

LV, 5FU with/without docetaxel in patients with inoperable or relapsed gastric cancer

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Purpose To estimate the effect and toxicity of leucovorin(LV) and fluorouracil(5FU) with/without docetaxel(LV5FU2D/LV5FU2) combination chemotherapy in patients with inoperable or postoperative relapsed gastric cancer. **Methods** Total 27 patients are enrolled in this study. 8 patients received LV 20mg/m²(bolus), 5FU 400mg/m²(bolus), 5FU 600mg/m²(24-hour continuous infusion) on day 1, 2, 15, and 16, every 4 weeks(LV5FU2). 19 patients received LV5FU2 plus docetaxel 60mg/m²(1-hour infusion) on day 15(LV5FU2D). **Results** A total of 17 cycles of LV5FU2 and 101 cycles of LV5FU2D were administered. Response is observed only in LV5FU2D group and the response rate were 40.0% with 2 complete response and 4 partial response in 15 evaluable LV5FU2D group patients. The median response duration is 183 days (95% CI, 57-183). As compared with LV5FU2 group, LV5FU2D had a higher likelihood of median time to progression (228 days (95% CI, 58-127) in LV5FU2D, 85 days (95% CI, 58-127) in LV5FU2; P<0.0001). The grade 3-4 toxicity of neutropenia(24.6%) is observed in LV5FU2D group and of neutropenia(5.7%), anemia(5.7%) is observed in LV5FU2 group. The grade 1 toxicity of injection site reaction is observed all patients and the grade 1-2 toxicity of alopecia is observed 60% in LV5FU2D group. **Conclusion** LV5FU2D significant increase response and time to progression in patients with inoperable or postoperative relapsed gastric cancer than LV5FU2, and is observed tolerable toxicity.

Comprehensive analysis of ERCC, XPD, and XRCC polymorphisms: Association with clinical outcomes in patients with advanced gastric cancer

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Purpose : Platinum-DNA adducts are repaired by nucleotide excision repair (NER) pathway, in which genes of the excision repair cross-complementation 1 (ERCC1), xeroderma pigmentosum group D (XPD) and X-ray repair cross-complementing group (XRCC) have an important role. The purpose of this study was to investigate the relationship between single nucleotide polymorphisms (SNPs) of these genes and the clinical outcomes to combination chemotherapy of 5-FU and oxaliplatin in advanced gastric cancer (AGC). Patients and **Methods** : We searched SNPs of NER pathway genes from database of the International Hapmap Project. Tagging SNPs and haplotype blocks were founded by linkage disequilibrium and haplotype analysis. We conducted genotyping using germ line DNA from peripheral blood mononuclear cells of the patients. And then germ line DNA from peripheral blood of the AGC patients were analyzed using SNaPshot methods. Seventy three metastatic or relapsed AGC patients received 2-hour infusions of OX (100mg/m²) and LV (100mg/m²) followed by a 46-hour infusion of FU (2400mg/m²) repeated every 2 weeks as a first-line palliative chemotherapy and were analyzed. **Results** : By searching the database of the International Hapmap Project, we found 17 SNPs in ERCC, 69 SNPs in XPD, 78 SNPs in XRCC. We found that some SNPs played a role as a tagging SNP and belonged to haplotype block (5 tagging SNPs and one haplotype block in ERCC, 8 tagging SNPs and two haplotype blocks in XPD, 9 tagging SNPs and two haplotype block in XRCC). Tagging SNPs were analyzed and matched with clinical significance. Among the 22 tagging SNPs of NER pathway genes, only XPD-C156A SNP (rs238406) showed clinical correlation. AA genotype of XPD C156A showed higher response rate (CC: CA: AA=29.2%: 43.3%: 63.2% p=0.083) and toxicities (neutropenia of grade 3 or 4) (CC: CA: AA=4.3%: 3.2%: 21.1%, p=0.060) than CC or CA genotypes. **Conclusions** : Our results suggest that some SNPs of ERCC, XPD, XRCC showed linkage disequilibrium and belonged to haplotype blocks. And XPD-C156A SNP showed clinical correlation in AGC patients treated with modified FOLFOX-6 regimen. These findings require independent prospective confirmation.