Aim: GC33 is a first-in-class recombinant, humanized mAb that binds to glypican-3 which is highly expressed in HCC. The aims of the analysis were to investigate AFP response after administration of GC33 in patients with advanced HCC and to assess the relationship between AFP response and PFS.

Methods: Placebo and GC33 1600 mg biweekly with two loading doses were administered to previously treated patients with advanced HCC in a double-blind manner with 1:2 randomization. Seventy-one patients (placebo: GC33 = 24:47) who had AFP measurements at baseline (AFPB) and 6 weeks post treatment (AFP6W) were evaluated. Patients with steady state GC33 trough concentration higher than 230 µg/ml (the median of the projected trough concentration on cycle 3 day1) were included in GC33 high exposure group. AFP response was defined as a 20% decrease in AFP at 6 weeks post treatment.

Results: Twenty seven out of 47 patients treated with GC33 had trough concentration higher than 230 µg/ml. AFP change (%) from baseline at 6 weeks post treatment (calculated as (AFP6W-AFPB)/AFPB) in high exposure group was significantly lower than that in placebo and GC33 low exposure group combined (p = 0.029). In addition, 2 out of 24 (8.3%), 2 out of 20 (10%), and 8 out of 27 patients (30%) were AFP responder in placebo, GC33 low exposure group, and GC33 high exposure group, respectively. In landmark analysis (n = 71), AFP response was a prognostic factor of PFS (HR = 0.63, 80%CI: 0.41-0.97) regardless of treatment. Within GC33 treatment group, hazard ratio of PFS comparing AFP non-responder (n = 37) vs. AFP responder (n = 10) was 0.56 (80% CI: 0.34-0.91).

Conclusions: GC33 high exposure group had better AFP response than placebo and low exposure group. Early assessment of AFP response may potentially be a valuable biomarker for predicting antitumor response in patients with advanced HCC.

Disclosure: Yuyan Jin, Jun Shi, Alex Phipps and Ruey-min Lee have declared: is an employee of Hoffmann-La Roche; Mikiko Nakamura and Toshihiko Ohtomo have declared: is an employee of Chugai Pharmaceutical Co. Ltd.Ya-Chi Chen is an employee of Hoffmann-La Roche and also holds stocks of Hoffmann-La Roche.