No Improvement in CRC Outcomes With Vitamin E Supplementation

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The study covered in this summary was published on ResearchSquare.com as a preprint and has not yet been peer reviewed.

Key Takeaways

- FOLFOXIRI (5-fluorouracil, oxaliplatin, and irinotecan) is used as an effective first-line treatment for metastatic colorectal cancer (mCRC) but carries significant toxicity risks.
- The researchers postulated that adding δ-tocotrienol, shown to be neuroprotective and anti-inflammatory, to a standard triplet chemotherapy regimen might reduce toxicities, including peripheral neuropathy.
- Adding δ-tocotrienol to FOLFOXIRI did not significantly prolong the time to first hospitalization or death as compared to FOLFOXIRI plus placebo; toxicity profiles were also similar in both groups.
- Fewer dose reductions of oxaliplatin in the δ-tocotrienol group may represent a neuroprotective effect of tocotrienol, but this did not translate into differences in progression-free survival (PFS) or overall survival (OS).

Why This Matters

- CRC is the second leading cause of cancer-related deaths in developed countries, with an overall 5-year survival rate of 55% to 60%.
- Triplet chemotherapy used in mCRC treatment confers better outcomes than doublet therapy but is more toxic. Reducing toxicity would theoretically improve patients' tolerability and continuation of treatment.
- δ-Tocotrienol has been shown to be neuroprotective and anti-inflammatory, so adding it to a chemotherapy regimen might reduce toxicity.
- This is the first randomized, double-blind, placebo-controlled trial to evaluate the potential effect of δ-tocotrienol for increasing tolerability of FOLFOXIRI.

Study Design

- Seventy mCRC patients were randomly assigned to receive either FOLFOXIRI plus δ-tocotrienol or FOLFOXIRI plus placebo.
- FOLFOXIRI was administered in eight cycles followed by four cycles of 5-FU. δ-Tocotrienol 300 mg or placebo three times daily was added during chemotherapy for a maximum of 2 years. The primary endpoint was time to hospitalization or death during chemotherapy treatment.
- Toxicity and quality-of-life assessments were conducted at regular intervals.
- Time to first hospitalization or death, PFS, and OS were calculated and reported using standard statistical methods.

Key Results

- The median time to first hospitalization or death was 3.7 months in the placebo group (95% CI , 1.93 to not reached [NR]) vs NR with δ-tocotrienol (95% CI, 1.87 to NR); the hazard ratio (HR) was 0.70 (95% CI, 0.36 – 1.36; P = .29). The proportion of patients who were hospitalized or died within 7 months from the start of treatment was 57% for placebo vs 42% for δ-tocotrienol (P = .15).

- There were 32 hospitalizations in the placebo group and 25 in the δ-tocotrienol group from the start of FOLFOXIRI to 1 month after the end of treatment. The median duration of hospitalization was 5.8 days in the placebo group vs 5.9 days in the δ-tocotrienol group (*P* = .92).
- The most common adverse events/toxicities were nausea, diarrhea, peripheral sensory neuropathy, pain, fatigue, and anemia (grade 1 or 2). Grade 3 or 4 toxicities were uncommon except for neutropenia. Notably, no grade 3 or 4 peripheral sensory neuropathy was noted.
- During FOLFOXIRI treatment, the oxaliplatin dose was reduced in 24 patients (71%) in the placebo group and 17 (47%) in the δ-tocotrienol group (*P* = .047).
- Disease progression occurred in 62 patients (89%); 30 (48%) were in the placebo group and 32 (52%) in the δ-tocotrienol group. Median PFS in the placebo group was 9.2 months (95% CI, 7.3 – 10.6) vs 9.5 months (95% CI, 7.4 – 11.9) in the δ-tocotrienol group (HR, 1.08; 95% CI, 0.65 – 1.78; *P* = .77).
- Median OS was 23.3 months (95% CI, 17.1 to NR) in the placebo group and 22.3 months (95% CI, 17.9 – 37) in the δ-tocotrienol group (HR = 1.1; *P* = .76). Preliminary 3-year survival rate was 41% in the placebo group and 37% in the δ-tocotrienol group.
- No significant difference between groups was found in general health assessments.

Limitations

- The study was limited by small sample size and single-center setup.
- The method of measuring patients' adherence to δ-tocotrienol/placebo regimen could be improved.

Study Disclosures

- This work was financially supported by Vejle Hospital, the University Hospital of Southern Denmark. American River Nutrition supplied δ-tocotrienol and placebo free of charge. The authors declare no conflicts of interest.

This is a summary of a preprint research study, "Delta Tocotrienol as a Supplement to FOLFOXIRI in First Line Treatment of Metastatic Colorectal Cancer. A Randomized, Double-blind, Placebo-controlled Phase II Study," published January 11 on ResearchSquare.com and led by Louise Raunkilde, MD, and colleagues from University Hospital of Southern Denmark. It is provided to you by Medscape. This study has not yet been peer-reviewed. The full text of the study can be found on ResearchSquare.com.

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