

Supplementation with Fish Oil Increases First-Line Chemotherapy Efficacy in Patients with Advanced Nonsmall Cell Lung Cancer

BACKGROUND:

- Patients with lung cancer are often not diagnosed until the cancer is at an advanced-stage of the disease, where standard treatment usually includes palliative chemotherapy or radiotherapy.
- Specially, for patients suffering from nonsmall cell lung cancer (NSCLC), the response rate to first-line chemotherapy is very low with little improvements.
- Recently, experimental studies have reported a possible increase in the efficacy of certain types of chemotherapy when patients are concomitantly consuming fish oil.

OBJECTIVE:

- To evaluate whether the combination of fish oil (FO) and chemotherapy provide a benefit over standard of care (SOC) on response rate and clinical benefit from chemotherapy in patients with nonsmall cell lung cancer (NSCLC).

METHODS:

- **Design:**Controlled experiment – nonrandomized, parallel designed, open-label trial
- **Duration:** Study accrual occurred during a 2 years period from 2007 to 2009; chemotherapy treatments were given for 3 weeks for 4 cycles with post-trial treatment follow-up
- **Inclusion criteria:**Patients with a clinical diagnosis of stage IIIB or IV nonsmall cell lung cancer, who were chemotherapy-naïve that had the ability to maintain oral intake and an Eastern Cooperative Oncology group performance states ≤ 2 as assessed by a physician.
- **Exclusion criteria:**Patients were excluded if they were ineligible for chemotherapy and participation in a clinical trial due to nonstandard chemotherapy regimen.
- **Patients enrolled:**Initial screening was performed on 204 patients.
Drug regimens:All patients received first-line platinum-based doublet chemotherapy of palliative intent with either carboplatin and vinorelbine or carboplatin and gemcitabine. The SOC group only received the chemotherapy of palliative intent. The FO group received the chemotherapy plus either 4 1-gram capsules of fish oil per day (containing 2.2 grams EPA and 240 mg DHA) or 7.5 mL liquid fish oil per day (containing 2.2 grams EPA and 500 mg DHA).
- **Primary outcome measure:**Chemotherapy response rate – defined as the sum of complete response and partial response after 4 cycles of chemotherapy divided by the number of patients
- **Secondary outcome measures:**
 - Clinical benefit – defined as the sum of complete responses, partial responses, and stable disease after 4 cycles of chemotherapy divided by the number of patients
 - Chemotherapy toxicity – graded by a nurse before each cycle of chemotherapy using the National Cancer Institute Common Toxicity Criteria
 - Survival – expressed as percentage of patients surviving 1 year after trial enrollment
- **Power:**No power is provided
- **Data handling:**Per protocol (exclusion of subjects)

RESULTS:

- **Completion of study:**
 - The standard of care (SOC) group had 31 patients complete the study
 - The fish oil (FO) group had 15 patients complete the study.
- **Primary outcome measure:** Response rate in FO group was 60%, compared to 25.8% in the SOC group ($p=0.008$)
- **Secondary outcome measures:**
 - Clinical benefit in FO group was 80, compared to 41.9% in the SOC group ($p=0.02$)
 - Chemotherapy toxicity consisting of overall incidence of any grade 3 or 4 toxicity (nausea, vomiting, hand-foot syndrome, neutropenia, constipation, and gastritis) was 13.3% in FO group, compared to 22.6% in SOC group ($p=0.46$)
 - 1-year survival in FO group was 60%, compared to 38.7% in SOC group ($p=0.15$)

- **Author's conclusion:** In patients with advanced NSCLC, who are chemotherapy-naïve, the addition of fish oil to standard first-line platinum based chemotherapy may increase response rates and clinical benefit, without affecting the toxicity of the treatment. Further research with additional randomized trials is needed to confirm these results.

STRENGTHS:

- It was a controlled study, which is gold standard.
- A contemporary control group was used, therefore the patients were able to receive standard of care with palliative chemotherapy for their cancer. In this patient population, patient interest in placebo-controlled studies is low, but this study was able to utilize a control and attract interest from patients.
- Data handling design of per protocol utilizes only those patients who completed the study, which allows the true efficacy of the drug regimen to be better determined.
- Compliance was determined in the FO group by measuring the amount of capsules or amount of liquid remaining at the end of the study. The amount of plasma phospholipid EPA and DHA was also measured in both the SOC and FO groups, which showed that patients in the FO group took their medication and that patients in the SOC group did not receive FO supplementation.

LIMITATIONS:

- Small sample size
- Non-random assignment can create bias and lead to patients with differences that could influence the study to be predominately in one group, making it more difficult to evaluate.
- Open-label (no blinding) trial can introduce bias.
- Only patients from the Cross Cancer Institute in Edmonton, Alberta, Canada were enrolled
- No power was calculated, which causes an unknown risk for Type II error.
- Data handling design of per protocol may not actually show the clinical usefulness of the drug because patients can dropout for reasons that can affect its usefulness in practice.

CONCLUSIONS:

- A majority of patients with advanced staged NSCLC do not respond to first-line chemotherapy treatment. If fish oil can increase the response rates and clinical benefit for patients with NSCLC, many of these patients will be able to have an improvement in symptoms and possibly an improvement in survival as well.
- Due to the limitations associated with this study, further research should be performed evaluating the use of fish oil supplementation in patients with NSCLC through randomized multicenter trials that are blinded with larger number of sample sizes.

Reference:

Murphy RA, Mourtzakis M, Chu QSC, Baracos VE, Reiman T, Mazurak VC. Supplementation with fish oil increases first-line chemotherapy efficacy in patients with advanced Nonsmall cell lung cancer. *Cancer*. 2011;117(16):3774-3780.

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