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127P - Better than RECIST and faster than iRECIST: defining the Immunotherapy Progression Decision score to better manage progressive tumors on immunotherapy



CentraleSupélec

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Introduction

- Immuno-Oncology (IO) therapy has revolutionized therapeutic strategies in the treatment of multiple tumor types.
- Most patients do not respond to immunotherapy, and some show atypical responses (like Pseudo Progression).
- iRECIST protocol takes this atypical response into consideration, but imposes a delay of 1 month.
- We retrospectively analyzed clinical (Table 1), biological (NLR, LDH, Albumin, ...) and radiological (tumor burden, target and non-target lesion progression, tumor locations, ...) parameters measured at the timing of progression and determined which parameters could help at predicting outcome.

We defined the immunotherapy Progression Decision score (iPD score) based on Biological values and CT-scan characteristics based on parameters collected at the time of progression, the iPD score predicts patients with poor or critical prognosis for whom immunotherapy should be discontinued.

Materials & Methods

- This retrospective study includes 107 metastatic patients of all cancer types in phase I clinical trials treated by anti-PD(L)1 as monotherapy or combotherapy at Gustave Roussy.
- All the patients were classified progressive disease according to the RECIST 1.1 criteria.
- We analyzed clinical, radiological and biological information relative to the patients, at both Baseline and the first evaluation, and chose nonredundant and relevant criteria for the building of our score.

The authors declare no potential conflicts of interest.

Results

The characteristics related to the 107 included patients are presented in Table 1. The most prevalent cancer type was colorectal cancer (19.2%), followed by urinary tract (15.4%) and lung cancer (14.4%). The median OS was 5.54 months (95% CI, 3.90-7 months). Our proposed iPD score is presented in Table 2. The parameters were all gathered at the time of first CT-scan after immunotherapy onset. The criteria were mostly uncorrelated, and are clinically relevant. For example, the liver involvement's effect on survival is presented in Figure 1. Three subgroups of patients were determined using quantiles of the score:

- Good prognosis (GP) : lower quartile (1 to 5)
- Poor prognosis (PP) : IQR (6 to 9)
- Critical prognosis (CP) : high quartile (10 to 13)

