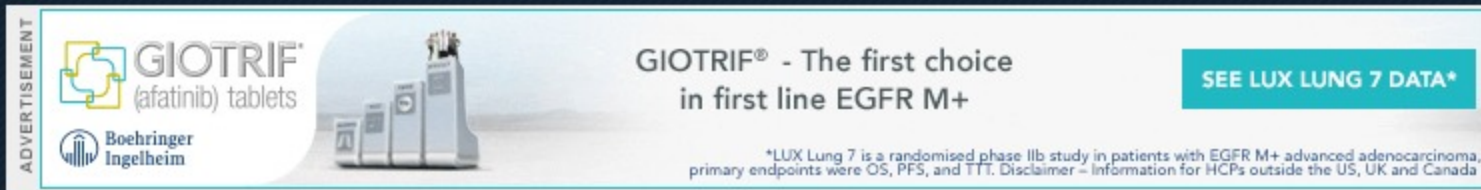


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Curcumin inhibits cancer stem cell phenotypes in *ex vivo* models of colorectal liver metastases, and is clinically safe and tolerable in combination with FOLFOX chemotherapy

Mark I. James¹, Chinenye Iwuji¹, Glen Irving, Ankur Karmokar, Jennifer A. Higgins, Nicola Griffin-Teal, Anne Thomas, Peter Greaves, Hong Cai, Samita R. Patel, Bruno Morgan, Ashley Dennison, Matthew Metcalfe, Giuseppe Garcea, David M. Lloyd, David P. Berry, William P. Steward, Lynne M. Howells, Karen Brown

¹ Joint first authors.

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Highlights

- Curcumin + FOLFOX inhibits growth of primary cancer stem cell (CSC) spheroid models.
- Curcumin + FOLFOX decreases expression of CSC markers in primary CSC spheroid models.
- Curcumin enhances proapoptotic effects of chemotherapy in explant culture.
- Curcumin is safe and tolerable in combination with FOLFOX chemotherapy.
- Curcumin is perceived by patients as an acceptable daily adjunct to chemotherapy.

Abstract

In vitro and pre-clinical studies have suggested that addition of the diet-derived agent curcumin may provide a suitable adjunct to enhance efficacy of chemotherapy in models of colorectal cancer. However, the majority of evidence for this currently derives from established cell lines.

Here, we utilised patient-derived colorectal liver metastases (CRLM) to assess whether curcumin may provide added benefit over 5-fluorouracil (5-FU) and oxaliplatin (FOLFOX) in cancer stem cell (CSC) models. Combination of curcumin with FOLFOX chemotherapy was then assessed clinically in a phase I dose escalation study. Curcumin alone and in combination significantly reduced spheroid number in CRLM CSC models, and decreased the number of cells with high aldehyde dehydrogenase activity (ALDH^{high}/CD133⁻). Addition of curcumin to oxaliplatin/5-FU enhanced anti-proliferative and pro-apoptotic effects in a proportion of patient-derived explants, whilst reducing expression of stem cell-associated markers ALDH and CD133. The phase I dose escalation study revealed curcumin to be a safe and tolerable adjunct to FOLFOX chemotherapy in patients with CRLM (n = 12) at doses up to 2 grams daily.

Curcumin may provide added benefit in subsets of patients when administered with FOLFOX, and is a well-tolerated chemotherapy adjunct.

Keywords:

Colorectal liver metastases, Curcumin, Cancer stem cells, Combination therapy

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