472P - Prognostic markers in patients (pts) with solid tumors submitted to bispecific T-cell engagers in phase I (phI) clinical trials

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BACKGROUND

Bispecific T cell engagers (BTE) are novel anticancer drugs that bind to both CD3 and cell surface antigens to promote immune activity. In solid tumors, they are currently being tested in early-phase clinical trials.

OBJECTIVE

To identify variables related to progression-free survival (PFS) ≥ 6 months in phI clinical trials evaluating bispecific T cell engagers.

PATIENTS AND METHODS

• Patients treated with BTE in phI studies at DITEP Gustave Roussy between June, 2016 and October, 2021.

• Collected data: sex, age, BMI, number of previous lines, ECOG-PS, RMH prognostic score, number of metastatic sites, albumin, LDH, CRP, fibrinogen, CBC, tumor burden (TB), tumor growth rate (TGR).

• TB: RECIST 1.1 in pre-enrollment, baseline, and first response assessment CT scans.

• TGR: calculated according to Ferté et al., 2014[1].

• Data balancing was done with SMOTE.

• XGBoost (XGB), was trained in a 5-fold CV to determine the most important variables.

• Unsupervised Gaussian Mixture Model (GMM) clustering was then used to group pts according to the selected features.

• Variables were submitted to univariate analysis between clusters

1. DOI: 10.1158/1078-0432.CCR-13-2098

RESULTS

Altogether, 25 pts were included in the analysis.

Total	25
Median Age	58 (IQR 53-66)
Sex	
Female	10 (40%)
Male	15 (60%)
Median Previous Lines of Treatment	4 (IQR 2-5)
Primary Site	
GI Tract	13 (52%)
Lung	12 (48%)
ECOG-PS	
0	9 (36%)
1	15 (60%)
2	1 (4%)
Royal Marsden Hospital Prognostic Score	
0	4 (16%)
1	11 (44%)
2	9 (36%)
Median Number of Metastatic Sites	2 (IQR 2-4)

Table 1: Characteristics of enrolled patients. IQR = interquartile range

• Cox analysis revealed post-enrollment TGR to be significant for PFS (HR 4.12; CI95% 1.53 - 11.10; p-value 0.01).

• SMOTE added nine new data points for data balance.

• XGB achieved a C-statistic of 0.72 (CI95% 0.60-0.84) in the 5-fold cross-validation. Features deemed important by the model were age, RMH prognostic score, TGR after enrollment, neutrophil-lymphocyte ratio, platelet count, serum lactate dehydrogenase, serum albumin, and serum C-reactive protein.

• GMM divided data points into six clusters. 14 out of 16 with PFS ≥ 6 months (including synthetic data points) were in one cluster (Cluster 0). A tridimensional graph of the data points used for clustering can be seen in Figure1.

• Univariate comparison of features between Cluster 0 and an aggregate of all other clusters showed that only LDH and CRP were significantly different between groups (p-value <0.01 and 0.03, respectively).

