Clinical implications of monitoring nivolumab immunokinetics in non-small cell lung cancer patients

Keywords: lung cancer, Immune checkpoint, cancer immunity, T-lymphocyte, Nivolumab

BACKGROUND

The PD-1–blocking antibody nivolumab persists in patients several weeks after the last infusion. However, no study has systematically evaluated the maximum duration that the antibody persists on T cells or the association between this duration and residual therapeutic efficacy or potential adverse events.

METHODS

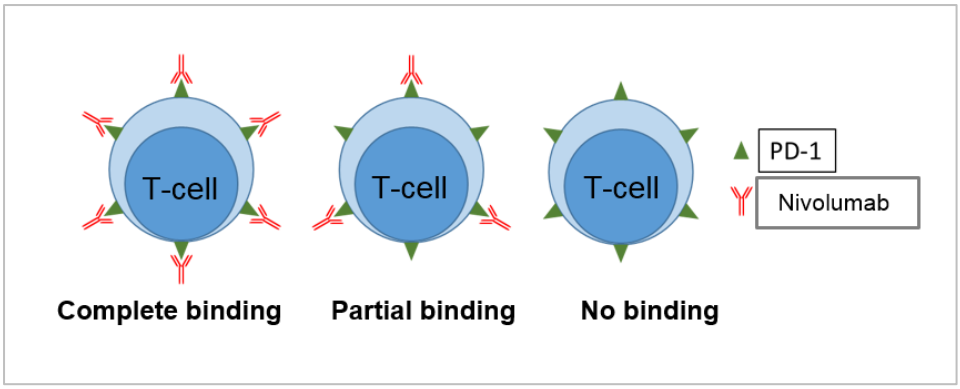
To define the duration of binding and residual efficacy of nivolumab after discontinuation, the authors developed a simplified strategy for T cell monitoring and used it to analyze T cells from peripheral blood from 11 non–small cell lung cancer patients previously treated with nivolumab. To determine the suitability of our method for other applications, they compared transcriptome profiles between nivolumab-bound and nivolumab-unbound CD8 T cells. The also applied T cell monitoring in 3 nivolumab-treated patients who developed interstitial lung diseases or progressive lung tumors.

RESULTS

Prolonged nivolumab binding was detected more than 20 weeks after the last infusion, regardless of the total number of nivolumab infusions (2–15 doses) or type of subsequent treatment, in 9 of the 11 cases in which long-term monitoring was possible. Ki-67 positivity, a proliferation marker, in T cells decreased in patients with progressive disease. Transcriptome profiling identified the signals regulating activation of nivolumab-bound T cells, which may contribute to nivolumab resistance. In 2 patients who restarted nivolumab, T cell proliferation markers exhibited the opposite trend and correlated with clinical response.

CONCLUSIONS

Although only a few samples were analyzed, their strategy of monitoring both nivolumab binding and Ki-67 in T cells might help determine residual efficacy under various types of concurrent or subsequent treatment.



The change in nivolumab-binding status.

The schematics present three different binding statuses: complete binding, partial binding, and no binding.

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