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Selective Internal Radiation Therapy in Metastatic Carcinoma of the Colon: A Story of Nonintegrated Care?

In June 2015 at the American Society of Clinical Oncology, there was a presentation by a European group presenting the results of the SIRFLOX trial. This was a randomized multicenter trial of 530 patients with carcinoma of the colon and unresectable liver metastases who were chemotherapy naïve.[1] Half of the group was treated with folinic acid, fluorouracil, and oxaliplatin chemotherapy with bevacizumab alone and in the other 50%, selective internal radiation therapy (SIRT) with Y-90 impregnated resin (sirtex) was administered. Patients were chosen if they had a known colorectal primary tumor and liver predominant liver metastases. It was found that in those that had received the addition of Y-90 SIRT, 79% of patients showed a partial or complete response to their liver metastases compared to 68% if chemotherapy alone was use. There was a significant improvement of progression-free survival (PFS) of disease in the liver with a median PFS of those who had the addition of SIRT achieved a median PFS of 20.5 months compared with 12.6 months for chemotherapy alone. However, what was disappointing was the overall mean PFS, and it was almost identical for the two groups being 10.2 months for chemotherapy alone and 10.7 months for chemotherapy and SIRT. How can such as disappointing result be explained?

The clue is seen in the subsequent resection rate which was 14% for both groups. This is a mystery as the partial and complete response rates for both groups were over 60%. In Cambridge, we were involved in a parallel study called FIRFOX which had similar treatment arms and was a multicenter trial in the UK but with smaller numbers. I started working on this trial as soon as I arrived in Cambridge and was pleased our first patient had an almost complete response and went on to have all his residual cancer resected. This caused a media storm in the UK and helped recruit more patients to the trial.[2] His story was not unique and where possible, we went on to resect tumor with an institutional resection rate of about double that seen in the SIRFLOX trial.

What was the difference between our patients and those on the SIRFLOX trial? To try and obtain some answers I headed off to a meeting in Barcelona where these results were being discussed and we were privileged to meet many of the SIRFLOX trialists. It became clear that in many of the centers performing the study, care was not integrated. A patient would be seen by the surgical team and deemed to be "unresectable." They would be referred to an oncologist for chemotherapy and recruited to the trial. However, in many centers, there was no reassessment made about resectability. Some of those presents expressed the difficulty concerning re-evaluating patients after SIRT and had not considered the use of sequential F-18 fluorodeoxyglucose positron emission tomography/computed tomography.[3] It appeared that because previous experiences had led the surgical teams to believe that once unresectable always unresectable, these patients were not reconsidered for surgery after SIRT. In some centers, there was a more multidisciplinary approach which included advice from both radiology and nuclear medicine staff. This lead to patients being reassessed and resection rates were closer to those from our unit. In patients with carcinoid, we have shown how vital it is that nuclear medicine is involved as an integral part of the continuing care of the patient with complex cancers.[4] It is clear that SIRFLOX demonstrates SIRT kills liver metastases but the lack of integrated care which should include the nuclear medicine physician and the lack of reassessment kills the patient.

The lessons of SIRFLOX is that new techniques such as SIRT can deem a previously unresectable patient resectable and that this needs a continued multidisciplinary (which must include nuclear medicine) assessment and reassessment of patients to ensure optimal outcomes.

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