



August 2, 2018

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

Sirtex Medical Inc.

300 Unicorn Park Drive
Woburn, MA 01801

Phone: +1 (781) 721-3800
+1 (888) 4-SIRTEX
Fax: +1 (781) 721-3880
Website: www.sirtex.com

NCCN Colon/Rectal/Anal Cancers Panel

Re: Yttrium 90 resin microspheres for chemo-refractory and chemo-intolerant colon cancer in the NCCN Clinical Practice Guidelines in Oncology® - Colon Cancer

We respectfully request formatting revisions to the guideline with the purpose of clarifying and supporting patient access and coverage of the existing NCCN recommendation of yttrium 90 treatment for chemo-refractory/chemo-intolerant colon cancer. This is due to practical challenges resulting from the current placement of the recommendation in Principles of Radiation Therapy (COL-E) instead of the guideline algorithm. Thank you for recommending yttrium-90 for this setting.

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

- **COL-6, “Unresectable synchronous liver and/or lung metastases only”, after “Remains unresectable”:** revise to “Systemic therapy (see COL-D) or radioembolization for highly select patients (see COL-E)^{footnote}”
 - **Footnote:** “Arterially directed catheter therapy, and in particular yttrium-90 microsphere-selective internal radiation, is an option in highly selected patients with chemotherapy-resistant/-refractory disease and with predominant hepatic metastases.”(current language in COL-E)
- **COL-11, “Unresectable metachronous metastases”, after “Remain unresectable”:** revise to “Systemic therapy (see COL-D) or radioembolization for highly select patients (see COL-E)^{footnote}”
 - **Footnote:** “Arterially directed catheter therapy, and in particular yttrium-90 microsphere-selective internal radiation, is an option in highly selected patients with chemotherapy-resistant/-refractory disease and with predominant hepatic metastases.” (current language in COL-E)
- **COL-D1: “Continuum of care”, “Patient not appropriate for intensive therapy”, after “No improvement in functional status”:** revise to “Best supportive care or radioembolization for elderly patients (see COL-E)”

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 (Floxuridine).¹

Rationale Summary:

This is an existing NCCN recommendation of radioembolization with yttrium 90 resin microspheres in the chemo-refractory setting. The long-term update of the Metastatic colorectal cancer liver metastases Outcomes after RadioEmbolization (MORE) study reported an updated median overall survival of 10.0 months with yttrium 90 resin microsphere treatment in 606 patients with pretreated (progressed or had become intolerant to at least one line of systemic therapy) unresectable colorectal cancer with liver metastases.² Patient age did not significantly affect survival outcomes. A further analysis showed similar overall survival between patients aged <75 years (9.6 mo) and those aged ≥75 years (9.3 mo, $P=0.987$).³ The majority of adverse events reported were mild, with grade 3/4 events in less than 20% of patients. Rates of adverse events were similar between the younger and elderly groups ($P=0.398$). Also, overall survival was similar between elderly (≥70 years) and younger patients (<70 years): 9.3 months and 9.7 months ($P=0.335$). There were no differences between cohorts for any grade adverse events ($P=0.433$) or grade ≥3 events ($P=0.482$). This is consistent with a separate study that also showed similar overall survival and safety in pretreated patients aged <70 years and ≥70 years with yttrium 90 radioembolization.⁴ These data showed that yttrium 90 resin microsphere is a reasonable option in the chemo-refractory and chemo-intolerant setting regardless of age, including elderly patients who may not be appropriate for intensive therapy.

Sincerely,

David Liu, MD
Chief Medical Officer
Sirtex Medical Inc.

References (enclosed):

- 1A. SIR-Spheres® microspheres PI. Sirtex Medical Inc.
- 2A. Kennedy A, et al. Updated survival outcomes and analysis of long-term survivors from the MORE study on safety and efficacy of radioembolization in patients with unresectable colorectal cancer liver metastases. *J Gastrointest Oncol*. 2017;8(4):614-624.
- 3A. Kennedy A, et al. Safety and efficacy of radioembolization in elderly and younger patients with unresectable liver-dominant colorectal cancer. *Clinical Colorectal Cancer*. 2015;15(2):141-151.
- 4A. Tohme S, et al. Survival and tolerability of liver radioembolization: a comparison of elderly and younger patients with metastatic colorectal cancer. *HPB (Oxford)*. 2014;16(12):1110-1116.