Efficacy and Safety of Oxaliplatin/ Capecitabine Based Chemotherapy plus Bevacizumab as First-Line Treatment for Advanced Colorectal Cancer (CRC): a Systematic Review and Meta-analysis

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INTRODUCTION

- Colorectal cancer (CRC) is a leading cause of cancer-related deaths. 1
- Current 1st line for CRC therapy usually consists of 5-Fluorouracil (5-FU) based combination chemotherapy along with a targeted antibody against VEGF or EGFR. 2
- The combination of 5-FU with Oxaliplatin (FOLFOX) is a commonly used treatment regimen for CRC.
- Capecitabine is an oral prodrug of 5-FU. 3
- The combination of capecitabine with oxaliplatin (XELOX) has been shown to be non-inferior to the FOLFOX regimen, albeit with slightly increased toxicity. 3

OBJECTIVE

To evaluate the efficacy and safety of oxaliplatin or capecitabine - based chemotherapy plus bevacizumab as first-line treatment for advanced CRC.

MATERIAL AND METHODS

- Literature searches were conducted in MEDLINE, Embase, the Cochrane Library, and clinicaltrials.gov. No language or date restrictions were imposed.
- In addition, references of included studies were searched for relevant studies.
- All randomized controlled trials (RCTs) examining the efficacy and safety of oxaliplatin/capecitabine based chemotherapy plus bevacizumab in adult patients with advanced CRC were included.

Outcomes:

- Primary: overall survival (OS) and progression free survival (PFS).
- Secondary: response rate, complete response, partial response, stable disease, progressive disease, disease control, and adverse events.
- Two authors independently selected papers, extracted data and assessed quality.
- Study quality of included trials were assessed using the Cochrane Risk of Bias Tool.

RESULTS

- A total of 3 RCTs involving a total of 1993 patients were included in this meta-analysis.
- A total of 997 Patients received Oxaliplatin/capecitabine based chemotherapy, and a total of 996 Patients received comparators.
- Overall, the risk of bias of included trials was low.
- Most common adverse events reported with bevacizumab included bleeding, hypertension, and venous thromboembolic events.

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<tr>
<th>Study or Subgroup</th>
<th>Experimental Group</th>
<th>Control Group</th>
<th>Odds Ratio [OR]</th>
<th>95% CI</th>
<th>Test for overall effect: Z = 0.49 (P = 0.63)</th>
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<tbody>
<tr>
<td>Study or Subgroup</td>
<td>Experimental Group</td>
<td>Control Group</td>
<td>Odds Ratio [OR]</td>
<td>95% CI</td>
<td>Test for overall effect: Z = 2.18 (P = 0.03)</td>
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<td>Study or Subgroup</td>
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<td>Odds Ratio [OR]</td>
<td>95% CI</td>
<td>Test for overall effect: Z = 3.17 (P = 0.002)</td>
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DISCUSSION

- Despite advances in the treatment of metastatic CRC (mCRC), most patients have a poor prognosis. 4
- Since many patients may not prefer, or are not candidates for aggressive treatment regimens, effort should be put to identify efficacious but less toxic chemotherapeutic regimens. 5
- Bevacizumab is a humanized, IgG monoclonal antibody against VEGF-A which does not have significant activity as monotherapy. 6
- When given as part of combination chemotherapy, bevacizumab has shown good activity, and its ADRs are not serious enough to lower QoL. 7
- Bevacizumab also has been shown to improve progression-free survival and overall survival when added to chemotherapy in first-line and second-line treatment settings. 8
- International guidelines recommend FOLFOX or capecitabine based chemotherapy plus bevacizumab as first-line treatment for mCRC where more intensive treatment is not appropriate. 9
- When bevacizumab was combined with fluorouracil/ folinic acid plus oxaliplatin (FOLFOX-4) in the second-line setting, there were significant benefits in OS, PFS and RR. 10

CONCLUSION

Bevacizumab plus Oxaliplatin/capecitabine based chemotherapy showed improvement in OS and RR as compared to other chemotherapy in patients with advanced CRC.

REFERENCES