Identification of Regorafenib Prognostic index (REP index) via recursive partitioning analysis in Advanced Hepatocellular Carcinoma Patients Receiving systemic treatment.

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BACKGROUND

The results of the pivotal RESORCE trial led to the approval of the second tyrosine kinase Regorafenib, as second line treatment in advanced HCC after Sorafenib failure *. Data about prognostic factors in a second-line HCC setting are scarce. We investigated the prognostic factors in a cohort of patients with advanced HCC treated with regorafenib and built a new prognostic score (the REP index).

METHOD

A survival tree regression to define risk groups in the cohort was performed. We performed univariate Cox proportional hazards regression for each predictor variable, and we included in groups of risk the covariates on the basis of the HR and statistical significance ($p<0.05$) for dichotomized the study cohort. Consequently, we recursively repeated the univariate Cox proportional hazards regression within each group until no variable met the criteria for the inclusion, and no statistical significance was found.

RESULTS

At the first-step univariate analysis for OS, AP resulted the most significant parameter in terms of OS, and was chosen as first node in our tree model. In the subpopulation of patients presenting AP ≤122 U/L (n=155) at the baseline, the most statistically significant split was by the PFS to Sorafenib treatment, between patients with a PFS ≥ 6 months (n=59) and patients with a PFS < 6 months (n=96). In the subpopulation of patients with AP ≤122 U/l and PFS to Sorafenib ≥6 months, the final split was determined between patients with HBV-related liver disease (n=22) and patients with no HBV-related liver disease (n=37). In the subpopulation of patients presenting AP >122 U/L (n=104) at the baseline, the most statistically significant split was by Aspartato-amino transferase (AST) value, between patients with AST ≤56 U/l (n=48) and patients with AST>56 U/l (n=56). We built the REP index which stratify the population in "low-risk", "medium-risk" and "high-risk" patients. The difference in mOS between the three groups of risk was statistically significant, being 20.8 months (95% CI 10.0-46.3) in the "low-risk" group, 8.35 months (95% CI 7.2-1435.8) in the "medium-risk" group and 5.5 months (95% CI 3.5-13.2) in the "high-risk". The median PFS was 7.7 months (95% CI 3.7-19.3), 2.5 months (95% CI 2.1-28.8) and 2.4 months (95% CI 1.6-9.1) for "low-risk", "medium-risk" and "high-risk" group, respectively.

Table 1. Patients characteristics

Parameters	N(%)
Age, years (median, range)	**61 (27-82)**
Gender	
Female	36 (14)
Male	223 (86)
ECOG PS	
0	62 (23.9)
>0	197 (76.1)
Etiology	
HBV	166 (66.1)
No-HBV	93 (33.9)
Child-Pugh	
A	249 (88.2)
B	10 (11.8)
BCLC Stage	
B	17 (5.4)
C	242 (94.6)
AFP	
>400 ng/mL	115 (44.6)
≤400 ng/mL	144 (55.4)
Albumin	
≤3.5 g/dl	115 (44.3)
>3.5 g/dl	144 (55.7)
GPT	
>56 U/L	94 (34.3)
≤56 U/L	165 (65.7)
Alkaline Phosphatase	
>122 U/L	104 (39)
≤122 U/L	155 (61)
PFS Sorafenib	
>6 months	86 (33.9)
≤6 months	173 (66.1)

Figure 1. The diagram of the recursive partitioning analysis

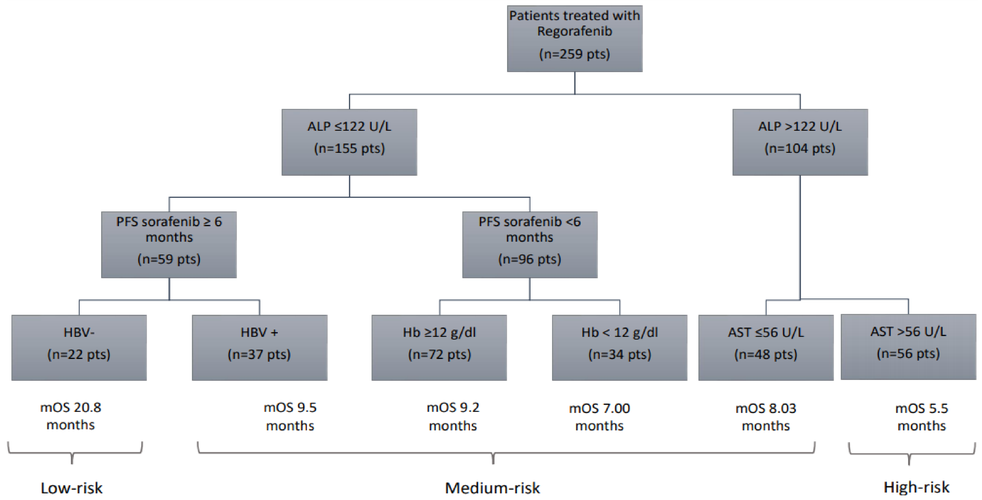
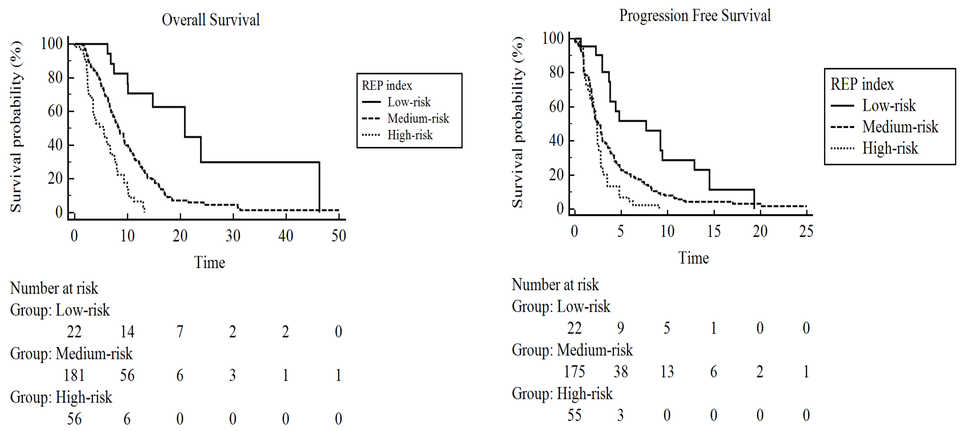


Figure 2. Kaplan Mayer for OS to regorafenib (A) and PFS to regorafenib (B) according the REP score.



CONCLUSIONS

The REP index is a independent prognostic factor for OS and PFS in patients with advanced HCC treated with regorafenib.

Moreover, this new index is easy to reproduce and, if validated on larger perspective trials, it could constitute a useful tool to stratify patients with advanced HCC progressed to sorafenib.

REFERENCES

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