Radiation Oncology Consultants

Excellence | Technology | Hope

ROC March 2013 Newsletter

Newsletter Announcements:

Successful launch of new and improved ROC website!

Dr. Christy Kesslering develops multi-disciplinary radio-embolization program at CDH Cancer Center.

1. Successful launch of new and improved ROC website!

The Physicians of Radiation Oncology Consultants are pleased to announce the successful launch of their brand new website!

www.chicagocancer.org

Some new features of this site include:

* Detailed explanation of all radiation treatments and technologies offered
* Easy referral physician hotline and second opinion line
* Comprehensive cancer references for our patients
* Access to all active clinical trials offered at our treatment locations
* Highlighting our physicians, locations and technologies in one location on the web

We hope you find the new website has a fresh look, is easy to use and is informative.

Please email us your feedback: info@chicagocancer.org

2. Dr. Christy Kesslering develops multi-disciplinary radioembolization program at Central Dupage Hospital (CDH) Cancer Center.

Over the past 6 months, Dr. Kesslering has collaborated with her Interventional Radiology colleagues Drs. Kim and Patel to perform 7 cases of selective internal radiation therapy (SIRT), also known as radioembolization, at CDH Cancer Center. SIRT is also offered at Alexian Brothers Medical Center and Advocate Good Shepherd Hospital.

SIRT is a liver-directed therapy for inoperable liver tumors. A micro catheter is used to deliver millions of radioactive microspheres into the hepatic artery, where they are carried into the arterioles and selectively lodge in the tumor microvasculature. There are 2 types of microspheres currently on the market: SIR-spheres (made by SIRTex) and TheraSpheres (made by Nodion). SIR-spheres are FDA-approved for liver metastasis from colorectal cancer, and TheraSpheres are FDA-approved for hepatocellular carcinoma. Given the similar mechanism of action, either technology can be used for both diagnoses as well as for liver metastases from other histologies.

SIR-Spheres microspheres are biocompatible resin microspheres containing yttrium-90 (Y-90) and have a median diameter of 32.5 microns. TheraSpheres are also Y-90 microspheres but are made of glass and also have a very small diameter of 20-30 microns. Yttrium-90 is a high-energy beta-emitting isotope with no primary gamma emission. The maximum energy of the beta particles is 2.27MeV with a mean of 0.93MeV. The maximum range of emissions in tissue is 11mm with a mean of 2.5mm. The half-life is 64.1 hours. Following administration, 94% of the radiation is delivered in 11 days.

The distribution of blood flow is 3 to 7 times greater within the tumor than the surrounding noncancerous tissue. Together with the properties of the microspheres mean that the microspheres lodge preferentially in the microvasculature of the tumor, maximizing tumoricidal effects and minimizing the effects on healthy liver parenchyma and adjacent tissues. Ex vivo analyses have shown that microspheres preferentially cluster around the periphery of tumor nodules with a high tumor:normal tissue ratio of up to 200:1. Toxicity is usually mild and temporary, including fatigue, anorexia, nausea, abdominal discomfort, and slight elevations of liver function tests.

At the CDH Cancer Center, we have chosen to use the SIR-spheres.

<u>SIR-Spheres Clinical Data (see links below for more information):</u>

The majority of SIR-spheres data (and where we see most of our patients currently) is for salvage or refractory disease where both the progression-free survival and overall survival were doubled over best supportive care or conventional therapy (median PFS 4-9mos vs. 2-3mos; median OS 7-16mos vs. 3-7mos). As expected, larger PFS and OS gains were seen with earlier use or SIR-spheres and in patients with liver-only distant metastasis. When adding SIR-spheres to first-line therapy, the median PFS increases from 3-9 months to 14-19 months and median OS increases from about to year to 2-4 years (Figure 1).

