Original Research Article

# Predictors of survival in a cohort of advanced Hepatocellular Carcinoma initiated on sorafenib

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## Abstract

**Background:** Hepatocellular carcinoma is the second common cause of cancer related mortality worldwide. The most accepted comprehensive classification of hepatocellular carcinoma is Barcelona clinic liver cancer (BCLC). Hepatocellular carcinoma with portal vein invasion and extra-hepatic metastasis corresponds to BCLC C or Advanced Hepatocellular carcinoma. Even if liver function is well preserved the median survival of this stage is only 10 months. Sorafenib is the first line drug for this disease group. With advent of newer treatment modalities like immune check point inhibitors and other anticancer drugs it is important to predict those who are likely to have inadequate response to sorafenib so that other second line chemotherapy can be tried.

**Aim and objectives:** To find out simple clinical and biochemical variables that can predict the response of sorafenib (Predictor of survival) in advanced hepatocellular carcinoma.

**Materials and methods:** It was a cross sectional study in which clinical and biochemical variables of the patient at the time of initiation of sorafenib was assessed and change in eosinophil count at the end of one month after initiation of sorafenib was assessed and patient's relatives were telephonically interviewed to assess the mortality at 6 months.

**Results:** 30 patients were taken up for the study, 26 were males and 4 were females. Most common etiology was HBV (33.3%) followed by Alcohol (30%). Among the variables analyzed, increase in eosinophil count after one month of treatment was the only variable that predicts 6 month survival. AUROC curve for increase in eosinophil was plotted and it was 0.789 in predicting 6 month survival.

**Conclusion:** Increase in eosinophil of >35 from baseline one month after initiation of Sorafenib in hepatocellular carcinoma can predict 6 month survival.

## Key words

Predictors, Survival, Cohort, HCC, Sorafenib, Hepatocellular carcinoma.

## Introduction

Hepatocellular carcinoma is the second common cause of cancer related mortality worldwide [1]. The most accepted comprehensive classification of hepatocellular carcinoma is Barcelona clinic liver cancer (BCLC) [2]. Hepatocellular carcinoma with Portal vein invasion and extra-hepatic metastasis corresponds to BCLC C or Advanced Hepatocellular carcinoma. Even if liver function is well preserved the median survival of this stage is only 10 months. Sorafenib is the first line drug for this disease group [3, 4, 5]. With advent of newer treatment modalities like Immune check point inhibitors and other anticancer drugs it is important to predict those who are likely to have inadequate response to sorafenib so that other second line chemotherapy can be tried.

## Aim and Objectives

- To find out simple clinical and biochemical variables that can predict the response of sorafenib (Predictor of survival) in advanced hepatocellular carcinoma.

## Materials and methods

It was a prospective study conducted in Department of Medical Gastronterology, Medical College, Trivandrum from June 2016 to May 2017. Clinical and biochemical variables of the patient at the time of initiation of sorafenib was assessed and change in eosinophil count at the end one month after initiation of sorafenib was assessed and patient's relatives were teliphonically interviewed to assess the mortality at 6 months.

## Results

30 patients were taken up for the study 26 were males and 4 were females (**Figure - 1** and **Table - 1**). Most common etiology among study population was HBV (33.3%) followed by Alcohol (30%) as per **Table – 2**.

Among the study variables analysed to predict survival following sorafenib initiation only change in eosinophil at one month following initiation of sorafenib can predict 6 month survival in advanced hepatocellular carcinoma as per **Table – 3**.

AUROC was plotted and found out that increase in eosinophil more than 35 from base line at 1 month following the initiation of sorafenib predict survival at 6 month in advanced hepatocellular carcinoma with Sensitivity of 67% and specificity of 77% (**Figure – 2**).
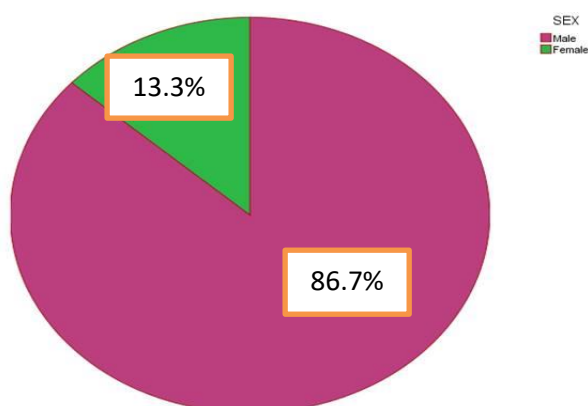
**Table - 1:** Sex distribution of study population.

