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EDITORIAL

COLLISION Trial Seeks to Answer Time-Honored Question: "Thermal Ablation or Surgery for Colorectal Liver Metastases?"

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We are honored to highlight the recently started COLLISION trial that will compare thermal ablation to surgical resection for small *resectable* colorectal liver metastases (CRLM 0–3 cm) [1]. Since colorectal cancer is the third most common malignancy worldwide and the second most common cause of cancer-related deaths in developed countries, this trial encompasses a major medical concern [2]. Although approximately half of all patients develop liver metastases in course of their disease, only 15–20% is considered eligible for curative intent surgical resection. For patients with an impaired general health status, history of extensive abdominal surgery, the presence of lesions with an unfavorable anatomical location or an insufficient future liver remnant to perform partial hepatectomy, thermal ablation nowadays is accepted worldwide to eliminate small *unresectable* CRLM. The minimal invasive and parenchyma-sparing nature, good and still improving efficacy with the potential to repeat procedures in case of local tumor progression, low costs and short hospital stay of thermal ablation have made it impossible to postulate generally accepted resectability criteria, especially for small and deep-seeded CRLM that require major hepatectomy [3].

With a remarkable difference in eight-year overall survival, 8.9% for the chemotherapy alone group vs. 35.9% for the radiofrequency plus chemotherapy group, the recently published long-term results of the EORTC-CLOCC trial demonstrate that aggressive local treatment can considerably prolong survival or in a subset of patients even provide cure [4].

Although previous series and meta-analyses routinely labeled thermal ablation inferior to surgical resection, these results have to be interpreted with caution as there is an apparent selection bias when comparing patients with unresectable disease (who receive ablation) to those who were surgical candidates. Recent series, using multivariate analysis or case matching, reported a comparable survival for ablation alone versus resection alone. [5–9] These results have revitalized the discussion whether thermal ablation, given its superior safety profile, should be favored over partial hepatectomy for smaller CRLM. We have designed a two-arm, multicenter, phase III, single-blind prospective randomized controlled trial for patients with liver-only *resectable* CRLM up to 3 cm to prove or disprove non-inferiority of thermal ablation compared to the current gold-standard: partial hepatectomy.

The COLLISION trial (registered at clinicaltrials.gov: NCT03088150) is initiated by the Amsterdam University Medical Center, in Amsterdam and part-funded by a research grant from Medtronic–Covidien. The trial is embedded within the Dutch Colorectal Cancer Group (DCCG), a multidisciplinary collaboration that aims to improve preclinical and clinical colorectal cancer research. At present, ten high-volume centers for liver surgery throughout the Netherlands and Italy are enrolling patients and several (inter)national institutions are awaiting local review board approval.

