META-ANALYSIS ON THE INCIDENCE OF HYPERPROGRESSIVE DISEASE DURING IMMUNE CHECKPOINT INHIBITOR THERAPY

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Background Hyperprogressive disease (HPD) is a distinct pattern of rapid tumor progression observed in patients with cancer who are undergoing immune checkpoint inhibitor therapy. Despite the growing evidence, a universal definition of HPD remains to be established, and incidence rates vary based on the defining criteria. Therefore, a refinement of currently existing criteria is warranted to better characterize this phenomenon and evaluate its incidence.

Methods Two independent investigators performed a systematic literature search in EMBASE and MEDLINE using keywords selected in Park et al.¹: checkpoint, immunotherapy, pd1, pdl1, ctla4, ipilimumab, nivolumab, pembrolizumab, atezolizumab, avelumab, durvalumab and hyperprogress. Studies published from March 3, 2020 to April 20, 2020 that included the incidence and definition of HPD in patients receiving immunotherapy were included for analysis. Selected studies were then combined with those included in the meta-analysis by Park et al.¹ Duplicates were removed, and the study with a larger cohort was selected in instances of overlap between two cohorts. In total, 50 studies were included for meta-analysis.²⁻⁵¹ Pooled incidence rates of HPD and prespecified subgroup analyses based on four categories defining HPD (tumor growth rate ratio, tumor growth kinetics ratio, early tumor burden increase, and combination) were obtained with 95% confidence intervals (CI) using a random effects model performed on R.

Results A total of 6009 patients from 50 studies were included in the meta-analysis. Incidences varied from 0.0% to 43.1% (figure 1), and the overall pooled incidence of HPD was 12.9% (95%CI, 11.1%–14.7%). Significant heterogeneity was observed ($I^2 = 77\%$; $p < 0.01$). Studies were also grouped into one of 4 categories (table 1) based on the definition of HPD used to calculate the tumor growth acceleration: tumor growth rate ratio (pooled incidence of HPD 10.5%; 95% CI, 7.9%–13.0%), tumor growth kinetics ratio (pooled incidence, 14.8%; 95% CI, 12.0%–17.5%), early tumor burden increase (pooled incidence, 17.2%; 95% CI, 9.7%–24.7%), and combinations of the above (pooled incidence, 12.2%; 95% CI, 9.2%–15.2%).

Abstract 238 Table 1 Subgroup analyses based on definitions of HPD

Factor	Pooled incidence of HPD (%)	P value			
		vs Category 1	vs Category 2	vs Category 3	vs Category 4
HPD definition					
Category 1 (TGR ratio)	10.5 (7.9–13.0)	-	0.025	0.097	0.385
Category 2 (TGK ratio)	14.8 (12.0–17.5)	0.025	-	0.552	0.223
Category 3 (early tumor burden increase)	17.2 (9.7–24.7)	0.097	0.552	-	0.229
Category 4 (combination)	12.2 (9.2–15.2)	0.385	0.223	0.229	-

Abbreviation: TGR, tumor growth rate; TGK, tumor growth kinetics.

Abstract 238 Figure 1 Overall pooled incidence of HPD. The overall pooled incidence of HPD was 12.9% (95% CI, 11.1%–14.7%). Significant heterogeneity was observed ($I^2 = 77\%$; $p < 0.01$).

Conclusions The overall incidence of HPD from 50 studies was 12.9% (95%CI, 11.1%–14.7%). HPD incidence varied from 0% to 43.1% depending on the definition each investigator chose. There is a growing need for a more uniform definition of HPD that does not underestimate or overestimate its incidence.

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