In Reply

We appreciate the interest and insightful comments from Dr. Al-Batran regarding our recent publication [1]. There is no doubt that the French FNCLCC/FFCD 9703 study is an important trial for evaluating the role of perioperative chemotherapy in the management of resectable gastroesophageal adenocarcinoma [2]. It has the distinction of being one of the few trials that predominantly evaluated gastroesophageal junction (GEJ) tumors, as opposed to most other prospective trials, which included only a small number of GEJ patients along with mostly gastric or esophageal cancer patients.

The purpose of our article was to review the literature for adjuvant treatment of gastric cancer and not GEJ or esophageal adenocarcinomas [1]. Most studies evaluating chemotherapy or chemoradiation in resectable gastric cancer included at least some patients with GEJ tumors, and a short section on GEJ was included in our review for the sake of completeness.

We agree with Dr. Al-Batran that based on results of the MAGIC trial and the FNCLCC/FFCD study, perioperative chemotherapy for resectable GEJ adenocarcinoma is a reasonable option [2, 3]. However, we suggest that more data are needed to clarify the role of radiation and that there is still a strong rationale for considering its integration into the treatment regimen. Almost 24% of patients in the CROSS trial had GEJ tumors, and even although results for GEJ tumors were not reported separately, a survival advantage for preoperative chemoradiation with a dose of 41.4 Gy versus surgery alone was noted [4]. The POET trial, which exclusively evaluated patients with GEJ tumors, reported improved pathologic complete response rates (15.6% vs. 2.0%) and a nonsignificant trend toward improved 3-year survival (47.4% vs. 27.7%, $p = .07$) with neoadjuvant chemoradiation to a dose of 30 Gy in 15 fractions compared with preoperative chemotherapy [5]. Unfortunately, this trial was closed prematurely because of poor accrual, and statistical significance could not be reached. The preoperative radiation doses utilized in both European trials were lower than what has been the U.S. standard of 45–50.4 Gy and were not delivered with intensity-modulated radiation therapy (IMRT); data from the MD Anderson Cancer Center suggest improved overall survival, locoregional control, and non-cancer-related death with IMRT versus three-dimensional conformal radiation therapy (3D-CRT) [6]. Moreover, another small Australian study that included GEJ tumors showed higher response rates and R1 resection rates favoring neoadjuvant chemoradiation over chemotherapy but failed to show an overall survival benefit, again, likely because of insufficient sample size [7].

Additional prospective trials in the modern radiation era with advanced imaging and delivery technologies that can account for respiratory-associated tumor motion with contours

drawn according to consensus guidelines are needed to clarify the role of radiation. Indeed, data on pancreatic cancer have shown the importance of adherence to protocol guidelines in the design of radiotherapy fields such that in the RTOG 9704 trial, failure to adhere was associated with reduced survival [8].

Based on the available data, we feel that the benefit of preoperative chemotherapy versus chemoradiotherapy remains controversial. We eagerly await results from the randomized TOPGEAR trial, which includes GEJ patients [9]. Until then, the debate regarding the role of radiation in GEJ tumors will continue.

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Disclosures

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