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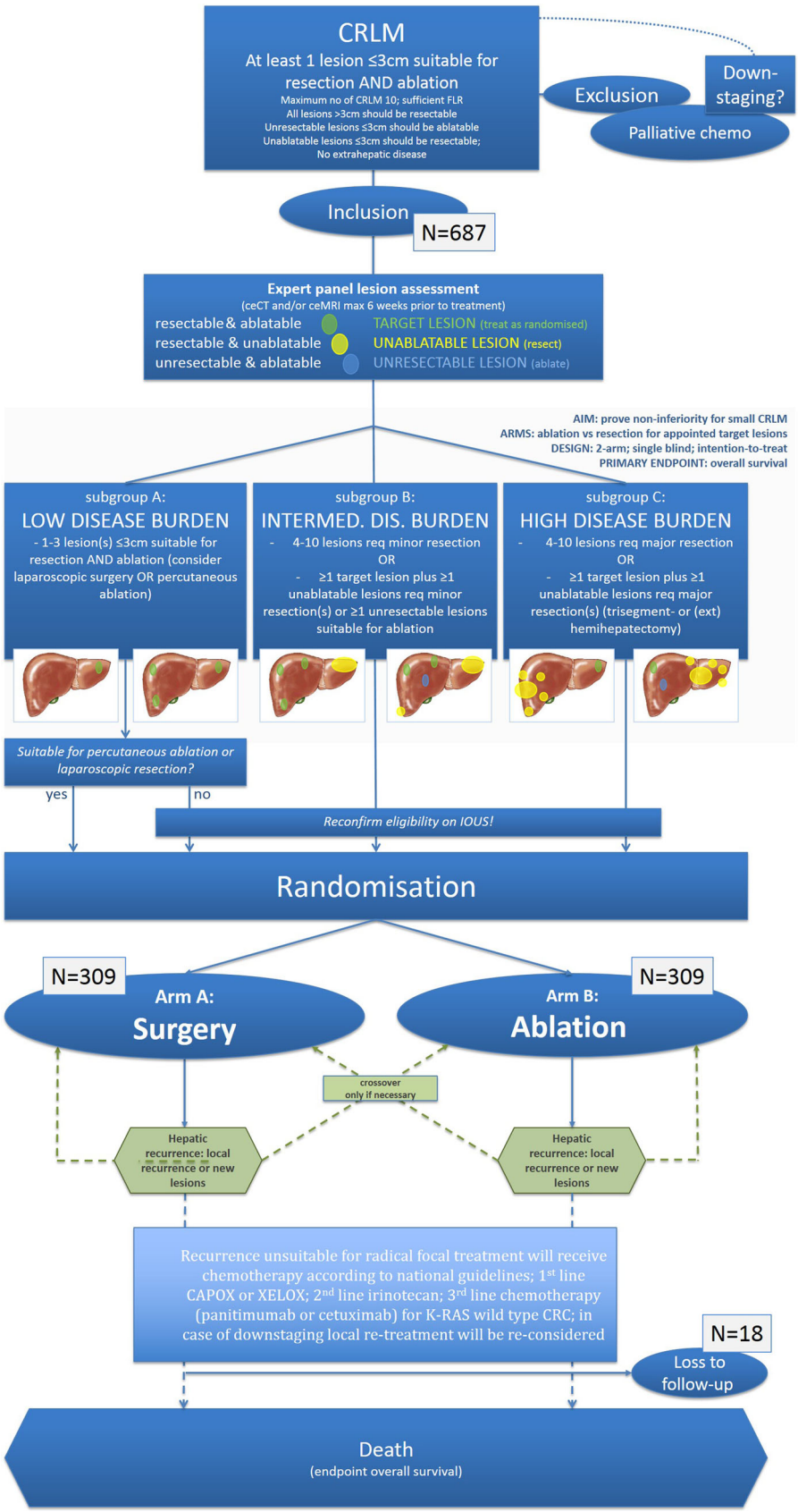
Fig. 1 Flowchart



Patients with at least 1 resectable and ablatable CRLM ($\leq$ 3 cm), up to ten lesions, a good performance status, no extrahepatic disease and no prior liver treatment are considered eligible (Fig. 1). Supplementary resection(s) for resectable tumors $>$ 3 cm and ablation(s) for unresectable tumors $\leq$ 3 cm are allowed. The primary endpoint is overall survival. Secondary endpoints are disease-free survival, time-to-(local)-progression, primary and assisted technique efficacy, mortality, length of hospital stay, assessment of quality of life and cost-effectiveness.

If thermal ablation proves to be non-inferior (i.e., equal or superior), a switch in treatment method will lead to a reduction in morbidity and mortality, length of hospital stay and incremental costs without compromising oncological outcome for patients with small resectable CRLM. The first study results are expected at the end of 2025.

Compliance with Ethical Standards

Conflict of interest Investigator Sponsored Research (ISR) grant by Medtronic PLC. The funders had no role in the design of the study; the collection, analysis or interpretation of the data; the writing of the manuscript; or the decision to submit the manuscript for publication.

Ethics Approval and Consent to Participate Review board approval was obtained at the Amsterdam University Medical Center. Reference Number 2016.561 (NL-Number NL58551.029.16). All participants will provide written informed consent.

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