Prospective study of UGT1A1*27 polymorphism for irinotecan therapy: result of lung oncology group in Kyushu (LOGiK1004B)

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Background: UGT1A1*27 is known that exist together with UGT1A1*28 as linkage disequilibrium and impair the effect of UDP-glucuronosyltransferase (UGT) in basic research, however, poor clinical investigation because of the rare frequency.

Purpose: To evaluate the effect of UGT1A1*27 gene polymorphism for safety and efficacy in irinotecan therapy. The effects of UGT1A1*28 and UGT1A1*6 gene polymorphism also examine at a time.

Patients and methods: Eligibility criteria were lung cancer patients scheduled the dose of irinotecan therapy as single >= 80 mg/m², combination >= 50 mg/m², radiation with single >= 50 mg/m², radiation with combination >= 40 mg/m²; age >= 20 years; performance status 0-2. After informed consents, patients were enrolled and collected the blood to examine UGT1A1*28 and UGT1A1*6 polymorphism and received irinotecan therapy. Examination of UGT1A1*27 were added when founding UGT1A1*28 polymorphism. We planned 111 enrollment for an accrual of 10 patients with UGT1A1*27 gene polymorphism.

Results: Fifty patients were enrolled and 48 patients were eligible. Patients’ characteristics were as follows: male/female = 41/7; performance status (PS) 0/1/2 = 14/33/1; median age (range) = 72 (51-87); Ad/Sq/La/Oth = 16/15/12/4. UGT1A1*27 were checked in 9 patients including ineligible one patients with *28/*28, however, no gene polymorphism was found. The study was stopped after interim analysis.

Evaluation of side effects of irinotecan, febrile neutropenia (FN) were only grade 3 toxicities and analyzed. In patients with UGT1A1*28 and UGT1A1*6 polymorphism, FN observed higher than that with wild type (29% and 33% vs. 14%) but not significant (p = 0.3830 and p = 0.1368, respectively).

Conclusions: UGT1A1*27 gene polymorphism was not found in our study. Further investigation might be warranted with UGT1A1*28 wild type.