



KEYNOTE-407: changing the way we treat stage IV squamous non-small cell lung cancer

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Introduction

Patients with stage IV squamous non-small cell lung cancer (NSCLC) were historically treated with first-line platinum-based therapy. Median overall survival (OS) with these regimens was 10–12 months and 5-year OS was estimated at 2% (1,2). Standard of care for patients with squamous NSCLC who developed progressive disease on platinum-based doublets was either (I) docetaxel with or without ramucirumab or (II) gemcitabine (3,4). Subsequently, four randomized phase III trials demonstrated significant improvements in survival when compared to docetaxel for patients receiving monotherapy with a programmed death-1 (PD-1) axis inhibitor (5-8). As a result, PD-1 axis inhibitors became the preferred second-line therapy after development of progressive disease on a platinum-based doublet.

Immune checkpoint inhibitors were then evaluated as initial treatment in combination with platinum-based chemotherapy. The PD-1 inhibitor pembrolizumab added to first-line platinum-based chemotherapy demonstrated superior objective response rate (ORR), progression-free survival (PFS) and OS in non-squamous NSCLC (9). Similarly, three phase III trials evaluated the addition of an immune checkpoint inhibitor to platinum-based doublets in advanced squamous NSCLC (10-13). The cytotoxic T-lymphocyte antigen-4 (CTLA-4) inhibitor ipilimumab combined with carboplatin and paclitaxel did not result in improved PFS or OS when compared

to chemotherapy alone (10). IMpower131 evaluated the addition of the programmed death ligand-1 (PD-L1) inhibitor atezolizumab to carboplatin plus nab-paclitaxel. IMpower131 demonstrated a PFS benefit for the addition of atezolizumab, but no OS benefit (11,12). KEYNOTE-407, which is the focus of this editorial commentary, evaluated the addition of pembrolizumab to carboplatin plus taxane. KEYNOTE-407 demonstrated an improvement in both PFS and OS for the addition of pembrolizumab to chemotherapy (13).

KEYNOTE-407

KEYNOTE-407 was a randomized, double-blind, phase III trial comparing pembrolizumab plus chemotherapy (n=278) versus placebo plus chemotherapy (n=281). Chemotherapy consisted of carboplatin plus a taxane (paclitaxel or nab-paclitaxel). Chemotherapy was administered every 3 weeks for up to 4 cycles. Pembrolizumab or placebo were continued until development of progressive disease, up to 35 total cycles of treatment or other discontinuation criteria were met. The primary endpoints of this study were PFS and OS. The median follow-up at time of analysis was 7.8 months (13).

The addition of pembrolizumab improved the ORR by blinded independent central review, 57.9% *vs.* 38.4%. Similarly, the ORR was greater across all PD-L1 subgroups

with the addition of pembrolizumab: 63.2% *vs.* 40.4% for PD-L1 negative, 49.5% *vs.* 41.3% for PD-L1 of 1–49% on tumor cells and 60.3% *vs.* 32.9% for PD-L1 \geq 50% on tumor cells. This improvement in ORR translated into a survival benefit for the addition of pembrolizumab to chemotherapy (13).

The median PFS by blinded independent central review was improved with the addition of pembrolizumab to chemotherapy, 6.4 *vs.* 4.8 months, HR 0.56 (95% CI, 0.45–0.70), $P < 0.001$. The median PFS was improved across all PD-L1 subgroups: 6.3 *vs.* 5.3 months [HR 0.68 (95% CI, 0.47–0.98)] for PD-L1 negative, 7.2 *vs.* 5.2 months [HR 0.56 (95% CI, 0.39–0.80)] for PD-L1 of 1–49% on tumor cells and 8.0 months *vs.* 4.2 months [HR 0.37 (95% CI, 0.24–0.58)] for PD-L1 \geq 50% on tumor cells (13).

