

5-FU dose monitoring and prevention of oxaliplatin-induced neurotoxicity in FOLFOX 4 regimen: Results of a phase II study.

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Introduction: FOLFOX4 is the most commonly used base chemotherapy regimen for treatment of colorectal cancer. Although pharmacokinetically-guided dose management has been shown to improve 5-FU efficacy and tolerance in other regimens, it has not been demonstrated to date with FOLFOX4. In this phase II study, FOLFOX4 was optimized with pre-therapeutic detection of DPD deficiency (genotyping and phenotyping), individual 5-FU dose monitoring based on a simple pharmacokinetic follow-up, and prevention of oxaliplatin neurotoxicity with Ca+Mg infusions. **Patients and Methods:** 119 patients with metastatic colorectal cancer were treated in first line therapy: 63±10 years old, metastasis: liver (57), lung (5), both (41), >2 (16); PS : 0 (68), 1 (37), 2 (14). **Results:** See the table below. **Conclusions:** FOLFOX4 with pharmacokinetically-guided 5-FU dose management and neuropathy prevention provides high efficacy and disease control, equivalent to that of combinations with targeted therapies, with better tolerance and much lower cost.

Pretherapeutic detection of major DPD deficiency	5 patients
5-FU plasma clearance variability	42-130 l/m ² x h
Quick 5-FU dose increase or decrease, from 2,500 mg/m²	
Dose increase >20 %	36%
Dose decrease > 20 %	12%
Response rate at 3 months: CR - PR - SD - PD (%)	2.5 - 67.2 - 23.5 - 4
Overall survival (months)	28 ± 2 (23-33)
Progression-free Survival (months)	16 ± 2 (11-21)
Secondary metastasis surgery	39 patients (33%)
Toxic side-effects (grade 3-4 NCI-CTC)	
Diarrhea	1.7 %
Mucositis	0.8 %
Neutropenia	12 %
Neuropathy	5 %