Poster

[P25-10] P25-10: Oncologic drugs (2)

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[P25-10-8] Impact of STAT3 genetic polymorphism on sunitinib-induced stomatitis in Japanese renal cell carcinoma patients

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Background

Stomatitis is a very frequent adverse event induced by molecular-targeted drugs. Signal transducer and activator of transcription (STAT) 3 is a key factor in homeostasis of the oral mucosa by regulating the production of inflammatory cytokines. It is known that the C allele of rs744166 leads to a higher basal expression level of STAT3. Sunitinib is a substrate of P-glycoprotein (multidrug resistance (MDR)-1/*ABCB1*) and breast-cancer resistance protein (BCRP/*ABCG2*) that regulate the excretion of drugs to saliva. These related genetic polymorphisms are well known to have ethnic differences. In this retrospective study, we evaluated the association between sunitinib-induced stomatitis and *STAT3*, *ABCB1*, and *ABCG2* polymorphisms in Japanese patients with metastatic renal cell carcinoma (mRCC).

Methods

Fifty-two patients with RCC treated with sunitinib were retrospectively genotyped to elucidate a potential association between *STAT3*, *ABCB1*, and *ABCG2* polymorphisms and stomatitis development. Incidence of stomatitis was followed up until 1 year since the start of therapy.

Results

Stomatitis occurred in 22 out of 52 patients. All analyzed genotype frequencies did not show significant deviation compared with those in the Japanese population. The *STAT3* rs744166 T allele frequencies were 50% and 70.5% in the non-stomatitis and stomatitis groups, respectively (odds ratio (OR), 2.39; 95% confident interval (CI), 1.05–5.43; $P = 0.045$). Furthermore, the *ABCB1* rs1128503 CT+TT genotypes exhibited a significant association with stomatitis development (OR and 95% CI, not applicable; $P = 0.033$). Serum creatinine in stomatitis patients was significantly lower compared with that in non-stomatitis patients ($P = 0.034$). In the Kaplan–Meier method for the cumulative incidence of stomatitis, a statistically significant difference was observed between the TT+TC and CC genotypes at *STAT3* rs744166 ($P = 0.037$). Both multiple logistic regression analysis and Cox proportional-hazards regression analysis show *STAT3* rs744166 TT+TC genotypes and serum creatinine in each patient were significant independent factors for stomatitis development. There are no significant association with *ABCB1* and *ABCG2* polymorphisms and stomatitis development in the multivariate analysis.

Conclusions

Our retrospective analysis indicates that *STAT3* polymorphism may be a significant risk factor for sunitinib-

induced stomatitis in Japanese patients with mRCC.