

Adjuvant therapy in resectable gastric cancer—the CRITICS trial

We read the final report of the eagerly awaited CRITICS trial¹ with interest, since its overall results showed a favourable outcome when compared with the previous landmark studies, INT0116² and MAGIC.³ Population-based data suggest that the approaches established by both studies have been successfully transferred into clinical practice. The authors provide comprehensive follow-up data, including long-term renal function tests, which will be useful to observe after longer follow-up. Reassuringly, toxicity with radiochemotherapy was not excessive versus chemotherapy alone, and the conclusion by Annemieke Cats and colleagues,¹ to direct research toward intensification of preoperative strategies, is reasonable. Until the results of TOPGEAR (NCT01924819) and other ongoing trials such as ARTIST-II (NCT01761461) become available, it would be useful if the authors could provide a more detailed subgroup analysis.

The CRITICS trial included a wide spectrum of clinical stages; however, data from a 2015 study⁴ in Asia indicate that the benefits of radiotherapy use in addition to chemotherapy and (high-quality) surgery might be restricted to patients with more advanced tumours. Cats and colleagues have provided subgroup analyses on relevant parameters, such as localisation and histology, and the latter was inconclusive relative to the data from Asia, which indicated a benefit of radiochemotherapy for intestinal subtypes.⁴ Unfortunately, no subgroup analysis that stratified by initial clinical tumour stage was included. Can such data already be retrieved from the currently available database? Additionally, a per-protocol analysis of patients who completed both pre-operative and postoperative treatment would be of interest, even if

this subset only includes only around 50% of patients.

The importance of sufficiently large treatment volumes has been suggested by the seminal patterns of failure analysis,⁵ the large treatment volumes used in INT0116,² and more recent use of intensity-modulated radiation therapy.

Although locoregional failure alone was rarely observed in the CRITICS trial, there might be a tight temporal relationship between occult peritoneal relapse and systemic failure. Therefore, it would be of note whether the authors examined the effect of treatment technique or treatment volumes on patterns of failure.

Finally, many patients were censored between 24 and 60 months, in the plateau-like region of the survival curves. Given that the survival curves started to separate at 24 months in INT0116,² do the authors plan to provide long-term follow-up data to detect later separation of the survival curves?

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- 1 Cats A, Jansen EPM, van Grieken NCT, et al. Chemotherapy versus chemoradiotherapy after surgery and preoperative chemotherapy for resectable gastric cancer (CRITICS): an international, open-label, randomised phase 3 trial. *Lancet Oncol* 2018; **19**: 616–28.
- 2 Smalley SR, Benedetti JK, Haller DG, et al. Updated analysis of SWOG-directed intergroup study 0116: a phase III trial of adjuvant radiochemotherapy versus observation after curative gastric cancer resection. *J Clin Oncol* 2012; **30**: 2327–33.
- 3 Cunningham D, Allum WH, Stenning SP, et al. Perioperative chemotherapy versus surgery alone for resectable gastroesophageal cancer. *N Engl J Med* 2006; **355**: 11–20.

- 4 Park SH, Sohn TS, Lee J, et al. Phase III trial to compare adjuvant chemotherapy with capecitabine and cisplatin versus concurrent chemoradiotherapy in gastric cancer: final report of the adjuvant chemoradiotherapy in stomach tumors trial, including survival and subset analyses. *J Clin Oncol* 2015; **33**: 3130–36.

- 5 Landry J, Tepper JE, Wood WC, Moulton EO, Koerner F, Sullinger J. Patterns of failure following curative resection of gastric carcinoma. *Int J Radiat Oncol Biol Phys* 1990; **19**: 1357–62.