Refining patients' selection for immunotherapeutic early-phase clinical trials (ieCTs): a single Phase I Unit experience

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Background

Identifying patients mostly benefitting from ieCTs is of crucial importance in the era of precision medicine. The Gustave Roussy Immune Score (GRImS) identifies two prognostic categories (low risk, 0-1; high risk, 2-3) based on three objective variables: LDH > ULN, albumin < 35 g/dl, NLR>6 and has been proved to work as a good prognostic index. However, no predictive score has been validated to be used in clinical practice so far.

Patients and methods

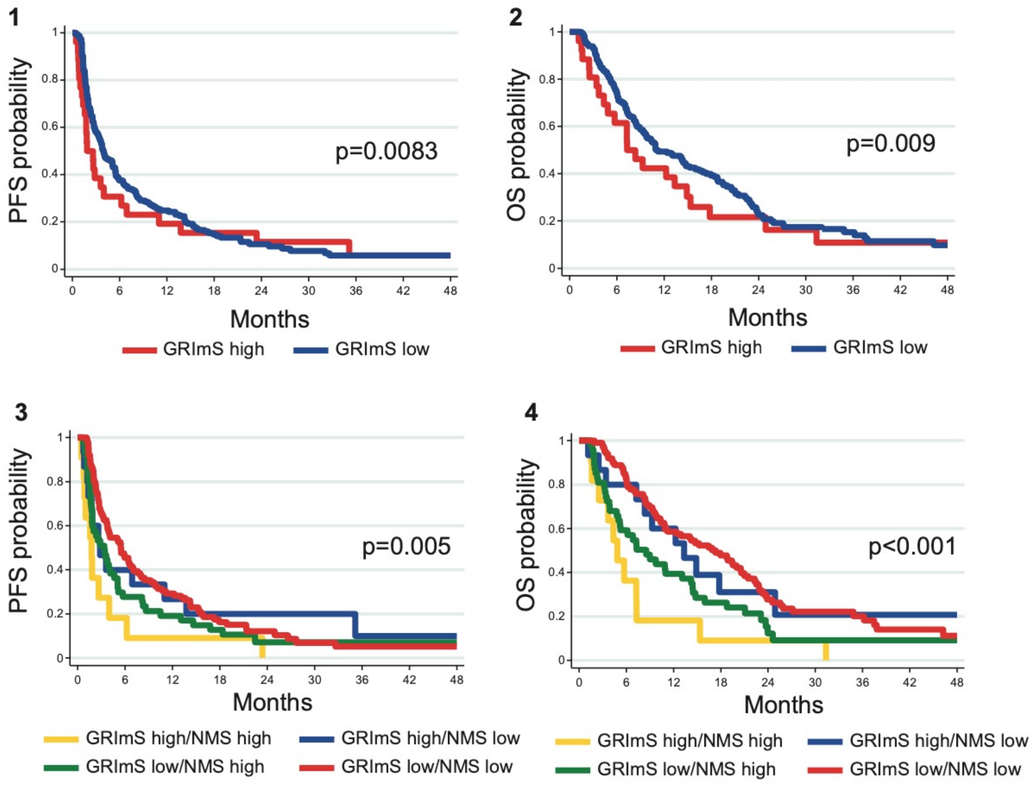
We retrospectively collected clinical-pathologic, laboratory and treatment-specific characteristic of consecutive patients, enrolled in ieCTs from January 2014 to July 2020 at Humanitas Research Hospital Phase I Unit. A large series of variables were correlated with progression-free survival (PFS) and overall survival (OS) through univariate and multivariate analysis (UVA; MVA). P-value for statistical significance was set at 0.050.

Results

A total of 205 pts (M/F:117/88; median age: 62.5 yrs) with advanced solid tumors treated into ieCTs have been selected. The most frequent histologies were NSCLC (26%), HCC (23%), and glioblastoma (11%). Patients' clinico-pathological characteristics are summarized in Table 1.

	N (%)
Sex	
Female	88 (43)
Male	117 (57)
Age	
<75	156 (76)
≥75	49 (24)
ECOG PS	
0	126 (61.5)
1	79 (38.5)
Smoking habit	
No	86 (42)
Yes	119 (58)
Tumor type	
NSCLC	53 (26)
HCC	48 (23)
GBM	23 (11)
Colorectal	14 (7)
Melanoma	11 (5)
Others	56 (27)
Therapy type	
Immunotherapy combo	86 (42)
Immunotherapy single agent	55 (27)
Immunotherapy + antiangiogenic	51 (25)
Immunotherapy + chemotherapy	13 (6)
Line of therapy	
1st	32 (16)
2nd	95 (46)
≥3rd	78 (38)
N metastatic sites	
1	61 (33)
2	63 (35)
3-4	58 (32)
Best response	
SD	95 (46)
PR	21 (10)
CR	4 (2)
PD	82 (42)
PD-L1 status	
<1%	77 (37.5)
≥1%	40 (19.5)
Not assessed	88 (43)
Microsatellite status	
Stability	108 (53)
Instability	2 (1)
Not assessed	95 (46)

Table 1. Patients' clinico-pathological characteristics.



With a median follow-up of 28.4 months (mos), the PFS was 3.6 mos, and the OS was 10.8 mos. At the UVA, among clinical-pathologic characteristics, the number of metastatic sites (NMS, 1-2 sites vs >2 sites) proved statistically significant in terms of both PFS and OS, while NLR predicted better OS and age did not influence prognosis. In the MVA, GRImS (PFS HR:1.36, p=0.083; OS HR:1.64, p=0.009) (Fig. 1-2) and NMS (PFS HR:1.49, p=0.018; OS HR:2.07, p<0.001) confirmed their prognostic effect. Thus, we crossed GRImS and NMS and observed a statistically significant prognostic trend, with GRImS low/NMS low (mPFS 5.7 mos; mOS 20.5 mos) reporting a statistically significant better mPFS and mOS compared to GRImS low/NMS high (mPFS 3.5 mos; mOS 8.5 mos), GRImS high/NMS low (mPFS 3 mos; mOS 10.4 mos), and GRImS high/NMS high (mPFS 1.1 mos; mOS 4.4 mos) (Fig. 3-4).

Conclusions

We assessed the prognostic accuracy of GRImS in our ieCTs cohort. We found that NMS might be usefully integrated into the GRImS in order to better refine prognosis and potentially identify patients who may benefit more from enrollment in ieCTs.

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