The OS was also improved with the addition of pembrolizumab to chemotherapy, median OS of 15.9 *vs.* 11.3 months, 1-year OS of 65.2% *vs.* 48.3%, HR 0.64 (95% CI, 0.49–0.85), $P < 0.001$. The addition of pembrolizumab improved OS regardless of PD-L1 staining. For PD-L1 negative patients the median OS was 15.9 *vs.* 10.2 months and 1-year OS was 64.2% *vs.* 43.3%, HR 0.61 (95% CI, 0.38–0.98). For patients with PD-L1 of 1–49% on tumor cells the median OS was 14 *vs.* 11.6 months and 1-year OS was 65.9% *vs.* 50.0%, HR 0.57 (95% CI, 0.36–0.90). Similarly, for patients with PD-L1 of \geq 50% on tumor cells the median OS was not reached *vs.* not reached and 1-year OS was 63.4% *vs.* 51.0%, HR 0.64 (95% CI, 0.37–1.10). Exploratory analyses did not reveal a particular subgroup that benefited more than another. Specifically, there was no significant difference in OS by whether patients received paclitaxel or nab-paclitaxel. Information on incidence of baseline liver metastases and any possible influence on survival benefit was not provided. Approximately 8% of patients had baseline brain metastases and due to these small numbers subgroup analysis was not performed comparing patients with or without baseline brain metastases (13).

The OS data are relatively immature due to the short follow-up. However, it is noteworthy that the OS curves were continuing to separate in favor of the pembrolizumab arm at the time of data analysis for patients who were PD-L1 $<$ 50% on tumor cells and for the whole study population. The addition of pembrolizumab resulted in a longer median duration of response, 7.7 *vs.* 4.8 months. Similarly, there were more patients on the pembrolizumab arm who had an ongoing response (57.1% *vs.* 41.7%) and who were still receiving study treatment (43.5% *vs.* 25.7%) (13). This suggests that the OS benefit for the addition of

pembrolizumab to chemotherapy may improve with longer follow-up.

There were 42.8% of patients who discontinued the placebo arm and subsequently received a PD-1 axis inhibitor. The effective cross-over rate for patients on the placebo group to receive subsequent PD-1 axis inhibition by different PD-L1 subgroups was not provided (13). However, patients with PD-L1 positive disease and/or higher PD-L1 staining may have been more likely to receive second-line treatment with a PD-1 axis inhibitor. The lack of significant OS benefit for the addition of pembrolizumab to chemotherapy in patients with PD-L1 of \geq 50% on tumor cells could be explained by a potentially higher rate of subsequent PD-1 axis inhibition for patients in this subgroup who were initially on the chemotherapy alone arm (13).

Adding pembrolizumab to chemotherapy did not significantly increase the any grade treatment emergent adverse event rate (TEAE) or grade \geq 3 TEAE when compared to chemotherapy alone, 98.2% *vs.* 97.9% and 69.8% *vs.* 68.2% respectively. However, there was a higher incidence of all grade immune mediated adverse events/infusion reactions with the addition of pembrolizumab, 28.8% *vs.* 8.6%. Additionally, the rate of discontinuation of all treatment (13.3% *vs.* 6.4%) or any component of treatment (23.4% *vs.* 11.8%) was numerically higher for the group receiving pembrolizumab (13).

How do we incorporate KEYNOTE-407 into clinical practice?

Many questions have arisen following publication of KEYNOTE-407. For instance, how do we select who should receive pembrolizumab plus chemotherapy and who should receive monotherapy with pembrolizumab? Additionally, what is the role for other chemotherapy backbones with immune checkpoint inhibition in squamous histology NSCLC? Also, how does pembrolizumab plus platinum plus taxane compare to other regimens that have been studied and/or are currently being investigated for first-line treatment of squamous NSCLC?

KEYNOTE-024 demonstrated a survival benefit for patients with any histology NSCLC and PD-L1 on tumor cells of \geq 50% who were treated with pembrolizumab when compared to platinum-based doublets (14,15). Subsequently, a retrospective study suggested that patients with PD-L1 on tumor cells of \geq 90% may have improved outcomes with pembrolizumab when compared to patients with PD-L1

of 50–89% on tumor cells. The ORR was 60% *vs.* 33%, median PFS was 14.5 months *vs.* 4.1 months (HR 0.50, $P < 0.01$) and median OS was not reached *vs.* 15.9 months (HR 0.39, $P = 0.002$) (16). A second retrospective study suggested a non-significant trend towards PFS improvement in patients with PD-L1 on tumor cells of $\geq 90\%$ who were treated with pembrolizumab when compared to patients with PD-L1 of 50–89% on tumor cells, 12 month PFS was 44.1% *vs.* 32.3%, hazard ratio 0.78, $P = 0.34$ (17). Efficacy outcomes for patients with PD-L1 of 50–89% on tumor cells treated with pembrolizumab in these retrospective studies were inferior to those seen in clinical trials of pembrolizumab plus chemotherapy for patients with similar or lower PD-L1 staining levels (9,13,16,17).