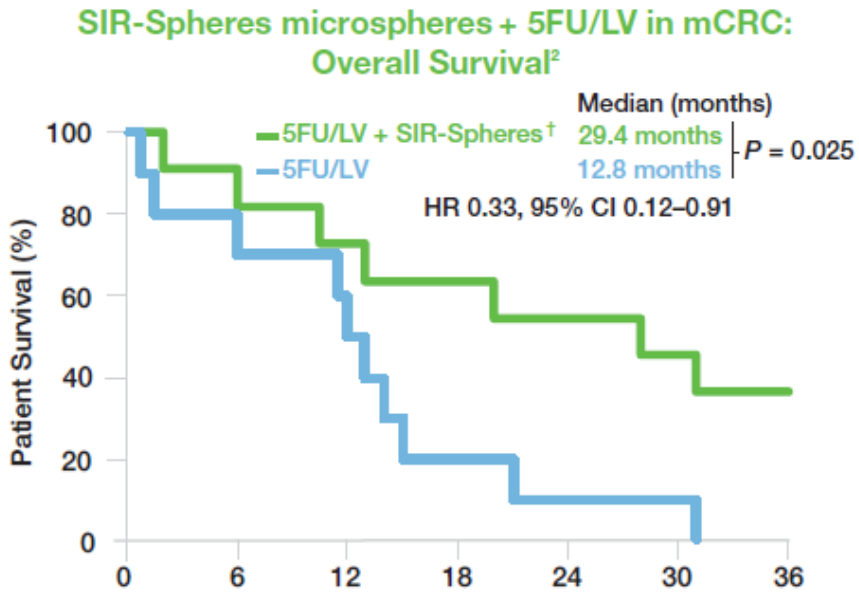

Figure 1—Prolongation of median OS with first-line application of SIR-spheres to 5FU-LV for patients with metastatic colorectal cancer (Hazel et al.).

Criticisms of these studies focus on their use of 5FU/LV, rather than FOLFOX which is commonly employed as first-line therapy for metastatic colorectal cancer. Sharma et al. reported results of dose-escalation trial using SIR-spheres + FOLFOX4. In this group of 20 patients, 65% had extra-hepatic metastases. 90% of patients had a response to treatment and 100% had stable to improved disease (Figure 2). The median PFS was 9.3 months in all patients and 14.2 months with liver-only disease. Median TTP (time to progression) in the liver was 12.3 months for all patients and 16.0 months for liver-only patients. These results compared favorably to historical data of FOLFOX4 alone, where the median TTP or PFS was 7.6-9.0 months and overall response rates was 32-59%.

Based on promising phase II data (Figure 3), a phase III trial evaluating the use of SIR-spheres in the first-line setting is currently underway.

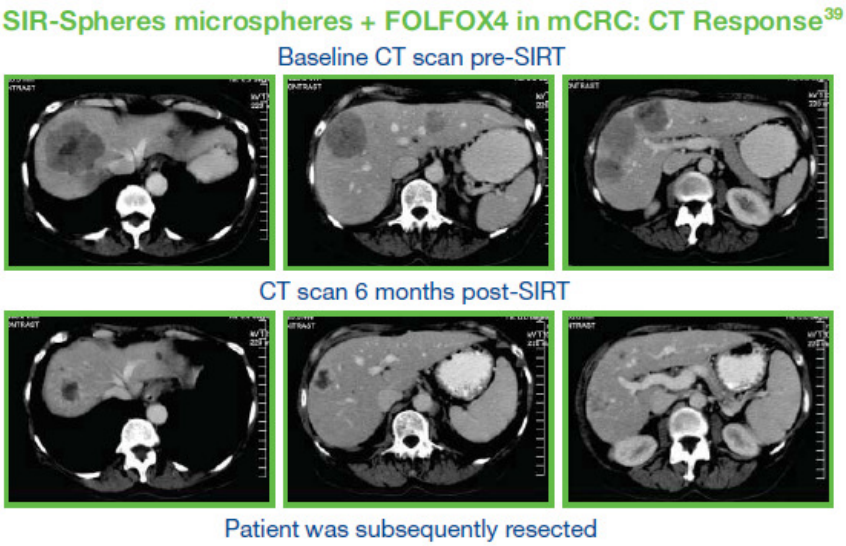

Figure 2—Sample case of partial radiographic response to the first-line use of SIR-spheres with FOLFOX4 (Sharma et al.).

