The GILDA trial finds no survival benefit from intensified screening after primary resection of colorectal cancer: the PulMiCC trial tests the survival benefit of pulmonary metastasectomy for detected asymptomatic lung metastases.

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Key message

The GILDA authors are unable to explain the apparently inverse relationship between early diagnosis and survival as it appeared in their trial. If treatment of metastases does not improve survival then there may be net harm done, explaining the inverse relationship. The PulMiCC trial seeks to resolve the uncertainty around clinical benefit of pulmonary metastasectomy.
We welcome the publication of the GILDA trials and admire the perseverance of the trial leaders and their team in bringing this study to successful conclusion.[1] We know just how hard this can be from the recovery of the CEASL trial, the results of which were unpublished for 20 years.[2] CEASL was eventually published under the “restoring invisible and abandoned trials” (RIAT) initiative led by the BMJ.[3] We share the view of the GILDA authors that viewed alongside the findings of CEASL and FACS, their findings ‘undermine the paradigm that earlier detection of recurrences may translate into either longer survival duration or enhanced quality of life in patients with colorectal cancer treated with curative intent.’

The GILDA authors write that they are ‘not able to explain the apparently inverse relationship between early diagnosis and survival’ as it appeared in their trial of intensified monitoring of patients after apparently successful resection of primary colorectal cancer. We know that for lung metastasectomy the hazard ratio for death is doubled for each of the well-known adverse prognostic factors: more than one metastasis, an interval of under three years since the primary resection and any elevation of CEA.[4] Occasional cure of a truly solitary metastasis remains possible but most of the supposed benefit may well be an illusion due to extreme case selection. We suspect that the same is true of metastasectomy from the liver, despite extravagant claims such as: ‘The surgical management of colorectal liver metastases (CRLMs) was a paradigm change in the management of metastatic disease and is one of the greatest advances in surgical practice of recent times.’[5] The surgery may be a technical tour de force but its benefit is unproven.

The ‘inverse relationship’ may well be due to the harms of surgery becoming evident in absence of net benefit. The GILDA authors note that the FACS trialists chose to ‘abandon its original principal endpoint (overall survival) with a surrogate but more practical endpoint’ which was opportunities for surgical treatment of recurrence with curative intent. As an endpoint it was more ‘practical’ only in the sense that it led to a statistically significant result. Increasing the number of metastasectomy operation has limited clinical significance unless ‘intent’ translates into survival benefit. Survival benefit has not been shown in CEASL, FACS or GILDA. We hope to provide evidence from the PulMiCC trial (https://clinicaltrials.gov/ct2/show/NCT01106261) with respect to pulmonary metastasectomy in colorectal cancer. Perhaps it is now at last time for an RCT of liver metastasectomy as mooted by Mayo Clinic surgeons as long ago as 1992.[6] Over the past 20 years a great deal of effort and health care costs have been expended on liver metastasectomy. Patients continue to be exposed to potentially hazardous interventions without any good evidence of a beneficial effect on survival.
Reference List


3 Godlee F: Colorectal cancer: a cautionary tale. BMJ DOI: 10.1136/bmj.g3311 (Published 15 May 2014).

