**Title：mFLOT Chemotherapy as First-line Treatment in GC**

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**Patient eligibility**

Chinese patients with metastatic gastric cancer were eligible if all the following criteria were met: histologically confirmed adenocarcinoma of stomach; untreated metastatic disease or recurrence over 6 months after finish of adjuvant chemotherapy; age from 18 to 75 years; Eastern Cooperative Oncology Group (ECOG) performance status of 0-2; estimated life expectancy more than 3 months; adequate hematological, hepatic, renal and coagulation function (White blood count $\geq 3.5\times10^9$/L, Absolute neutrophil count $\geq 1.5\times10^9$/L, Platelets $\geq 80\times10^9$/L, Hemoglobin≥75g/L). Exclusion criteria were: second primary malignant disease, central nervous system metastasis, peripheral nerve disease, uncontrollable medical illness, contraindication or known hypersensitivity reaction to any of the study drugs, patients with pregnant. All patients provided written informed consents. The protocol was approved by ethics committee of Ruijin Hospital, Shanghai Jiaotong University School of Medicine, Shanghai, People's Republic of China.

**Treatment plan**

Classical 3+3 design was used in present study. The starting doses of docetaxel and oxaliplatin were at 80% of original doses of FLOT regimen. Dose escalation started at 40mg/m$^2$ of docetaxel (level 1) and 65mg/m$^2$ of oxaliplatin (level 1). The plan of dose escalation was listed in Table 1. The increment doses of docetaxel and oxaliplatin were about 10% of highest doses, respectively. At least

3 patients were enrolled at each dose level. If no patient experienced DLT, the dosage was increased to next level and 3 new patients were enrolled. If DLTs occurred in one patient, another 3 patients were enrolled in this level. MTD was defined as if 2 or more patients in one level suffered DLTs (two of three patients or two of six patients). The RD was defined as the dose level below the MTD.

Leucovorin (200mg/$m^2$) and 5-FU (2200mg/$m^2$ 48 hours continuous infusion) were given in fixed dose. Antiemetic prophylaxis could be given before treatment. Dexamethasone was administered orally before and after treatment of docetaxel following the protocol to prevent fluid retention and allergic reactions. Prophylactic use of G-CSF was not permitted. The treatment was administered every 2 weeks until disease progression, unacceptable toxicity, patient's refusal or maximum 12 cycles. If patients were evaluated as SD or better after 8 cycles, S-1 as maintenance therapy or another 4 cycles intravenous treatment could be given decided by physicians and patients together.

Dose modification was not permitted in first two cycles unless severe adverse events occurred. Dose reductions were performed for all three drugs when treatment related grade 3 or 4 toxicities occurred after first two cycles. The dose of docetaxel, oxaliplatin and fluorouracil were reduced by 20% for the subsequent cycle. Dose reduction could be performed only once. If grade 3 or 4 toxicities still occurred after dose reduction, drug which caused distinction toxicities would be excluded in following treatment. Treatment initiated when following criteria was met, absolute granulocyte count was $\geq 1.5\times10^9$/L, platelet count was $\geq 100\times10^9$/L, and all treatment related toxicities were resolved to grade $\leq$1.

**Toxicity evaluation**

Adverse events were recorded and evaluated every week during the first two cycles according to the National Cancer Instituted Common Terminology Criteria for Adverse Events (NCI-CTCAE, version

4.0), and every 2 weeks after. Dose-limiting toxicities (DLTs) were determined during the first two cycles, including: febrile neutropenia, grade 4 neutropenia, grade 4 thrombocytopenia, ≥grade 3 infection, ≥grade 3 non-hematological toxicities, treatment delay ≥ 2 weeks[9].

**Response evaluation**

Response were classified according to the RECIST guideline (version 1.1)[10]. Enhanced computed tomography scans of chest, abdomen and pelvis were performed within 1 week before start of the treatment and were repeated every 8 weeks irrespective of treatment delay. If clinical symptoms, like increasing ascites, worse of pain, which indicated progression of disease during treatment, the imaging examination would be performed ahead of schedule decided by physicians to assess status of disease. Progression free survival (PFS) was measured from the date of treatment start until disease progression or death of any cause. Overall survival (OS) was measured from the date of diagnosis until death of any cause.