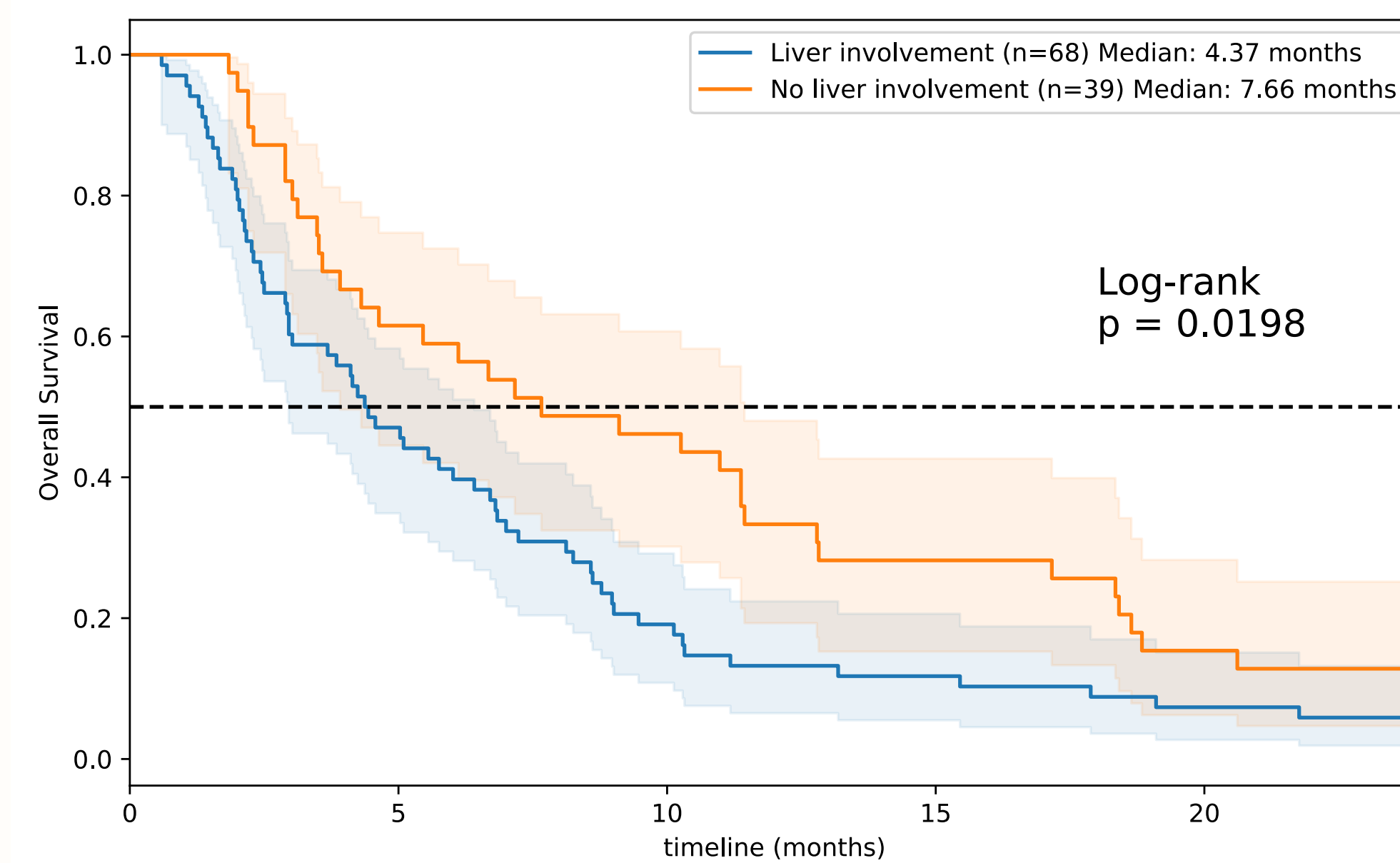


Figure 1: The effect of liver involvement on the OS.

Table 1: Patient's characteristics.

Variable	Patients (n=107)
Age-years	
Median (IQR)	58 (48-65)
Range	25-88
Sex	
Male	65 (60%)
Female	42 (40%)
Previous Immunotherapy	
Yes	2 (2%)
No	105 (98%)
Number of previous treatments	
0	1 (1%)
1	27 (25%)
2	24 (22%)
≥ 3	55 (51%)
Number of metastasis at baseline	
1	13 (12%)
2	39 (36%)
≥ 3	55 (51%)
Liver metastasis	
Yes	68 (64%)
No	39 (36%)
IO therapy	
Anti-PD1	52 (49%)
Anti-PDL1	55 (51%)
Combo Therapy	
No combo	16 (15%)
Another ICI	76 (71%)
Radiotherapy	15 (14%)