KEYNOTE-042 reported improved OS for pembrolizumab monotherapy when compared to platinum-based doublets in patients with PD-L1 $\geq 1\%$ on tumor cells. However, this survival benefit was only significant for patients with PD-L1 of $\geq 50\%$ on tumor cells. For patients with PD-L1 of 1–49% on tumor cells there was no significant survival benefit for pembrolizumab when compared to chemotherapy, median OS of 13.4 *vs.* 12.1 months, HR 0.92 (95% CI, 0.77–1.11) (18). In cross trial comparisons pembrolizumab monotherapy appears to have less OS benefit than pembrolizumab plus chemotherapy for patients with PD-L1 of 1–49% on tumor cells (9,13,18). Thus, pembrolizumab plus chemotherapy should be favored in patients with PD-L1 of 1–49% on tumor cells unless there are contraindications to chemotherapy.

It is reasonable to treat patients with PD-L1 $\geq 50\%$ on tumor cells with pembrolizumab monotherapy and patients with PD-L1 of $< 50\%$ on tumor cells with pembrolizumab plus chemotherapy. However, there is a possibility that certain patients with PD-L1 $\geq 50\%$ on tumor cells may do better with chemoimmunotherapy as opposed to pembrolizumab monotherapy. Perhaps the patients that may do better with pembrolizumab plus chemotherapy are those with PD-L1 50–89% on tumor cells or maybe certain mutations may help with selecting which patients among those with PD-L1 $\geq 50\%$ on tumor cells should receive pembrolizumab versus pembrolizumab plus chemotherapy. Future trials will help in determining which patients with PD-L1 $\geq 50\%$ on tumor cells do better with pembrolizumab monotherapy versus pembrolizumab plus chemotherapy.

The presence of KRAS and specific co-mutations has been associated with efficacy or lack thereof in patients treated with immune checkpoint inhibitors (19,20). However,

KRAS mutations only occur in about 1% of squamous histology NSCLC (21). KEAP1 mutations have been associated with lack of significant benefit from the addition of pembrolizumab to chemotherapy (20). KEAP1 mutations are present in about 12% of squamous NSCLC (21). ARID1A mutations were associated with benefit of PD-L1 inhibition plus CTLA-4 inhibition when compared to platinum-based chemotherapy, but did not have an association with benefit from PD-L1 inhibition alone (22). ARID1A mutations are present in 7% of squamous histology NSCLC (21). The association of ARID1A mutations with efficacy of chemoimmunotherapy regimens has not been reported.

The chemotherapy backbone in KEYNOTE-407 consisted of carboplatin plus a taxane (13). The benefit and/or toxicity of PD-1 axis inhibitors plus carboplatin plus gemcitabine is unclear. Investigating pembrolizumab or other PD-1 axis inhibitors in combination with different platinum-based doublets besides carboplatin plus taxane could be beneficial.

IMpower131 demonstrated a PFS benefit, but no OS benefit, for the addition of atezolizumab to carboplatin plus nab-paclitaxel in metastatic squamous NSCLC. There were 42.1% of patients on the chemotherapy arm of IMpower131 who received subsequent therapy with an immune checkpoint inhibitor (11,12). This rate of cross-over was similar to the 42.8% seen on the chemotherapy arm of KEYNOTE-407 (13). Thus, a higher incidence of subsequent immune checkpoint inhibitor therapy on the chemotherapy alone arm does not explain the lack of OS benefit seen on IMpower131. About 1/3 of patients on KEYNOTE-407 were PD-L1 negative, while approximately 50% of patients on IMpower131 were PD-L1 negative. However, KEYNOTE-407 demonstrated improved OS in the PD-L1 negative subgroup, while IMpower131 did not (11–13). This suggests that a higher rate of PD-L1 negative patients is also not the reason for the lack of OS benefit seen with the addition of atezolizumab to chemotherapy in IMpower131. It is noteworthy that the chemotherapy arm had better OS on IMpower131 than the chemoimmunotherapy arm for patients who were PD-L1 low/intermediate, the exact reasons for this are unclear (11,12). Whether differences in the patient populations between IMpower131 and KEYNOTE-407 (e.g., incidence of baseline liver metastases, baseline brain metastases, oligometastatic disease or receipt of subsequent therapy) contributed to differing OS outcomes with these chemoimmunotherapy regimens is unknown. Pembrolizumab blocks the interaction of both PD-L1 and