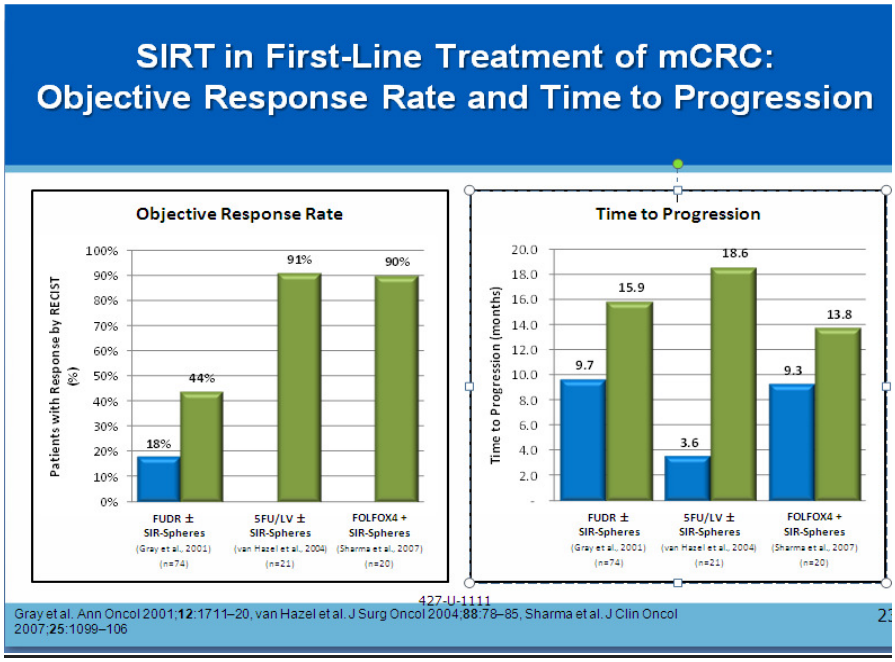

Figure 3—Summary of clinical data demonstrating favorable response rates with the first-line use of SIR-spheres with conventional chemotherapy for metastatic colorectal cancer.

Appropriate patients:

Appropriate patient selection is critical to maximizing benefit and minimizing side effects of the SIRT procedure. SIR-spheres should be used in patients with unresectable liver lesions with:

- Liver-dominant or liver-only disease;
- Good performance status (ECOG/WHO PS 0-2)
- Life expectancy > 3 months
- Adequate liver function (bilirubin < 2.0 mg/dL)

Of note, once a patient is deemed a good candidate for treatment, turn-around time for insurance pre-certification is typically less than 1 week.

Mapping procedure:

The treatment work-up includes a thorough angiographic evaluation of the liver vasculature to detect and occlude any vessels that could carry microspheres away from the liver to the stomach, duodenum, or gallbladder and to plan for the subsequent administration of SIR-Spheres microspheres. (If these vessels are not detected or occluded, the risks of ulceration or other significant side effects significantly increase.)

During this arteriography, the tip of the catheter is placed in the same position where the SIR-Spheres microspheres will be delivered, and Tc-99m MAA is administered into the hepatic artery as a tracer to determine the extent of arterio-venous shunting to the lungs and confirm the absence of gastric and duodenal flow. Some patients may have vasculature that will preclude accurate and reliable placement of the catheter and therefore prohibit the safe delivery of the microspheres. In addition, the amount of lung shunting may alter the activity that can be safely implanted commensurate with an acceptable risk of radiation pneumonitis. In such cases, you may make the decision not to treat the patient.

Once the extent of extrahepatic shunting has been evaluated and the patient deemed acceptable for treatment, SIR-Spheres microspheres will be administered at a subsequent visit.

Treatment:

Once the micro catheter has been correctly sited in the hepatic artery, the proximal end of the micro catheter is connected to the SIR-Spheres microspheres Delivery System. SIR-Spheres microspheres are then slowly delivered into the trans-femoral catheter. The radiologist should periodically check the position of the micro catheter to ensure it remains correctly sited during the delivery procedure and confirm that blood is flowing forward without stasis.

SIR-Spheres microspheres are delivered slowly at a rate of no more than 5mL per minute to allow for optimal distribution in the tumor microvasculature. Too rapid delivery of microspheres may cause reflux back down the artery into other organs. At the conclusion of the procedure, the micro catheter is removed and the patient returned to the recovery area for observation before discharge.

Post-treatment verification:

A SPECT scan of the upper abdomen is performed within 24 hours after implantation of SIR-Spheres microspheres. The SPECT scan will detect the Bremsstrahlung radiation from the yttrium-90 to confirm placement of the microspheres in the liver.

The treatment of the whole liver is often divided into two separate procedures, treating the lobe with the greatest burden of disease first and following this with treatment to opposite lobe about 3-4 weeks later. At a minimum, a repeat bilirubin should be obtained to confirm there is sufficient residual hepatic function to allow for the completion of treatment. Of note, in patients who have not been heavily pretreated with chemotherapy and have lower burdens of tumor, the whole liver can be treated in a single procedure.

Follow-up:

Following the procedure, the patients will return to routine screening with CEA levels and CT or other imaging as per standard of care and the medical oncologist's preference. Patients may become candidates for surgical resection, ablation, or SBRT, so staying in the loop (even if it is to just review images as opposed to seeing the patient in follow up) may be of value to the patient.

For more information visit: www.sirtex.com or
http://www.nordion.com/therasphere/

For publication data you can go directly to these links:
http://www.sirtex.com/media/34437/summary_of_sir-spheres_in_mcrc_638-u-1112.pdf http://www.nordion.com/therasphere/physicians_us/publications.asp