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Radiosensitization for TARE: Does Duration of Chemotherapy Affect PFS?

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BACKGROUND

Capecitabine and temozolomide (CapTem) are classic radiosensitizers used in combination with radiation therapy for many cancers. A feasibility study of integrated CapTem and Y90 transarterial radioembolization (TARE) for neuroendocrine tumors (NETs) suggests synergy with PFS of 31 months exceeding historical controls. The impact of duration of chemotherapy after TARE on PFS is not known.

METHODS

36 subjects with liver-domianant grade 2 metastatic NETwere treated with capecitabine 600 mg/m2 twice daily for 14 days and temozolomide 150-200 mg/m2 in two divided doses on day 10-14, with 14 days between cycles. During the initial cycle of chemotherapy, the patient underwent simulation angiography with Tc99m-MAA SPECT. The dominant lobe was treated on day 7 of the second cycle of CapTem. Resin Y90 microspheres (SIR-Spheres; Sirtex Medical) were administered according to the body surface area method. Patients with bilobar disease had the other lobe was treated on day 7 of the third or fourth cycle. Clinical and laboratory assessment was done monthly and imaging performed every 3 months. CapTem was continued until progression or intolerance. Subjects were categorized by duration of CapTem into 3-6 mo, 7-12 mo, and >12 mo. PFS was estimated by Kaplan-Meier method and the groups compared by log rank test.

RESULTS

Mean duration of CapTem was 12 months. 10 subjects were on CapTem for 3-6 months, 15 for 7-12 months, and 11 for 13-32 months. 14/36 (39%) stopped CapTem due to toxicities prior to disease progression. Median PFS was > 36 months in the 3-6 month chemo group; 23 months for the 7-12 month chemo group, and 30 months for those on chemo > 12 months (p= NS).

CONCLUSIONS

This limited subset analysis suggests the following hypotheses:

1. Prolonged administration of radiosensitizing chemotherapy does not increase PFS. A limited course of chemotherapy at the time of TARE maybe sufficient to achieve synergy. This could be tested in a prospective trial.

2. Chemotherapy-related toxicities leading to intolerance occur in a substantial proportion of patients, offering an opportunity to investigate de-escaltion of chemotherapy to improve quality of life without sacrificing disease control.

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