Hyperprogressive Disease in Advanced NSCLC Treated With PD-1/PD-L1 Inhibitors

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Key Points

- Hyperprogressive disease was observed in 13.8% with PD-1/PD-L1 inhibitors and was associated with higher metastatic burden at baseline.
- Hyperprogressive disease was observed among 5.1% of patients receiving chemotherapy.

In a French study reported in *JAMA Oncology*, Ferrara et al found that hyperprogressive disease appeared to be more common with programmed cell death protein 1 (PD-1)/programmed cell death ligand 1 (PD-L1) inhibitor treatment than single-agent chemotherapy among previously treated patients with advanced non–small cell lung cancer (NSCLC).

Study Details

The retrospective study included 406 consecutive eligible patients treated with PD-1/PD-L1 inhibitors as monotherapy in second-line or later treatment at 8 institutions between November 2012 and April 2017, and 59 eligible patients who had failed a platinum-based regimen and received single-agent chemotherapy (taxane, pemetrexed [Alimta], vinorelbine, or gemcitabine) in 4 institutions between August 2011 and June 2016. Hyperprogressive disease was defined as RECIST v1.1 progressive disease on the first computed tomography scan during treatment with an absolute increase in tumor growth rate exceeding 50%.

Frequency of Hyperprogressive Disease

Among the patients receiving PD-1/PD-L1 inhibitor treatment, hyperprogressive disease was observed in 56 (13.8%). Pseudoprogression was observed in 19 (4.7%). Patients with hyperprogressive disease were more likely to have more than two metastatic sites prior to treatment vs those without hyperprogressive disease (62.5% vs 42.6%, $P = .006$). Median overall survival was poorer among patients with

hyperprogressive disease in the first 6 weeks of treatment vs those with progressive disease (3.4 months vs 6.2 months, hazard ratio = 2.18, *P* = .003).

By comparison, 3 (5.1%) of 59 patients receiving single-agent chemotherapy exhibited hyperprogressive disease. Median overall survival was 4.5 months in those with hyperprogressive disease vs 3.9 months in 18 patients with progressive disease at first evaluation (*P* = .60).

The investigators concluded, "Our study suggests that [hyperprogressive disease] is more common with PD-1/PD-L1 inhibitors compared with chemotherapy in pretreated patients with NSCLC and is also associated with high metastatic burden and poor prognosis in patients treated with PD-1/PD-L1 inhibitors. Additional studies are needed to determine the molecular mechanisms involved in [hyperprogressive disease]."

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