PD-L2 with PD-1 on T-cells, while atezolizumab only blocks the interaction of PD-L1 with PD-1 on T-cells. The exact role of PD-L2 in immunosuppression in squamous NSCLC is unclear and whether PD-1 blockade has better enhancement of efficacy in combination with chemotherapy than does PD-L1 blockade remains to be determined.

Currently pembrolizumab plus carboplatin plus taxane is the only chemoimmunotherapy regimen approved for first-line treatment of squamous histology NSCLC. Pembrolizumab monotherapy is approved for initial treatment of patients with metastatic NSCLC of any histology and PD-L1 of $\geq 50\%$ on tumor cells. CheckMate-227 reported an OS benefit for nivolumab plus ipilimumab when compared to platinum-based doublets in advanced NSCLC patients of any histology. Specifically, for the subset of patients with squamous histology NSCLC there was a significant benefit for nivolumab plus ipilimumab in patients of any PD-L1 status and for patients with PD-L1 $\geq 1\%$ on tumor cells, the relative benefit was similar to that seen in KEYNOTE-407 (13,23). Data for PD-L1 subgroups (negative, 1–49% on tumor cells or $\geq 50\%$ on tumor cells) was not provided for the squamous NSCLC subset. For patients of any histology NSCLC on CheckMate227 there was only an OS benefit with nivolumab plus ipilimumab for patients with PD-L1 $\geq 50\%$ on tumor cells or PD-L1 negative with tumor mutational burden ≥ 10 mutations per megabase by Foundation Medicine tumor tissue testing (23). In contrast, in KEYNOTE-407 the OS benefit of pembrolizumab added to chemotherapy was seen regardless of PD-L1 status (13). Whether ARID1A mutations may help predict a subset of patients that may preferentially benefit from a chemotherapy free first-line regimen of nivolumab plus ipilimumab remains to be determined.

The MYSTIC trial compared durvalumab with or without tremelimumab versus platinum-based chemotherapy in any histology NSCLC. There was no OS benefit for either immunotherapy regimen when compared to chemotherapy in this trial (22). These regimens are not approved for first-line treatment of metastatic NSCLC.

The POESEIDEN trial had a press release suggesting durvalumab with or without tremelimumab plus platinum-based chemotherapy resulted in significantly improved PFS compared to chemotherapy alone (24). Similarly, the CheckMate 9LA trial had a press release suggesting nivolumab plus ipilimumab plus platinum-based chemotherapy resulted in significantly improved OS compared to chemotherapy alone (25). However, data has not been

presented for either of these trials. Thus, these regimens should not be used outside the setting of a clinical trial.

IMpower110 compared atezolizumab monotherapy versus platinum-based doublets in patients with any histology NSCLC. There was a significant OS benefit for atezolizumab monotherapy in the subgroup of patients who expressed PD-L1 $\geq 50\%$ on tumor cells or $\geq 10\%$ on immune cells. While exploratory analysis by histology did not suggest a significant OS benefit for squamous histology in this high PD-L1 group, there was a strong trend towards significance [HR 0.56 (95% CI, 0.23–1.37)] which may have been limited by the small sample size (n=50) (26). Atezolizumab is not approved as first-line monotherapy in patients with metastatic NSCLC and as a result should not be used in this setting outside of a clinical trial.

