

UNDERSTANDING THE DEFINITION OF HYPERPROGRESSIVE DISEASE (HPD) AND ITS INCIDENCE – A NEW PATH FORWARD

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Background Hyperprogressive disease (HPD) is a phenomenon where tumors grow exponentially following immunotherapy. Multiple definitions have been proposed, and the incidence of HPD varies from 5.9% to 43.1% depending on the definition.¹ As HPD is associated with worse patient outcomes, it is important to have a clear definition of HPD to identify and prevent such cases.^{2,3} There is much discussion about how to best define HPD as RECIST criteria only considers the target lesions.⁴ iRECIST and irRECIST have been newly proposed to incorporate new lesions. This study proposes a new, modified definition for HPD using RECIST 1.1 and taking the sum of new lesions into consideration.

Methods This study retrospectively analyzed 128 lung cancer patients' data (N of patients = 128) and 144 total number of regimens (N of regimens = 144) at a large metropolitan academic medical center. This study compares the incidence of hyperprogression using different definitions including Champiat, Saada-Bouزيد, and Ferrara et al.⁵⁻⁷ As a modification to these definitions, the new lesions were included into the sum of lesions. The difference of incidence between original and modified definitions was evaluated with Chi-squared test.

Results The incidence rate of hyperprogression ranged from 5% to 15%, depending on the original definitions and modified definitions. Among the 144 treatment regimens, hyperprogression was detected in 5% (N=7), 10% (N=14), and 0% (N=0) using the original Champiat, Saada-Bouزيد, and Ferrara et al. definitions respectively. The incidence of hyperprogression increased when new lesions were included in the definition. The incidence rate with modified Champiat, Saada-Bouزيد and Ferrara et al. definitions were 11% (N=16), 15% (N=21) and 6% (N=9) respectively (table 1). Incorporating new lesions enabled the detection of more HPD cases, and the change in the sum of lesions are depicted in figure 1. The difference in incidence between original and modified definitions was statistically significant only for the Champiat et al. (X² = 3.0, p=0.05).

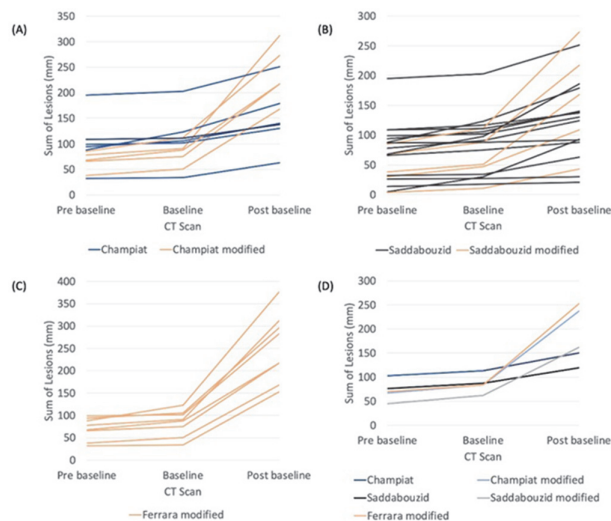
Conclusions Incorporation of new lesions in the definition of hyperprogression resulted in an increase in HPD incidence for all three definitions. However, statistically significant difference was observed only for the Champiat et al. definition. There are limitations of utilizing RECIST 1.1 in the identification of HPD as it does not take new lesions into consideration. This study highlights the importance of including new lesions when defining HPD to accurately capture HPD.

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Ethics Approval The study was approved by Northwestern University's Institutional Review Board, study number STU00207117.



Abstract 1407 Figure 1 The changes of sum of lesions depending on patients with hyperprogression according to different definitions of hyperprogression and modification.

Abstract 1407 Table 1 A summary of the incidence of hyperprogression according to main different definitions of hyperprogression and modified definitions

Component	Source		
	Champiat et al ^[5] , November 2016	Saada-Bouزيد et al ^[6] , April 2017	Ferrara et al ^[7] , November 2018
Definitions*	RECIST progression and TGR-exp/ TGR-ref >2	TGK-exp/ TGK-ref >2	RECIST progression and TGR-exp - TGR-ref >50
Modified Definition	The modification was made to include new lesions on CT scans into the sum of lesions.		
Single	n=128		
RECIST 1.1	6 (5%)	11 (9%)	0 (0%)
Modification	15 (12%)	19 (15%)	9 (7%)
Multiple	n=144		
RECIST 1.1	7 (5%)	14 (10%)	0 (0%)
Modification	16 (11%)	21 (15%)	9 (6%)

*Indexes are calculated using TGR and TGK values before (ref) and during (exp) therapy.

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