The Editor

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Predictors of Sorafenib Benefit in Patients with Hepatocellular Carcinoma

Sir,

We read with interest the paper by Bruix et al1.

The authors analysed the combined data from the SHARP and Asia-Pacific trials of sorafenib compared to placebo in patients with advanced hepatocellular carcinoma (HCC). They claim to demonstrate a benefit, across all sub-groups, in overall survival due to Sorafenib. Unfortunately, many of their conclusions cannot be substantiated by the data presented.

Specifically, the authors claim that there is `significant clinical benefit in patients who are HBV-positive’. However, this statement is not supported by the evidence presented. The HR for sorafenib compared to placebo in the HBV-positive group was 0.78 [0.57 – 1.06] and therefore does not reach the benchmark for statistical significance. Furthermore, and perhaps more importantly, neither the univariate nor the multivariate modelling of patients who received sorafenib identify HBV status as a covariate that has any impact on overall survival. This is in striking contrast to HCV-positive patients where the HR was 0.47 [0.32–0.69], a finding confirmed visually in the Fig. 2 (A&B) survival curves.

Thus the findings of Bruix et al., are entirely in line with our recent meta-analysis2, showing that whilst in HCV-positive patients there is significant benefit for sorafenib, in HBV positive and/or HCV negative patients, there is little or no benefit.

Such findings are of considerable clinical importance because the great majority of HCCs worldwide are HBV positive (and HCV negative). Such observations may also be one important factor in explaining why sorafenib has failed to have even an additive effect when combined with surgical resection3 or transarterial chemoembolization (TACE)4. In these trials most patients were HCV negative and it is therefore not surprising that the addition of a drug that is minimally effective in this subgroup did not enhance the overall survival after resection or TACE.

On the other hand, the opportunity to prescribe a drug according to viral status offers a dramatic example of true personalised oncological therapy.

**REFERENCES**

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Yours faithfully,

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