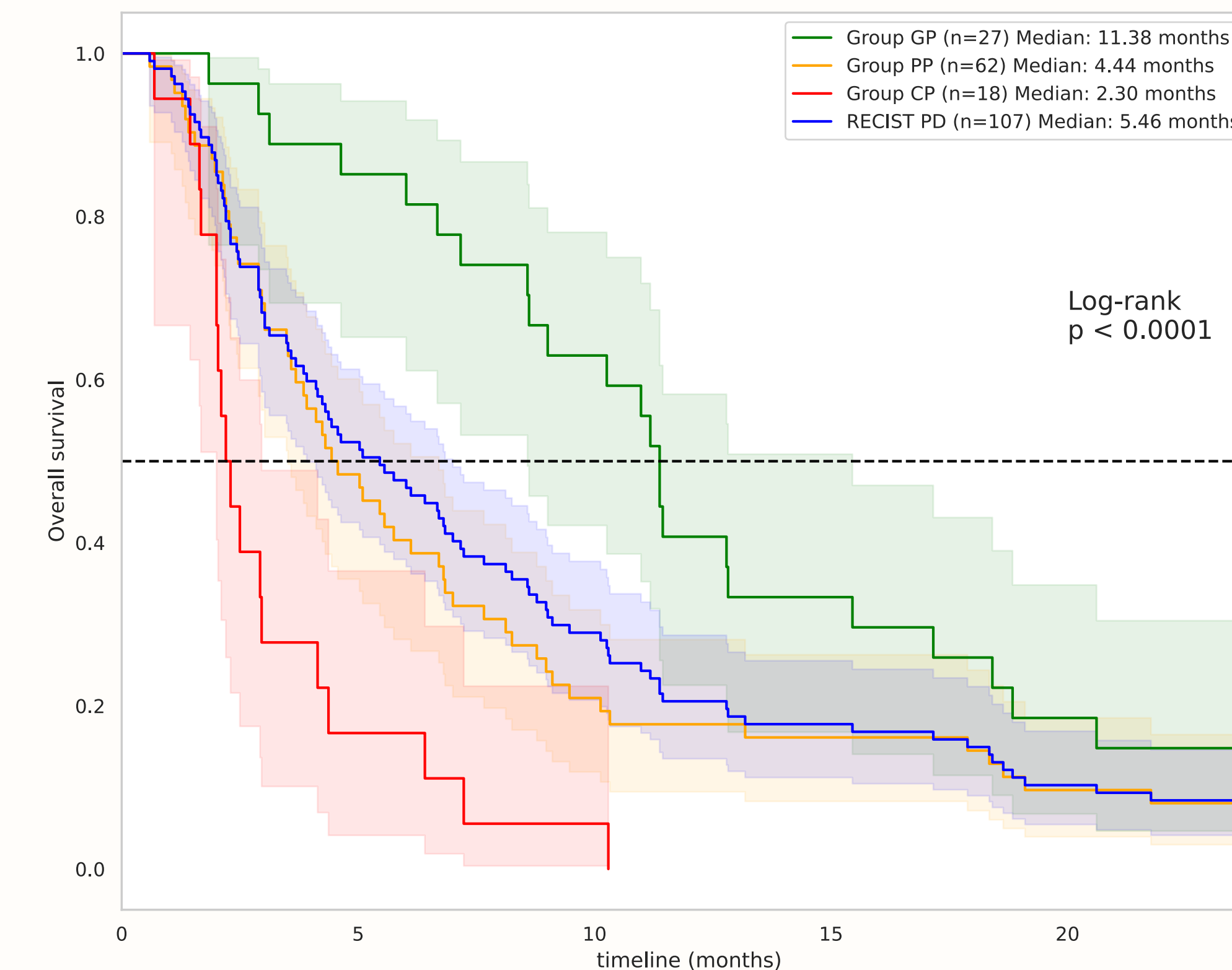


Figure 2: Overall survival curves of groups iPD score GP, PP, and CP.

Table 2: Immunotherapy Progression Decision score (iPD score)

Category	Criterion	Score weight
Biology	NLR > 6	1
	LDH > ULN	1
	Albumin < ULN	1
General CT	Tumor burden > 15cm	1
	Liver involvement	1
	Number of organs involved	1, 2, or 3
Specific CT	Target lesions increase > 20%	1
	Non-target lesions increase > 50%	1
	New lesions	Emergence, ∑ Size > 10cm, New organ
	TOTAL	∑

iPD score	Prognosis status	Median OS
scores 1 to 5	good prognosis (GP)	11.4 m
scores 6 to 9	poor prognosis (PP)	4.4 m
scores 10 to 13	critical prognosis (CP)	2.3 m

We analyzed the distribution of PSPD patients within the different iPD subgroups and observed that no PSPD was observed in the critical prognosis group (CP) (Table 3).

We compared the different known scores are baseline for the prediction of the overall survival, using a fitted cox model (Figure 4).

Table 3: Distribution of PSPD according to the iPD subgroups, GRIm and RMH scores. All scores are ranked from best (0) to worst (2 or 3). The proportion of pseudo-progressor is indicated in each class.

