Tolerance and efficacy of adjuvant chemoradiotherapy with FOLFIRI in adenocarcinoma of stomach and GI junction

Tolérance et efficacité de la radiochimiothérapie adjuvante avec FOLFIRI dans les adénocarcinomes de l’estomac et du cardia

Based on the results of major studies performed to compare surgery and surgery + chemoradiotherapy (INT 0016) [1], chemoradiotherapy following surgery could be considered as standard treatment. We noted the significant effectiveness of combined treatment, but the problem is the toxicity of this combination, which seems to be important.

It therefore seems to be necessary to test an effective but less toxic treatment. In metastasis, FOLFIRI is more effective than LV5FU2 or LV5FU2—CDDP. Moreover, patient tolerance supports the use of FOLFIRI compared to LV5FU2—CDDP [2].

Eleven patients (WHO < 1) with a median age of 43 years, range (36—61 years), underwent surgery for gastric adenocarcinoma and then were treated between January 2004 and January 2005. The treatment protocol was FOLFIRI three cycles every two weeks, followed by chemoradiotherapy (with two cycles of LV5FU2S and 45 Gy daily. 1.8 Gy daily) again followed by three cycles of FOLFIRI. FOLFIRI: LV5FU2S (folinic acid 200 mg/m², two hours, 5FU 400 mg/m², bolus, 5FU infusion 1200 mg/m², 44 hours + CPT 11: 180 mg/m², two hours, d1—d15).

Considering hematological toxicity, 44 cycles of FOLFIRI were well-tolerated: no neutropenic fever, neutropenia grade IV, thrombocytopenia grade I/IV. Anemia grade I was observed in three patients who were also treated with EPO.

Toxicity is obviously gastro-intestinal. For 44 cycles of FOLFIRI before and after radiotherapy: nausea grade II and vomiting grade I: 14/44 (32%), diarrhea grade I: 6/44 (14%) grade III 1/44(2%), asthenia grade I: 6/41 (14%) grade II 5/44(11%). One of these patients had to stop treatment due to toxicity grade III, (vomiting in the first cycle), Campto® was then stopped and then five cycles of LV5FU2 were administered without radiotherapy. One patient had toxicity grade III (diarrhea) with radiotherapy.

All but one of six patients were free of disease (> 36 months follow-up). Five patients had local relapse with peritoneal carcinomatosis and died. It should be noted that these five patients could not receive full treatment due to digestive toxicity grade III in one, to grade II intolerance in another and finally, to very early disease progression in a third patient. Two patients could not continue treatment, one due to loss of contact and the other due to surgery for digestive perforation after the second cycle. Thus, only 44 cycles could be analysed.

The goal of new drug combinations is to develop standard treatments such as ECF or FU cisplatin. New metastatic chemotherapies are now based on taxanes [3], but also on combinations with CPT11 [4]. The combination of chemoradiotherapy and FOLFIRI has never been tried. FOLFIRI may be promising considering the results in metastatic disease. FOLFIRI is well tolerated in the metastatic setting. In our study of 11 patients, the hematological tolerance was good. Nevertheless, more gastrointestinal toxicity was observed, especially at the end of radiotherapy.

This protocol with FOLFIRI might be feasible but the toxicity of chemoradiotherapy remains a problem (additional treatment delayed or cancelled), especially after radiotherapy. Based on these results, a multicentre trial has begun with the choice of neo-adjuvant or adjuvant chemoradiotherapy. Chemotherapy will not be proposed after radiotherapy.

Références


