PHASE I TRIAL OF PANITUMUMAB IN COMBINATION WITH CISPLATIN, FLUOUROURACIL AND DOCETAXEL (MDCF) IN ADVANCED/METASTATIC GaSTRIC CANCER

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Background: To determine the maximum tolerated dose (MTD) of docetaxel, cis-platin and 5-Fluourouracil (5-FU-lecovorin (LV) (modified DCF regimen) plus panitumumab in patients with advanced/metastatic gastric adenocarcinomas.

Methods: Patients received Panitumumab 6 mg/kg as 1h iv infusion, followed by the administration of mDCF: escalated doses of docetaxel in 3 dose’s level (dose 30, 35 and 40 mg/m²) as 1 hour iv infusion on day 1 and standard doses of cis-platin (40 mg/m² as 1 hour iv infusion on day 1), LV (400 mg/m² as a 2-hr i.v infusion, on day 1), 5-FU bolus infusion (400 mg/m² on day 1) and 5-FU continuous infusion (100 mg/m²/day on days 1-2), every 2 weeks. At least 3 patients were treated on the same dose-level.

Dose limiting toxicities were evaluated in the first cycle and were defined as the occurrence of any grade 4 hematologic toxicity or any >= grade 3 non-hematologic toxicity and any treatment delay due to toxicity.

Results: Fifteen patients (median age 58 years; male/female 8/7; PS (ECOG) 0-1 in 93% and 2 in 7%) with advanced/metastatic HER-2 negative gastric cancer were enrolled, 3 in level 1, 5 in level 2 and 9 in level 3. The DLT level was not reached: one patient (1%) developed febrile neutropenia in the level 3 (40mg/m² of docetaxel). A total of 127 treatment cycles have been administered (median 8 cycles/patient). Skin rush was the most common toxic effect of the combination. Grade 3 rush was observed in 4 (27%) patients while another 4 (27%) develop grade 2 rush. Grade 3 fatigue occurred in one (6%) patients and grade 3 diarrhea in another one (6%). Hematological toxicity was mild with one (6%) patient presenting grade 3 febrile neutropenia and another one (6%) grade 3 anemia. There were no treatment related deaths. Objective response was observed in 5 (34%, 95% CI: 10.7-61.8) patients: 2 in the 1st, 1 in the 2nd and 2 in the third dose’s levels. The median Progression Free Survival was 6.2 months (95% CI: 3.4 – 8.9 months) while the median overall survival was 12.9 (95% CI: 4.8 – 21.0) with a probability of 1 year survival of 74%.

Conclusion: The Panitumumab could be safely added to the standard doses of mDCF. The combination is well tolerated, with promising efficacy results. The trial is continued as a phase II multicenter study.