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Response

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In reply: We thank Dr Komuro, Watanabe, Tsurita and Muto, for your interest[1] in our article discussing Survivin Expression in 49 ovarian carcinomas.[2] Your study evaluating survivin expression in rectal carcinoma with preoperative radiation shows essentially the same results; namely, there is no correlation of survivin expression with age or stage and no correlation with overall and disease-free survival.[1] However, both studies show a correlation between the presence of survivin in the carcinoma and histology. We did show correlation with mutant p53 that, however, was not demonstrated in your series of rectal carcinoma.

As indicated, in Table IV in our paper,[2] variable results have been obtained based on differential localization of survivin expression in different carcinomas. You have not indicated whether the expression of survivin was nuclear or cytoplasmic. However, several other studies (as indicated in Table IV),[2] have shown cytoplasmic survivin expression by immunohistochemistry to be associated with a decreased 5-year survival and increased recurrence rate in colorectal carcinomas. Your lack of significant correlation between survivin expression and survival following preoperative radiation in rectal carcinoma may be related to the fact that the expression you report is nuclear rather than cytoplasmic.

The timing of the radiotherapy and/or antisurvivin therapy may be of great importance. As you indicated, survivin is a member of the inhibitor of the apoptotic protein family. Thus, its expression could decrease the effectiveness of both chemo- and radiation therapies that function via increasing apoptosis. However, if survivin expression is present in a carcinoma, initial antisurvivin therapy could decrease the existing survivin, so that it will no longer have as depressing an effect on the effectiveness of chemo- or radiotherapy. Thus, there should be an increase in apoptosis and an increased response to subsequent chemo- and radiotherapy.[3–6] This suggests that combined antisurvivin and chemo- and/or radiotherapy might be useful in the treatment of patients with carcinomas showing survivin expression, with the antisurvivin therapy given at earlier stages in the treatment. The five cases who received radiation had a mean OS and DFS similar to those who were not irradiated ($P=0.97$, and $P=0.72$). Markers of apoptosis (survivin, bcl-2, bax) were also similar in the two groups with and without radiotherapy. Bax expression was present in 40% of the radiated group, and in 82% of the nonirradiated group, but this was not a statistically significant difference ($P=0.676$). Too few carcinomas were bcl-x-negative to allow for statistical analysis. Only proliferation (MIB-1 index) was significantly lower in the irradiated group ($P=0.0113$). Thus, we do not believe it is necessarily correct that if the prognosis of a sub-group with adjuvant therapy correlates with survivin expression, it will more strongly support antisurvivin therapies in this group.

In our 49 patients with ovarian cancer, only five were given radiation therapy in combination with surgery and chemotherapy. The remainder had surgery alone (seven), surgery plus chemotherapy (28), no therapy at all (two) and no follow-up of therapy (seven) at our institution available.

We certainly agree with you that we require studies including larger number or cases with standardized methods of immunohistochemistry indicating the exact localization of the survivin expression, and more standardized methods of treatment, in order to clarify the action of survivin expression in malignant tumors. At that stage, we may be able to include antisurvivin therapies in order to assess their efficacy.

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