Prognostic Implication of Serum Alpha-Fetoprotein in Patients with Unresectable Hepatocellular Carcinoma Treated with Regorafenib

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BACKGROUND
- Regorafenib is standard therapy for patients with unresectable hepatocellular carcinoma (uHCC) after progression on sorafenib.
- Serum alpha-fetoprotein (AFP) was reported as a significant predictive factor for the outcome of patients with advanced HCC on sorafenib treatment.
- In this multinational retrospective cohort study, implication of serum alpha-fetoprotein (AFP) in the prediction of effectiveness of regorafenib in uHCC was investigated.

METHODS
- Study design: Multinational, retrospective, cohort study
- Study population: A total of 581 patients with uHCC, previously treated with sorafenib after failure to sorafenib from 12 institutions in Korea and Italy were included. All patients had received sorafenib as first line treatment. All patients had at least one dose of regorafenib after sorafenib, BCLC stage of B or C, and Child-Pugh class A at the time of regorafenib initiation.
- Baseline AFP: Serum AFP was measured at the initiation of regorafenib treatment and during the treatment. Patients were classified according to baseline AFP using a cutoff of 400 ng/mL.
- AFP response: A patient was considered an AFP responder if there was an event of 20% reduction of serum AFP during treatment with regorafenib compared to baseline AFP (minimum AFP / baseline AFP < 80%).
- Statistical analysis: Baseline characteristics in relation to baseline AFP and AFP response were compared using chi-square tests. Univariate analysis were done using Kaplan-Meier graphs and log-rank tests. Multivariate analysis were done using Cox proportional hazard regression model with backward likelihood ratio method.

RESULTS
- Baseline characteristics according to baseline AFP
  - Baseline AFP: Below 400ng/mL (n=312) Above 400ng/mL (n=266) P value
  - Sex
    - Male 275 (88.1%) 229 (86.1%) 0.46
    - Female 37 (11.9%) 37 (13.9%) 0.0002
  - Age (Below 60) 113 (36.3%) 130 (48.9%) 0.002
  - HBV 193 (61.9%) 184 (69.2%) 0.15
  - HCV 45 (14.4%) 35 (13.2%) 0.70
  - Others 74 (23.7%) 47 (17.7%) 0.02
  - ECOG PS 0.02
    - 0 90 (28.8%) 52 (19.9%) 0.01
    - 1 220 (70.5%) 207 (77.8%) 0.25
    - 2 0 (0.6%) 6 (2.3%) 0.01
  - BCLC Stage 0.544
    - B 24 (7.7%) 17 (6.4%) 0.01
    - C 288 (82.9%) 249 (93.6%) 0.01
    - BCLC prior TACE 0.02
    - Prior TACE 221 (70.8%) 193 (72.6%) 0.32
    - Prior RT 121 (38.8%) 130 (48.9%) 0.02
    - Prior Surgery 137 (43.9%) 102 (38.3%) 0.18
  - Extrahepatic Disease 0.50
    - Extrahepatic Disease 229 (73.4%) 201 (75.8%) 0.50
  - AFP Response (cutoff of 20%) 0.06
    - AFP Response (cutoff of 400 ng/mL) 108 (37.2%) 88 (35.3%) 0.65

- PFS and OS by baseline AFP
  - OS
    - AFP <400 ng/mL
    - AFP >400 ng/mL

- PFS and OS by AFP response

- Multivariate analysis of overall survival
  - Variables Hazard Ratio 95% CI P value
  - OS
    - Etiology (HBV vs non-HBV) 0.69 0.52-0.91 0.009
    - Prior TACE 0.77 0.54-1.09 0.10
  - AFP Baseline (<400 ng/mL vs ≥400 ng/mL) 0.55 0.42-0.71 <0.001
  - AFP Response (Responder vs Non-responder) 0.35 0.26-0.48 <0.001
  - Overall Response to Sorafenib (CR, PR, SD vs PD) 0.69 0.53-0.90 0.007
  - HFSR 0.51 0.39-0.67 <0.001

- Multivariate analysis of progression-free survival
  - Variables Hazard Ratio 95% CI P value
  - PFS
    - Sex (Male vs Female) 1.36 1.02-1.82 0.04
    - Prior TACE 0.79 0.63-0.99 0.04
  - AFP Baseline (<400 ng/mL vs ≥400 ng/mL) 0.71 0.58-0.87 0.001
  - AFP Response (Responder vs Non-responder) 0.52 0.42-0.64 <0.001
  - Overall Response to Sorafenib (CR, PR, SD vs PD) 0.67 0.55-0.83 <0.001
  - HFSR 0.67 0.55-0.82 <0.001

CONCLUSIONS
- Baseline AFP and on-treatment AFP response were independent prognostic factors for advanced HCC patients treated with regorafenib.
- Serum AFP may be a useful clinical indicator to predict the clinical outcomes of regorafenib treatment in patients with advanced HCC.

None of the authors have any conflict of interest.