Adjuvant therapy in resectable gastric cancer—the CRITICS trial

We read the final report of the eagerly awaited CRITICS trial with interest, since its overall results showed a favourable outcome when compared with the previous landmark studies, INT0116 and MAGIC. 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, 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 study 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. 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, the large treatment volumes used in INT0116, 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, do the authors plan to provide long-term follow-up data to detect later separation of the survival curves?


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