August 10th, 2018

David Liu, MD
Chief Medical Officer
Sirtex Medical Inc
300 Unicorn Park Drive, Woburn, MA 01801
(781) 721-3800
David.liu@sirtex.com

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NCCN Colon/Rectal/Anal Cancers Panel

Re: Yttrium 90 resin microspheres for right-sided primary colon cancer in the NCCN Clinical Practice Guidelines in Oncology® - Colon Cancer

On behalf of Sirtex Medical, I respectfully request the NCCN Colon Cancer Panel to review the enclosed recent publication¹ in support of the addition of yttrium 90 resin microspheres to standard first-line mFOLFOX6 chemotherapy in patients with right-sided primary (RSP) colon cancer with liver-dominant or liver-only metastases.

Suggested Changes: We respectfully ask the NCCN Panel to consider the following:

Colon Cancer Guideline:

- **COL-6, “Unresectable synchronous liver and/or lung metastases only”, under “treatment”, “Systemic therapy”:** Add “mFOLFOX6 + yttrium 90 resin microspheres ± bevacizumab (liver-dominant or liver-only metastases, right-sided tumors only)”

- **COL-D, 1 of 10, under “Initial therapy”:** Add “mFOLFOX6 + yttrium 90 resin microspheres ± bevacizumab (liver-dominant or liver-only metastases, right-sided tumors only)”

FDA Clearance: SIR-Spheres® (yttrium 90 resin microspheres) was approved by the FDA under a premarket approval application in 2002. SIR-Spheres® is indicated for the treatment of unresectable metastatic liver tumors from primary colorectal cancer with adjuvant intra-hepatic artery chemotherapy (IHAC) of FUDR (Flouxuridine).²

Clinical Rationale:

Patients with RSP colorectal cancers have worse prognosis for survival and fewer treatment options than patients with left-sided primary (LSP) tumors.³ A recent published analysis on tumor sidedness included 2 randomized phase 3 studies, SIRFLOX and FOXFIRE Global
(n=739), that compared the combination of selective internal radiation therapy (SIRT) using yttrium 90 resin microspheres (SIR-Spheres) plus first-line mFOLFOX6 with mFOLFOX6 alone in patients with liver-only or liver-dominant metastatic colorectal cancer. In the 179 patients (24.2%) with RSP (defined as splenic flexure through cecum), addition of yttrium 90 resin microspheres to standard chemotherapy was associated with statistically significant benefit in overall survival compared with chemotherapy alone (median OS, 22.0 mo vs 17.1 mo; HR, 0.641; \( P = 0.008 \)). There was a clinically meaningful improvement of 4.9 months in median overall survival. Consistent gain of OS in both studies (4.8 mo for SIRFLOX and 7.9 mo for FOXFIRE Global) suggest this finding is not the consequence of a chance imbalance of prognostic factors. Rates of treatment-emergent grade \( \geq 3 \) adverse events were similar in the yttrium 90 resin microspheres plus chemotherapy arm (77.2%) versus the chemotherapy alone arm (77.4%) for patients with RSP \( (P=1.000) \). These data support the addition of yttrium 90 resin microspheres to first-line chemotherapy as an effective and safe treatment option for patients with liver-only or liver-dominant RSP colon cancers.

Sincerely,

David Liu, MD
Chief Medical Officer
Sirtex Medical, Inc

References (enclosed):
2. SIR-Spheres® microspheres PI. Sirtex Medical Inc.