Background Hyperprogressive disease (HPD) is the accelerated growth of tumor size after treatment with immunotherapy. As HPD is associated with poorer outcomes, it is important to understand the risk factors (RF) to prevent HPD. Some RF for HPD include age, primary lesion size, and presence of metastases in the contralateral lung, pleura, liver, and bone. Others identified Eastern cooperative oncology group scale of performance status (ECOG PS) >1, having more than two metastasis sites, and liver metastasis as significant RF. With existing findings showing varying results, this study aims to complement and identify potential RF for HPD in lung cancer patients.

Methods This study retrospectively analyzed 128 patients’ data (N of patients = 128) and 144 total number of regimens (N of regimens = 144) at a large metropolitan academic medical center. Multiple variables were analyzed using chi-squared tests and t-tests to identify RF using two definitions of HPD by Champiat and Saada-Bouzid et al. The variables that were analyzed are treatment line, regimen, immunotherapy type, histology, PD-L1 status, tumor mutational burden (TMB), diagnosis age, sex, smoking status, ECOG PS, neutrophil-to-lymphocyte ratio (NLR), TNM staging, platelets, number of metastases, and the presence of metastases in the brain, bone, and liver.

Results Among the 144 cases, immunotherapy was used as the first line in 27% (N=34), second line in 51% (N=65), and third or more line in 23% (N=29). Immunotherapy was used as a single agent in 77% of cases (N=111) and as a combination with other chemotherapy, targeted therapy in 23% of cases (N=33).

Using the Champiat et al. definition of HPD, immunotherapy only regimen, non-adenocarcinoma histology of tumor (histology was classified as adenocarcinoma, squamous cell carcinoma, small cell lung cancer and other), and bone metastasis were associated with HPD (table 1). Using the Saada-Bouzid et al. definition, histology and immunotherapy only regimen was shown to be marginally associated with HPD. However, no associations were identified between HPD and other clinicalopathological variables, including, but not limited to, age, the number of sites of metastatic disease, genomic alterations, and peripheral blood biomarkers, including the NLR.

Conclusions Bone metastasis, non-adenocarcinoma histology, and immunotherapy only regimens were associated with HPD. Given the small sample size, further investigation is warranted to elucidate the correlation with hyperprogression and other clinicopathologic and genomic features.

REFERENCES
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