

GS04-4 **Enhancement of therapeutic efficacy of DDS preparation by improving tumor microenvironment**

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DOXIL[®], a formulation of doxorubicin (DXR) encapsulated in PEGylated liposomes, increases the circulating time of encapsulated DXR and enhances accumulation of the drug to the tumor tissue, and thus contributes to an improved efficacy and toxicity profile over conventional DXR. However, in the tumor acidic environment, DXR itself may be difficult to penetrate through cellular membrane of tumor cells, because DXR is ionized in such acidic environment due to the basicity of DXR. To improve the tumor acidic environment, in this study, we focused on “sodium bicarbonate (SBC)”, which is used for the treatment of acidosis or as an antacid drug in clinical cases. Bicarbonate ions were supplied by oral administration of SBC into C26 murine colorectal carcinoma-bearing mouse in order to ameliorate the tumor acidic environment. Then, the tumor growth suppressive effect of DOXIL[®] (weekly three injections) was evaluated in those mice. During the treatments, pH in the urine, which may be an indication that the tumor environment has been neutralized, is also monitored. As we expected, the therapeutic effect of DOXIL[®] was improved by combination with SBC treatment. The uric pH of the mice treated with SBC was kept in alkaline during the tumor growth has been suppressed. However, the uric pH has become acidic when the tumor growth was restarted. These results indicate that oral administration of SBC improves the therapeutic efficacy of DOXIL[®], and the monitoring of uric pH after oral administration of SBC during anticancer treatment may be an indication to predict the therapeutic efficacy of anticancer agent.