Conclusions

Pembrolizumab plus carboplatin plus taxane is the only approved chemoimmunotherapy regimen for metastatic squamous NSCLC. This regimen should be utilized in fit patients with PD-L1 $< 50\%$ on tumor cells and it may benefit some patients with PD-L1 $\geq 50\%$ on tumor cells more than pembrolizumab monotherapy. However, further improvement is needed to optimize selection of which patients should receive pembrolizumab monotherapy versus chemo-immunotherapy. KEYNOTE-407 investigated a maximum of 2 years of pembrolizumab therapy in combination with 4 cycles of carboplatin plus taxane. However, whether 2 years is the optimal duration of pembrolizumab treatment and the safety of stopping pembrolizumab at 2 years in ongoing responders is unclear. Additionally, the role of consolidative local therapy in patients with limited remaining sites of disease following chemoimmunotherapy and of radiation to oligoprogressive disease in patients on first-line chemoimmunotherapy remains to be determined. KEYNOTE-407 was a major advancement; however, there is still a lot of room to improve outcomes for patients with metastatic squamous NSCLC.

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Footnote

Conflicts of Interest: Advisory board/consulting role

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Ethical Statement: The author is accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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References

1. Cetin K, Ettinger DS, Hei Y, O'Malley CD. Survival by histologic subtype in stage IV nonsmall cell lung cancer based on data from the Surveillance, Epidemiology and End Results Program. *Clin Epidemiol* 2011;3:139-48.
2. Schiller JH, Harrington D, Belani CP, et al. Comparison of four chemotherapy regimens for advanced non-small-cell lung cancer. *N Engl J Med* 2002;346:92-8.
3. Crinò L, Mosconi AM, Scagliotti G, et al. Gemcitabine as second-line treatment for advanced non-small-cell lung cancer: A phase II trial. *J Clin Oncol* 1999;17:2081-5.
4. Garon EB, Ciuleanu TE, Arrieta O, et al. Ramucirumab plus docetaxel versus placebo plus docetaxel for second-line treatment of stage IV non-small cell lung cancer after disease progression on platinum-based therapy (REVEL): a multicentre, double-blind, randomised phase 3 trial. *Lancet* 2014;384:665-73.
5. Borghaei H, Paz-Ares L, Horn L, et al. Nivolumab versus Docetaxel in Advanced Nonsquamous Non-Small-Cell Lung Cancer. *N Engl J Med* 2015;373:1627-39.
6. Brahmer J, Reckamp KL, Baas P, et al. Nivolumab versus Docetaxel in Advanced Squamous-Cell Non-Small-Cell Lung Cancer. *N Engl J Med* 2015;373:123-35.
7. Herbst RS, Baas P, Kim DW, et al. Pembrolizumab versus docetaxel for previously treated, PD-L1 positive, advanced non-small-cell lung cancer (KEYNOTE-010): a randomised controlled trial. *Lancet* 2016;387:1540-50.
8. Rittmeyer A, Barlesi F, Waterkamp D, et al. Atezolizumab versus docetaxel in patients with previously treated non-small-cell lung cancer (OAK): a phase 3, open-label, multicentre randomised controlled trial. *Lancet* 2017;389:255-65.
9. Gandhi L, Rodríguez-Abreu D, Gadgeel S, et al. Pembrolizumab plus Chemotherapy in Metastatic Non-Small-Cell Lung Cancer. *N Engl J Med* 2018;378:2078-92.
10. Govindan R, Szczesna A, Ahn MJ, et al. Phase III Trial of Ipilimumab Combined with Paclitaxel and Carboplatin in Advanced Squamous Non-Small-Cell Lung Cancer. *J Clin Oncol* 2017;35:3449-57.
11. Jotte RM, Cappuzzo F, Vynnychenko I, et al. IMpower131: Primary PFS and safety analysis of a randomized phase III study of atezolizumab + carboplatin + paclitaxel or nab-paclitaxel vs carboplatin + nab-paclitaxel as 1L therapy in advanced squamous NSCLC. *J Clin Oncol* 2018;36:LBA9000.
12. Jotte R, Vynnychenko I, Stroyakovskiy D, et al. IMpower131: Final OS Results of Carboplatin + Nab-Paclitaxel +/- Atezolizumab in Advanced Squamous NSCLC. Abstract OA14.02. Barcelona, Spain: IASLC 20th Annual World Conference on Lung Cancer, 2019.
13. Paz-Ares L, Luft A, Vicente D, et al. Pembrolizumab plus Chemotherapy for Squamous Non-Small-Cell Lung Cancer. *N Engl J Med* 2018;379:2040-51.
14. Reck M, Rodríguez-Abreu D, Robinson AG, et al. Pembrolizumab versus Chemotherapy for PD-L1 Positive Non-Small-Cell Lung Cancer. *N Engl J Med* 2016;375:1823-33.
15. Reck M, Rodríguez-Abreu D, Robinson AG, et al. KEYNOTE-024 3-Year Survival Update: Pembrolizumab Versus Platinum-Based Chemotherapy for Advanced NSCLC. Barcelona, Spain: IASLC World Conference on Lung Cancer, 2019.
16. Aguilar EJ, Ricciuti B, Gainor JF, et al. Outcomes to first-line pembrolizumab in patients with non-small-cell lung cancer and very high PD-L1 expression. *Ann Oncol* 2019;30:1653-9.
17. Edahiro R, Kanazu M, Kurebe H, et al. Clinical outcomes in non-small cell lung cancer patients with an ultra-high expression of programmed death ligand-1 treated using pembrolizumab as first-line therapy: A retrospective multicenter cohort study in Japan. *PLoS One* 2019;14:e0220570.
18. Mok TSK, Wu YL, Kudaba I, et al. Pembrolizumab versus

