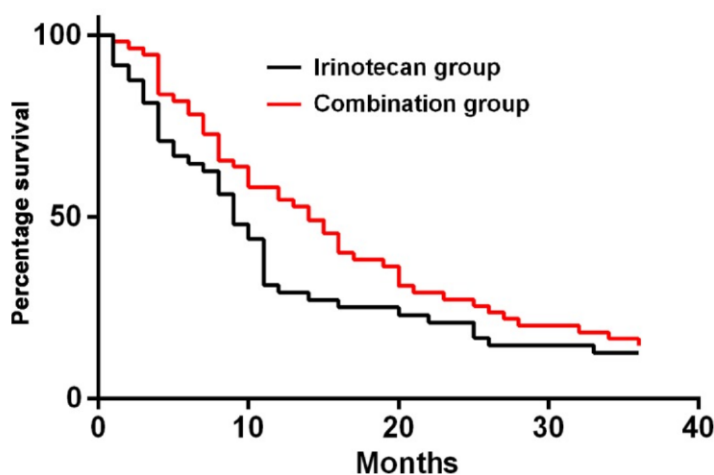


# Abstract from Clinical Trials

Clinical effects of high frequency hyperthermia-assisted irinotecan chemotherapy on patients with middle and advanced colorectal cancer and its safety assessment.



Analysis of 3-year survival rate in two groups of patients. The 1-, 2- and 3-year survival rates of patients in irinotecan group were 31.25% (15 cases), 22.92% (11 cases) and 12.50% (6 cases), respectively. Those in combination group were 58.18% (32 cases), 29.09% (16 cases) and 16.36% (9 cases), respectively.

"Clinical effects of high frequency hyperthermia-assisted irinotecan chemotherapy on patients with middle and advanced colorectal cancer and its safety assessment were investigated. A retrospective analysis was performed on the medical records of 103 patients with middle and advanced colorectal cancer treated in Cancer Center of Guangzhou Medical University from May

2011 to June 2015, including 48 patients receiving irinotecan plus conventional treatment (irinotecan group) and 55 patients receiving high frequency hyperthermia-assisted irinotecan plus conventional treatment (combination group). The treatment effects, severity and incidence of adverse reactions, quality of life and 3-year survival rates of patients were analyzed and

compared between the two groups. After 4 courses of treatment, there were statistically significant differences in the proportions of patients with partial remission and objective remission, with those in combination group higher than those in irinotecan group (both  $P < 0.05$ ). After 4 courses of treatment, no patient died. After 4 courses of treatment, those that increased in different degrees (all  $P < 0.05$ ), compared with those in combination group were significantly higher than those in irinotecan group (all  $P < 0.05$ ). The 1-, 2- and 3-year survival rates of patients in irinotecan group were 31.25% (15 cases), 22.92% (11 cases) and 12.50% (6 cases), respectively. Those in combination group were 58.18% (32 cases), 29.09% (16 cases) and 16.36% (9 cases), respectively. The results of K-M survival curve analysis showed that there was no statistically significant difference in survival rate between the two groups of patients ( $P = 0.050$ ). High frequency hyperthermia-assisted chemotherapy for patients with middle and advanced colorectal cancer can effectively improve its treatment effects and patients' quality of life, with better treatment safety, worthy of clinical promotion."

Liu Z. *Clinical effects of high frequency hyperthermia-assisted irinotecan chemotherapy on patients with middle and advanced colorectal cancer and its safety assessment*. *Oncol Lett*. 2019 Jan;17(1):215-220. doi: 10.3892/ol.2018.9574. Epub 2018 Oct 12. PMID: 30655758; PMCID: PMC6313175.

Effective heating of tumours is often difficult to achieve. In a trial involving 71 patients with locally advanced colorectal cancer, only 35 tumours were heated optimally. Fatty tissue was the biggest challenge in heating tumours in this trial. Of the tumours that reached target temperatures 54% showed either complete or partial regression, whilst only 36% of tumours demonstrated partial or complete response in the group in which the target temperatures were not achieved.

Six randomised clinical trials published between 1990 and 2007, with a total of 520 patients, compared the effects of RT (N=258) versus RT and HT (N=262) for rectal carcinoma. Four of the studies (424 patients) reported OS rates. 2-year OS was significantly better in the RHT group ( $p = 0.001$ ), but this difference had disappeared by the 3-, 4- and 5-year follow ups. A significantly higher complete response rate was observed in the RHT group ( $p = 0.01$ ). No significant differences in toxicity were noted in the two studies that reported on toxicity.

Although preoperative radiochemotherapy in locally advanced rectal cancer can induce down staging, the incidence of local recurrence is still high. 37 patients with T3 or T4 rectal carcinoma were treated in a phase II trial with 5-Fluorouracil (300-350 mg/m<sup>2</sup>) and leucovorin (50 mg) and regional HT followed by RT. Surgery followed four to six weeks after completion of the regime. 16% of patients developed grade III toxicity. The overall resectability rate was 89%, and 31 of resection specimens had negative margins. 46% of patients

demonstrated a partial remission and the survival rate after surgery was 86% at 38 months. None of the patients with negative margins developed local recurrence, however five patients developed distant metastases.

122 patients were randomly assigned to receive preoperative HT combined with RT (N=44), preoperative RT alone (N=38) or surgery without any preoperative treatment (N=40). 5-year survival rate was 66.7% in the HRT group, 50% in the RT group and 40.5% in the control group. The percentage of survival at five years was 73.7%, 57.1% and 58.8% for the HRT, RT and control group, respectively. The results strongly suggest a benefit to the addition of HT to preoperative radiation treatment in rectal carcinoma patients.

24 patients with adenocarcinoma of the rectum who had been previously irradiated were treated with re-irradiation (median dose of 39.6 Gy), 5-fluorouracil

and HT (twice a week within one hour after radiotherapy).

The median local progression-free survival was 15 months and the OS rates at 1- and 3-years were 87% and 30%, respectively. Pain relief was achieved in 70% of patients and no grade 3 or 4 hematologic or skin toxicity occurred.

In a double armed, controlled trial, 56 patients with locally advanced carcinoma of the rectum (T4N0M0) received HT combined with RT as a pre-operative treatment and a control group of 59 patients received only RT followed by surgery. In the HT group, 16.1% of patients showed complete response and 53.6% showed regression of the primary tumour. The difference in results between the group which received HT and the control group (1.7% complete response and 33.9% significant regression of the primary tumour) was significant. The 5 -year OS rates were also significantly better in the HT group (35.6% versus 6.6%;  $p < 0.05$ ).

## References

Nishimura Y., Hiraoka M., Akuta K., et al. (1992) [Hyperthermia combined with radiation therapy for primarily unresectable and recurrent colorectal cancer](#) International Journal of Radiation Oncology, Biology and Physics Vol. 23, No. 4, pp: 759-768

Rau B., Wust P., Hohenberger P., et al. (1998) [Preoperative hyperthermia combined with radiochemotherapy in locally advanced rectal cancer: a phase II clinical trial](#) Annals Surgery Vol. 227, No. 3, pp: 380-389 Humboldt University of Berlin, Germany

Milani V. Pazos M., Issels R.D., et al, (2008) [Radiochemotherapy in combination with regional hyperthermia in preirradiated patients with recurrent rectal cancer](#) Strahlentherapie und Onkologie Vol. 184, No. 3, pp: 163-168 University Hospital Grosshadern , Munich, Germany Available online from: <http://www.ncbi.nlm.nih.gov/pubmed/18330513>