



Immunotherapy-based approaches have become a treatment option for patients with non-small-cell lung cancer (NSCLC). Importantly, evidence from preclinical studies suggests that radiotherapy stimulates an antitumour immune response. In order to investigate this hypothesis, Percy Lee, Narek Shaverdian and collaborators undertook a secondary analysis of the KEYNOTE-001 trial data; their positive results have now been published.

Pembrolizumab, a monoclonal antibody against programmed cell death protein 1 (PD-1), is approved by the FDA for the first and second-line treatment of patients with metastatic NSCLC. KEYNOTE-001, a phase I trial of 2 and 10 mg/kg pembrolizumab, is one of the studies that led to these approvals. Lee and his team had access to the data from patients involved in the trial (98 of 495) who received treatment at University of California Los Angeles (UCLA). As Lee clarifies “the ideal approach to determine a synergy between radiotherapy and immunotherapy would be to conduct a prospective trial, but we would need to wait at least 2–3 years before the results of such a study are available.”

Of 97 patients, 42 had previously received radiotherapy, which was delivered extracranially to 38 of the patients. Patients who previously received radiotherapy had longer progression-free survival (PFS) and overall survival durations than those who did not (4.4 months and 10.7 months, respectively, versus 2.1 months and 5.3 months). Of note, PFS and overall survival were

also longer for the patients who had received extracranial radiotherapy compared with those who didn't (6.3 months and 11.6 months versus 2 months and 5.3 months). Lee declares his optimism: “our findings suggest the presence of a synergistic effect between radiotherapy and immunotherapy. Only around 20% of patients with NSCLC respond to immunotherapies, but these results suggest that prior use of radiotherapy would improve antitumour immunity in these patients.”

Lee and collaborators have different plans to take this research forward. Firstly, preclinical studies need to be conducted to determine the mechanism underlying the synergy observed. In addition, Lee explains, “we do not know how radiation was delivered to all patients because they received radiotherapy before enrolling at UCLA. Prospective trials will help determine the optimal dosing and timing to potentiate the observed effect.” Finally, Lee is the lead investigator of the phase I/II trial NCT03148327, in which the combination of radiotherapy with durvalumab, an antibody against the PD-1 ligand (PD-L1), will be tested in patients with inoperable early stage NSCLC.

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**ORIGINAL ARTICLE** Shaverdian, N. et al. Previous radiotherapy and the clinical activity and toxicity of pembrolizumab in the treatment of non-small-cell lung cancer: a secondary analysis of the KEYNOTE-001 phase 1 trial. *Lancet Oncol.* [http://dx.doi.org/10.1016/S1470-2045\(17\)30380-7](http://dx.doi.org/10.1016/S1470-2045(17)30380-7) (2017)

**FURTHER READING** Garon, E. B. et al. Pembrolizumab for the treatment of non-small-cell lung cancer. *N. Engl. J. Med.* **372**, 2018–2028 (2015)