- chemotherapy for previously untreated, PD-L1 expressing, locally advanced or metastatic non-small-cell lung cancer (KEYNOTE-042): a randomised, open-label, controlled phase 3 trial. *Lancet* 2019;393:1819-30.
19. Skoulidis F, Goldberg ME, Greenawalt DM, et al. STK11/LKB1 Mutations and PD-1 Inhibitor Resistance in KRAS Mutant Lung Adenocarcinoma. *Cancer Discov* 2018;8:822-35.
 20. Skoulidis F, Arbour KC, Hellman MD, et al. Association of STK11/LKB1 genomic alterations with lack of benefit from the addition of pembrolizumab to platinum doublet chemotherapy in non-squamous non-small cell lung cancer. *J Clin Oncol* 2019;37:abstr 102.
 21. Available online: https://www.cbiportal.org/study/summary?id=lusc_tcga. Accessed 12/24/2019.
 22. Rizvi N, Cho BC, Reinmuth N, et al. Mutations Associated with Sensitivity or Resistance to Immunotherapy in mNSCLC: Analysis from the MYSTIC Trial. Barcelona, Spain: IASLC World Conference on Lung Cancer, 2019.
 23. Hellmann MD, Paz-Ares L, Bernabe Caro R, et al. Nivolumab plus Ipilimumab in Advanced Non-Small-Cell Lung Cancer. *N Engl J Med* 2019;381:2020-31.
 24. Imfinzi and Imfinzi plus tremelimumab delayed disease progression in Phase III POSEIDON trial for 1st-line treatment of Stage IV non-small cell lung cancer. Available online: <https://www.astrazeneca.com/media-centre/press-releases/2019/imfinzi-and-imfinzi-plus-tremelimumab-delayed-disease-progression-in-phase-iii-poseidon-trial-for-1st-line-treatment-of-stage-iv-non-small-cell-lung-cancer.html>. Accessed 11/19/2019.
 25. CheckMate -9LA, a Phase 3 Trial Evaluating Opdivo (nivolumab) Plus Low-Dose Yervoy (ipilimumab) Combined with Chemotherapy, Meets Primary Endpoint Demonstrating Superior Overall Survival Compared to Chemotherapy Alone in First-Line Lung Cancer. Available online: <https://news.bms.com/press-release/corporatefinancial-news/checkmate-9la-phase-3-trial-evaluating-opdivo-nivolumab-plus-l>. Accessed 11/19/2019.
 26. Spigel DR, De Marinis F, Giaccone G, et al. IMpower110: Interim OS Analysis of a Phase III Study of Atezolizumab (atezo) vs Platinum-Based Chemotherapy (chemo) as 1L Treatment (tx) in PD-L1-selected NSCLC. Barcelona, Spain: European Society of Medical Oncology Annual Meeting, 2019.

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