• mPFS of all patients was 123 days (CI95% 75-188), while that of Cluster 0 was 265 days (83-435) and that of all other clusters was 75 days (28-111). Log-rank showed a significant difference of PFS between Cluster 0 and other clusters (p-value <0.01). A Kaplan-Meier plot stratified by cluster group can be seen in Figure 2.
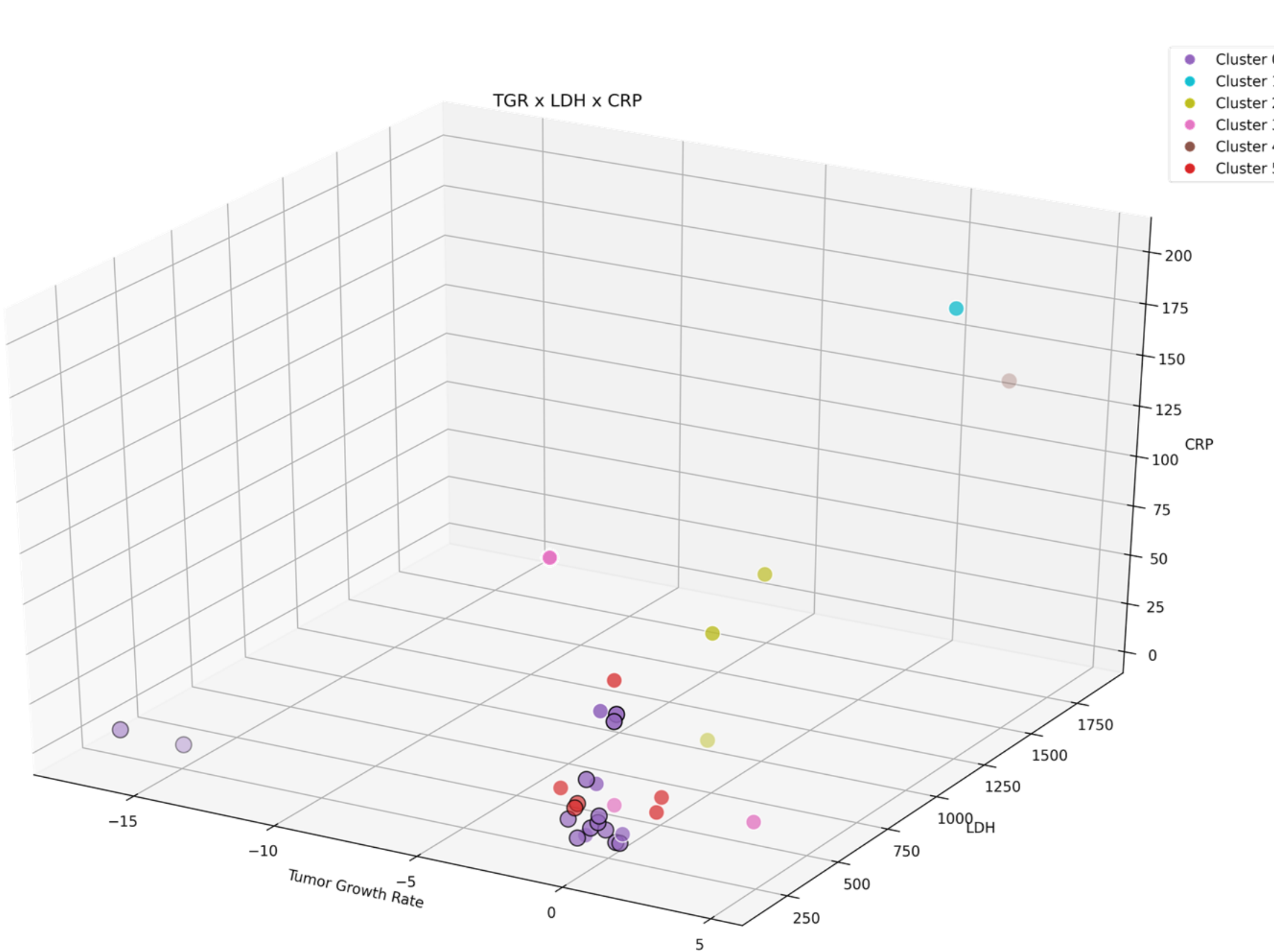

