced post weighting** (|standardized differences **<0.1**|) Chemoimmunotherapy was associated with no survival advantage versus immunotherapy during the entire follow-up period (IPW-adjusted Hazard Ratio [aHR] 0.98, 95% CI 0.86-1.12), but was associated with a survival benefit during the first 6 months (**aHR 0.74, 95% CI 0.61-0.90**). Similarly, in the subgroup of patients with a PD-L1 score ≥90%, chemoimmunotherapy 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

Chemoimmunotherapy was associated with no overall survival advantage over immunotherapy alone, although was associated with a survival benefit in the first 6 months. Among PD-L1 score ≥90% (subgroup), chemoimmunotherapy 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 chemoimmunotherapy over immunotherapy versus their long-term equivalence

REFERENCES

Reck, M., et al., *Updated analysis of KEYNOTE-024: pembrolizumab versus platinum-based chemotherapy for advanced non-small-cell lung cancer with PD-L1 tumor proportion score of 50% or greater.* 2019.

Aguilar, E.J., et al., *Outcomes to first-line pembrolizumab in patients with non-small-cell lung cancer and very high PD-L1 expression.* Annals of Oncology, 2019. **30**(10): p. 1653-1659.

***Shah was supported by a NIH NIGMS T32 pharmacoepidemiology fellowship award (T32GM-075766)**

Penn Medicine