| Sex | Frequency | Percent | Valid Percent | Cumulative Percent |
|---|---|---|---|---|
| Male | 26 | 86.7 | 86.7 | 86.7 |
| Female | 4 | 13.3 | 13.3 | 100.0 |
| Total | 30 | 100.0 | 100.0 | |

**Table - 2:** Etiology of HCC and cirrhosis in the study population.

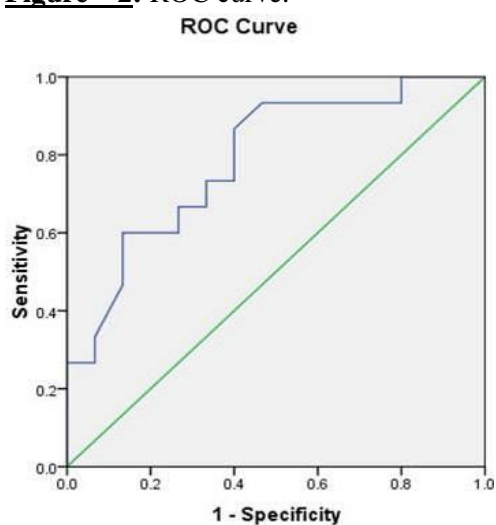| Etiology | Frequency | Percent | Valid Percent | Cumulative Percent |
|---|---|---|---|---|
| Alcohol | 9 | 30.0 | 30.0 | 30.0 |
| HBV | 10 | 33.3 | 33.3 | 63.3 |
| HCV | 9 | 30.0 | 30.0 | 93.3 |
| NAFLD | 2 | 6.7 | 6.7 | 100.0 |
| Total | 30 | 100.0 | 100.0 | |

**Figure - 1:** Sex distribution of study population.



**Table - 3:** Predictors of 6 month survival in advanced hepatocelluar carcinoma initiated on sorafenib.

| Parameter | P value | Mean difference | Standard error |
|---|---|---|---|
| Age | .235 | -4.200 | 3.461 |
| Hb | .616 | -.3933333 | .7756206 |
| TC | .272 | -1155.333 | 1030.160 |
| Initial | .758 | 8.800 | 28.245 |
| Final | .055 | -65.133 | 29.447 |
| Change | .004 | -68.867 | 21.661 |
| PLT | .613 | -.1173333 | .2291539 |
| Bilirubin | .229 | .8340000 | .6786928 |
| INR | .285 | .1020000 | .0935335 |
| Albumin | .246 | -.3533 | .2984 |
| Creatinine | .807 | .0193333 | .0784958 |
| CTP | .121 | .733 | .458 |
| Na | .901 | -.200 | 1.597 |
| AFP | .231 | -3197.000 | 2612.446 |

**Figure – 2:** ROC curve.



| Area under the curve | | | | |
|---|---|---|---|---|
| Area | Std. Error[a] | Asymptotic Sig.[b] | Asymptotic 95% Confidence Interval | |
| | | | Lower Bound | Upper Bound |
| .789 | .083 | .007 | .626 | .952 |

## Discussion

30 patients were taken up for the study in which 26 were males and 4 were females. Most common etiology among study population was Hepatitis B (33.3%) followed by Alcohol. Among the study variables analyzed to predict survival following sorafenib initiation only change in eosinophil at one month following initiation of sorafenib can predict 6 month survival in advanced hepatocellular carcinoma. AUROC was plotted and found out that increase in eosinophil more than 35 from base line at 1 month following the initiation of sorafenib predict survival at 6 month in advanced hepatocellular carcinoma with Sensitivity of 67% and specificity of 77%. At the time of malignancy there will be increased level of cytokine and chemotactic factors and there will be tissue destruction. It can result in margination and sequestration of eosinophil in the tissue and can result in decrease in circulatory eosinophils [6, 7]. We postulate that increase in eosinophil count following initiation of sorafenib predict tumor response to sorafenib and better the response, more will be the eosinophil released into the systemic circulation. In short increase in eosinophil following initiation of sorafenib can predict a better survival.

## Conclusion

Increase of eosinophil more than 35 from baseline at one month after initiation of sorafenib can predict 6 month survival in advanced hepatocellular carcinoma with Sensitivity of 67% and specificity of 77%.

## References

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