Rank	GRIm	RMH	iPD Score	Group
0	3/36 (8%)	3/25 (12%)	5/27 (19%)	GP
1	1/41 (2%)	0/41 (0%)	1/62 (2%)	PP
2	2/23 (7%)	3/36 (8%)	0/18 (0%)	CP
3	0/7 (0%)	0/5 (0%)		

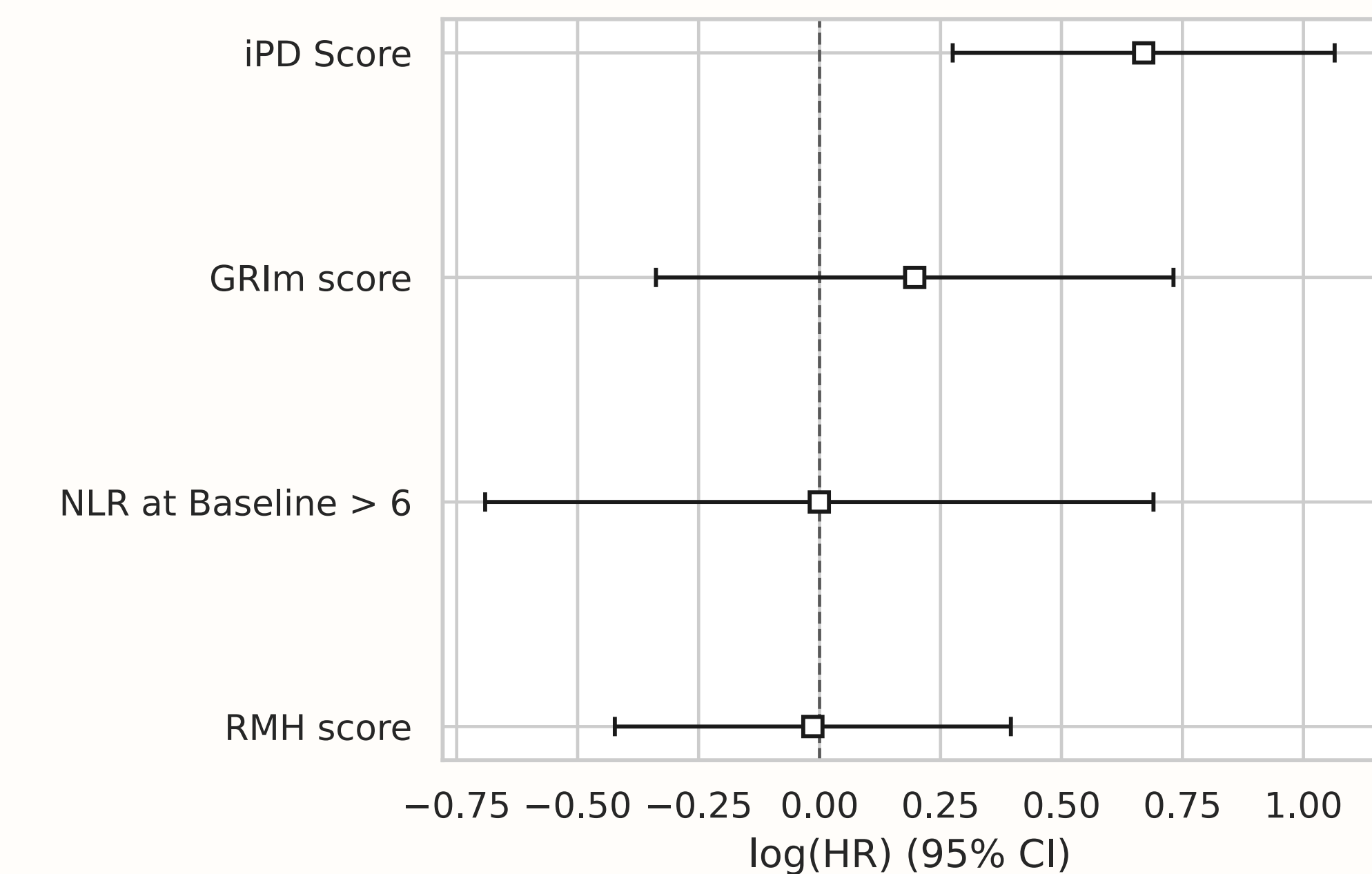


Figure 3: Cox model fitted on all criteria to predict overall survival. The biggest HR was affected to the iPD score by the model (HR = 2, p < 0.005)

Summary

- Progressive disease affects the majority of immunotherapy-treated patients.
- There exists scores that predict the outcome at baseline, but none to our knowledge that aim to identify the outcome after progression.
- The iPD score is based on a more precise characterization of CT-observations combined with biological factors.
- The iPD outperforms other scores in predicting survival and pseudo-progression patients.
- Further validation is warranted to confirm the validity and clinical use of this score.

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