Capsule Summary

Evaluation of Low-dose Pembrolizumab therapy in NSCLC patients

Advent of immune checkpoint inhibitors has created a paradigm shift for the treatment of numerous malignancies. Inhibitors targeting Programmed Cell Death-1 (PD-1) receptor and its ligand PD-L1, alone or in combination with chemotherapy drugs represent the new standard of treatment for difficult to treat malignancies such as non-small cell lung carcinoma (NSCLC).

Although the pharmacokinetics studies using Pembrolizumab demonstrated PD-1 receptor saturation at 1 mg/kg, the clinical efficacy of Pembrolizumab in Phase III studies was evaluated at 2 mg/kg, and it is currently recommended at a dose of 200 mg every 3 weeks [1, 2]. However, biologics such as Pembrolizumab are very expensive therapeutics, and a dose reduction to achieve equivalent efficacy could be cost-effective for the patients and also reduce the overall healthcare burden.

Objective

Study objective: A study by Low et al. aimed to perform a retrospective analysis of the therapeutic benefit of low dose Pembrolizumab (100 mg) in Asian patients with advanced NSCLC [3].

Key methods and patient characteristics

- Retrospective observational study among advanced stage NSCLC patients, receiving Pembrolizumab therapy between January 2016, and March 2020 at National University Hospital, Singapore.
- 100 mg dose was routinely administered in patents lacking adequate financial resources or based on physician's treatment preference.
- Retrospective observational study among advanced stage NSCLC patients, receiving Pembrolizumab therapy between January 2016, and March 2020 at National University Hospital, Singapore.
- Response classified as – progressive disease (PD), stable disease (SD), partial response (PR) or complete response.
- Retrospective observational study among advanced stage NSCLC patients, receiving Pembrolizumab therapy between January 2016, and March 2020 at National University Hospital, Singapore.

Key study characteristics:

	Pembrolizumab 100 mg	Pembrolizumab 200 mg
Age at diagnosis (median, range)	60.5 (28.4 – 80.0)	69.9 (42.8 – 92.2)
Smoking history	107 (38.6 %)	98 (35.4 %)
Median overall Survival in high PD-L1 expression patients	Current – 32 Never Smoked - 17	Current – 49 Never Smoked - 16
PD-L1 Tumour Proportion score (TPS)	0 % = 11, 1 % - 49 % =18, >50 % = 19, Unknown = 1	0 % = 5,1 % - 49 % = 13,>50 % = 44,Unknown = 3

Outcomes

	Pembrolizumab 100 mg	Pembrolizumab 200 mg	Hazard Ratio
Progression Free Survival (PFS in months)	6.8	4.2	**HR 0.6, P value = 0.16**
Overall Survival (OS in months)	14.3	19.8	**HR 1.08, P value = 0.86**

Interpretation: PFS and OS were not significantly different between the low dose 100 mg groups versus the 200 mg groups, in patients with pembrolizumab as a single agent therapy

Other key study findings & Conclusion

PFS and OS were also not significantly different between the low dose versus high dose Pembrolizumab groups in patients receiving additional chemotherapy. No difference in response rates or >G3 immune-related toxicities observed. Cost analysis revealed a cost saving of astounding SGD 39,942 per patient in the Pembrolizumab 100 mg group.

A lower dose of Pembrolizumab (100 mg) appears to be effective in an Asian patient cohort, without any significant difference observed with respect of PFS, OS and adverse events as compared to the standard higher dose of 200 mg. Further studies employing randomised clinical trials are warranted, which if prove the equal efficacy of 100 mg Pembrolizumab, could save enormous expenditure on this expensive biologic treatment.

Information Source

Low et al. Low-dose pembrolizumab in the treatment of advanced non-small cell lung cancer International journal of Cancer, 2021 Jul 1;149(1):169-176.
PMID: 33634869 DOI: 10.1002/ijc.33534.
Article access: https://onlinelibrary.wiley.com/doi/10.1002/ijc.33534
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Reference

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3. Low, J.L., et al., Low-dose pembrolizumab in the treatment of advanced non-small cell lung cancer. Int J Cancer, 2021. 149(1): p. 169-176.
4. Schwartz, L.H., et al., RECIST 1.1-Update and clarification: From the RECIST committee. Eur J Cancer, 2016. 62: p. 132-7.