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THE OVERALL SURVIVAL (OS) AND PROGRESSION-FREE SURVIVAL (PFS) OF HYPERPROGRESSIVE DISEASE (HPD) IN LUNG CANCER PATIENTS

¹Youjin Oh, ¹Trie Ami Djunadi, ¹Liam Il-Young Chung, ²Soowon Lee, ³Timothy Hong, ¹Zunairah Shah*, ¹Joo Hee Park, ¹Sung Mi Yoon, ¹Richard Duan, ¹Young Kwang Chae. ¹Feinberg School of Medicine, Northwestern University, Chicago, IL, USA; ²Baylor University, WACO, TX, USA; ³Northwestern University, Evanston, IL, USA

Background Hyperprogressive disease (HPD) is the acceleration of tumor growth observed in patients treated with immunotherapy. HPD was seen to be negatively associated with the overall survival (OS) and progression-free survival (PFS) when compared to patients without HPD.¹⁻⁵ Various definitions of HPD have been used to evaluate the relationship between HPD and OS/PFS.^{2,6-11} This study uses two HPD definitions from Champiat and Saada-Bouزيد et al. to evaluate the association between HPD and OS/PFS in lung cancer patients.^{8,11}

Methods This study retrospectively analyzed 128 patients (N=128) and 144 regimens (N=144) at a large metropolitan academic medical center. The overall survival (OS) and progression free survival (PFS) were analyzed using cox regression to produce a hazard ratio. Clinicopathologic variables were controlled for.

Results Among the 128 patients that were analyzed in this study, immunotherapy was used as the first line in 27% (N=34) and second line in 51% (N=65) of them. Immunotherapy was also used as a single agent in 77% (N=111) of all 144 regimens. In a survival analysis, the presence of hyperprogression was strongly negatively associated with PFS and OS in both definitions (figure 1.) Using the Champiat et al. definition, patients with HPD were about 20 times more likely to show future progression [Hazard ratio (HR) 22.30; 95% confidence interval (CI) 7.84-63.42, p<0.001]. Also, OS was greater in patients without hyperprogression [HR 2.69; 95% CI 1.11-6.5, p=0.029, table 1]. This trend was also seen with the Saada-Bouزيد et al. definition, revealing a higher risk of future progression [HR 4.46; 95% CI 1.78-11.18, p<0.001] and death [HR 3.17, 95% CI 1.61-6.2, p<0.001] among patients with HPD (table 2). According to the Champiat et al. definition, patients who were female or had Eastern cooperative oncology group scale of performance status (ECOG PS) 3-4 were more likely to experience future disease progression. The Saada-Bouزيد et al. definition showed that patients who were female, ECOG PS 3-4, or had immunotherapy as third line treatment or beyond resulted in a higher chance of future disease progression.

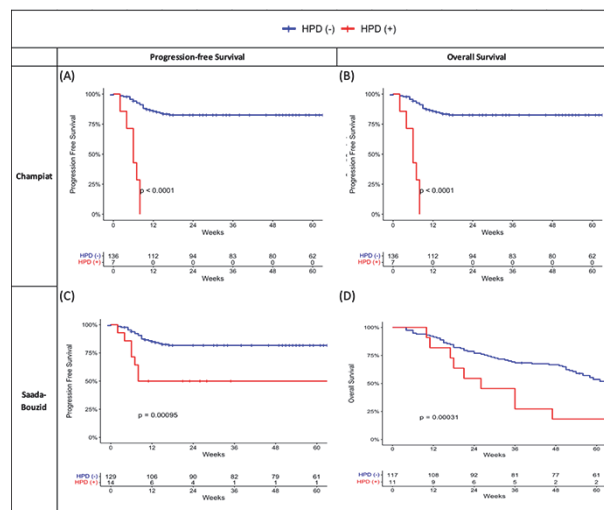
Conclusions Both definitions of HPD were associated with worse OS and PFS in lung cancer patients even after adjusting for confounding variables. Given its clinical importance associated with the poorer prognosis of patients, further attention and efforts are needed to identify hyperprogression and prevent its detrimental effects. Further studies with larger cohorts are warranted.

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



Abstract 1413 Figure 1 Overall survival and progression free survival between hyperprogression (HPD) and non-HPD patients defined by Champiat et al. and Saada-Bouزيد et al.

Abstract 1413 Table 1 Multivariate Analysis of overall survival and progression free survival including hyperprogression defined by Champiat et al.

Dependent	PFS			OS		
	HR	95%	p	HR	95%	p
Diagnosis Age	0.97	6.50-50.27	<0.001	1	0.98-1.0	0.627
Sex						
Female						
Male	0.32	0.14-0.72	0.006	0.75	0.51-1.1	0.15
Hyperprogression	18.08	6.50-50.27	<0.001	2.88	1.2-6.9	0.018
ECOG						
1-2						
3-4	4.12	1.26-13.48	0.019	1.49	0.70-3.2	0.302

Abstract 1413 Table 2 Multivariate Analysis of overall survival and progression free survival including hyperprogression defined by Saada-Bouزيد et al.

Dependent	PFS			OS		
	HR	95%	p	HR	95%	p
Diagnosis Age	0.97	0.93-1.00	0.081	1	0.98-1.0	0.828
Sex	Reference					
Female	Reference					
Male	0.4	0.17-0.91	0.025	0.77	0.51-1.2	0.223
Hyperprogression	3.92	1.55-9.88	0.004	2.76	1.40-5.4	0.003
Line of Immunotherapy	Reference					
1st line	Reference					
2nd line	1.82	0.59-5.56	0.294	0.92	0.55-1.5	0.751
3+ line	3.19	1.04-9.80	0.043	1.97	1.09-3.6	0.025
ECOG	Reference					
1-2	Reference					
3-4	3.28	1.01-10.64	0.048	1.76	0.81-3.8	0.151

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