Background While reported in other types of systemic therapy as well, evidence for hyperprogressive disease (HPD) following onset of immunotherapy has increased in the past decade. Despite such growing evidence, the lack of a consensual definition precludes a better understanding of this phenomenon.

Methods A systematic literature search was done on PubMed, Embase, Web of Science, and Cochrane Database of Systematic Reviews based on a search algorithm that included key terms including immune checkpoint inhibitor, immunotherapy, and hyperprogress. Studies published until June 21, 2022 which used a definition based on tumor kinetics were included. All studies were categorized according to one of three definitions of HPD: A) RECIST-defined progressive disease (PD) and tumor growth rate (TGR) ratio $< u > 2$; B) RECIST-based tumor growth kinetics (TGK) ratio $< u > 2$; and C) RECIST-defined PD and ATGR > 50%. A generalized linear mixed-effects model was used, and multivariable analysis was conducted to explore differences in the incidence across tumor types and HPD definitions.

Results A total of 34 studies comprising 4117 patients and 5 different tumor types (renal cell carcinoma (RCC), mixed or other, hepatocellular carcinoma (HCC), non-small cell lung cancer (NSCLC), and advanced gastric cancer (AGC)) were included in the meta-analysis. The overall pooled incidence of HPD was 12.40% (95% CI, 10.28 – 14.89%) and ranged from 0.0% to 36.73% (figure 1 and 2). Statistical heterogeneity was significant ($I^2 = 72.3%$; $P < 0.01$). Patients diagnosed with AGC (odds ratio (OR), 10.83; 95% CI, 2.15-66.02; P <0.01), HCC (OR, 7.99; 95% CI, 1.68-38.10; P = 0.03), NSCLC (OR, 7.14; 95% CI, 1.58-32.27; P <0.004), and mixed or other (OR, 5.09; 95% CI, 1.12-23.12; P = 0.03) were more likely to experience HPD than patients with RCC. Across definitions, differences in the HPD incidence were significantly higher for definition B (OR, 1.81; 95% CI, 0.58-1.80; $P = 0.025$) compared to definition C.

Conclusions Significant differences in HPD incidence are observed across tumor types and HPD definitions. To better characterize these differences, further studies — as well as efforts to agree on a consensual definition — are warranted.


Abstract 519 Figure 2

Forest Plot of HPD incidence across definitions


Abstract 519 Figure 1

Forest Plot of HPD incidence across tumor types


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