First-line hepatic infusion of pirarubicin in patients with isolated liver metastases: is it really promising?

In a recent issue of *Annals of Oncology*, Zelek et al. reported on a combination treatment of systemic [5-fluorouracil (5-FU), leucovorin (LV) and irinotecan] and hepatic arterial (pirarubicin) chemotherapy in the first-line treatment of non-resectable, metastatic colorectal cancer limited to the liver [1]. In their article, the authors report a response rate of 48% and a median survival of 20.5 months. Thirty-one patients were enrolled on the study and liver resection was possible in 11 responding patients. The median survival of resected patients was not reached, while the unresected group had a dismal median survival of 13.9 months. The authors conclude that regimens combining systemic and hepatic infusion chemotherapy deserve further investigation.

Reviewing this study, I find the results obtained very disappointing. By limiting patient enrollment to patients with hepatic metastases only, one would expect that the study outcome would be more favorable than what had been described with systemic chemotherapy alone. Instead, as the authors point out, responses were similar to what has been described with FOLFOX or FOLF-IRI combinations [2–4]. Furthermore, the outcome of patients with unresected disease was disturbingly poor compared to newer combinations.Attributing these findings to a poor prognosis patient population is certainly not justified given the strict eligibility criteria.

Of further concern is the lack of a favorable disease control rate with this combination. This is exemplified by a stable plus partial response rate of 71%, which does not compare favorably with a rate exceeding 80% with systemic combinations of 5-FU/LV and oxaliplatin or irinotecan. This could be secondary to the inability to administer full doses of effective systemic chemotherapy. The study does not even suggest a better hepatic disease control as evidenced by first-site disease progression in the liver in >80% of the initial responders. As far as the high resectability rate in this highly selected population, it can certainly be attributed to patient selection rather than the addition of hepatic arterial infusion.

The authors also point out that this combination therapy compares favorably to other combinations of systemic chemotherapy and hepatic arterial infusion, citing studies by Copur et al. [5] and Kemeny et al. [6]. In my opinion, these are unjustified comparisons as the first study involved a clearly inferior systemic chemotherapy (5-FU/LV) alternating with hepatic infusion, while the other enrolled a majority of pre-treated patients.

Caution should be exercised when developing newer combinations of systemic and hepatic chemotherapy in the front-line therapy of patients with metastatic colorectal cancer. Such combinations may be associated with significant patient inconvenience and increased expenditure to the health care system while a patient benefit continues to be lacking.

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References


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