Figure 1: tridimensional plot of all data points (TGR x serum lactate dehydrogenase [LDH] x serum C-reactive protein [CRP]), colored according to cluster. Data points with black borders were patients with PFS ≥ 6 months.
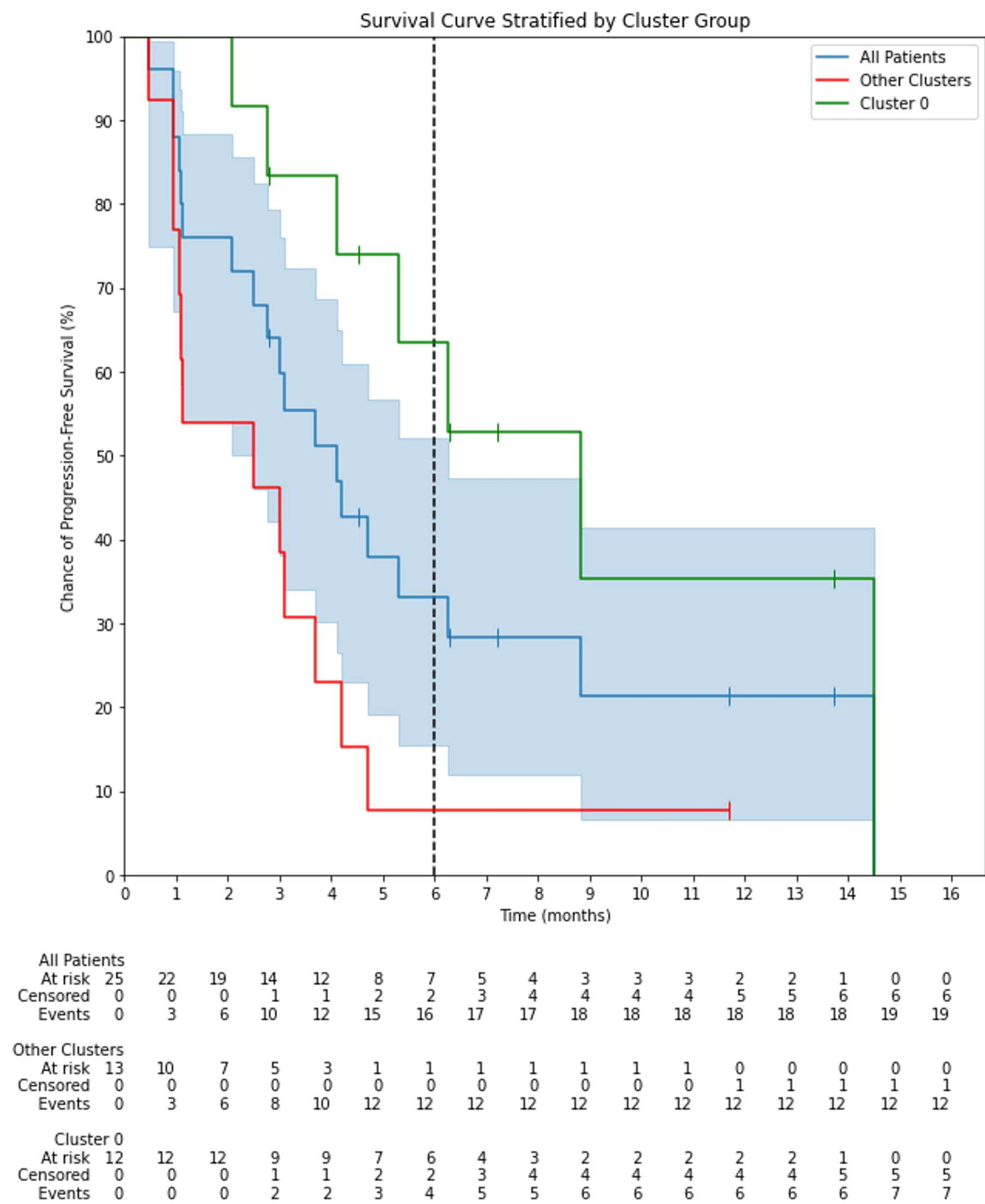

Figure 2: Kaplan-Meier plot of PFS of all patients (blue), with 95% confidence interval (light-blue area), patients from Cluster 0 (green), and all other patients (red). The black dashed line represents the six-month mark.

CONCLUSION

Lower C-reactive protein and LDH at baseline and tumor growth rate under bispecific CD3 T cell engagers might be useful to identify pts who will benefit with higher mPFS. Larger datasets and external validation are required to confirm these results.

ACKNOWLEDGMENT

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PARIS 2022 ESMO congress
PARIS FRANCE
9-13 SEPTEMBER 2022