E. Vasile*, C. Caparello, S. Caponi, L. Ginocchi, C. Vivaldi, improved overall survival was met [4]. This topic considering that the primary end point of the study of paclitaxel versus paclitaxel alone, will add new information on metastatic gastric cancer. The results of the RAINBOW trial, a and could become a new standard for second-line treatment of metastatic gastric cancer. The role of further treatments after chemotherapy in metastatic gastric cancer is reinforced.

Two different options, chemotherapy and anti-VEGFR therapy, are available and con

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Log(Hazard ratio)</th>
<th>SE</th>
<th>Weight</th>
<th>Hazard ratio IV, Fixed, 95% CI</th>
<th>Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thuss-Patience</td>
<td>-0.734</td>
<td>0.3324</td>
<td>4.7%</td>
<td>0.48 (0.25, 0.92)</td>
<td>2011</td>
</tr>
<tr>
<td>Kang, Docetaxel Arm</td>
<td>-0.2744</td>
<td>0.1813</td>
<td>15.8%</td>
<td>0.76 (0.53, 1.08)</td>
<td>2012</td>
</tr>
<tr>
<td>Kang, Irinotecan Arm</td>
<td>-0.543</td>
<td>0.193</td>
<td>13.9%</td>
<td>0.58 (0.40, 0.85)</td>
<td>2012</td>
</tr>
<tr>
<td>Cook</td>
<td>-0.4005</td>
<td>0.1607</td>
<td>20.1%</td>
<td>0.67 (0.49, 0.92)</td>
<td>2013</td>
</tr>
<tr>
<td>Fuchs</td>
<td>-0.2536</td>
<td>0.1285</td>
<td>31.4%</td>
<td>0.78 (0.60, 1.00)</td>
<td>2013</td>
</tr>
<tr>
<td>Li, Arm B</td>
<td>-0.9943</td>
<td>0.2643</td>
<td>7.4%</td>
<td>0.37 (0.22, 0.62)</td>
<td>2013</td>
</tr>
<tr>
<td>Li, Arm C</td>
<td>-0.8916</td>
<td>0.2803</td>
<td>6.6%</td>
<td>0.41 (0.24, 0.71)</td>
<td>2013</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td></td>
<td></td>
<td></td>
<td>100.0% 0.64 (0.56, 0.74)</td>
<td></td>
</tr>
</tbody>
</table>

Test for overall effect; $Z = 6.20 \ (P < 0.00001)$

Heterogeneity: $\chi^2 = 11.05, \ df = 6 \ (P = 0.09); I^2 = 46\%$

Figure 1. Meta-analysis of overall survival of second-line treatment versus best supportive care.

With these results, the role of further treatments after first-line chemotherapy in metastatic gastric cancer is reinforced. Two different options, chemotherapy and anti-VEGFR therapy, are available and confirmed efficacy in this setting. The combination of the two strategies as used in other cancers is promising and could become a new standard for second-line treatment of metastatic gastric cancer. The results of the RAINBOW trial, a phase III study evaluating ramucirumab in combination with paclitaxel versus paclitaxel alone, will add new information on this topic considering that the primary end point of the study of improved overall survival was met [4].


Oncology Center, Azienda Ospedaliero-Universitaria Pisana, Istituto Toscano Tumori, Pisa, Italy
(*E-mail: envasile@tin.it)

disclosure

The authors have declared no conflicts of interest.

references


do: 10.1093/annonc/mdt570

Can tumor location predict effectiveness of bevacizumab conducted in the first-line setting for metastatic colorectal cancer

Bevacizumab has been confirmed to improve progression-free survival (PFS) when combined with chemotherapy for metastatic colorectal cancer (MCRC). Although some molecular markers were investigated to predict effectiveness of bevacizumab, none was clearly proved in clinical practice [1]. Boisen et al. [2] published an interesting paper, which suggested that tumor site could be a marker for the use of bevacizumab.

Boisen et al. [2] explained that vascular endothelial growth factor (VEGF-A), target of bevacizumab, was present in higher levels in left-sided colon and rectal cancers than in right-sided colon cancers, thus leading to higher effectiveness of bevacizumab in treating the former tumor than the latter. However, published study indicated that expression level of VEGF-A could not predict effectiveness of bevacizumab [1]. Thereby, the explanation by Boisen et al. for tumor location as a marker for use of bevacizumab may not be tenable.

The study method of Boisen et al. [2] may not be appropriate. They selected two cohorts of patients, one was treated with capecitabine and oxaliplatin (CAPEOX) from 2003 to 2006 and the other CAPEOX plus bevacizumab from 2006 to 2011. Results showed that tumor location was a significant predictor of oncologic outcome in the CAPEOX plus bevacizumab group, while no association was found between tumor location and survival in CAPEOX group. Could that prove tumor location predicted effectiveness of bevacizumab, though which differed in the two cohorts? In our opinions, their evidence was not convincible. To achieve their study goal, they may need to compare survival between patients who received bevacizumab combined with chemotherapy and those who received chemotherapy alone in subgroups of cecum and ascending colon cancer, right flexure and transverse colon cancer, left flexure and descending colon cancer, sigmoid colon, and rectal cancer. Or, they may just divided all the patients into two large groups, one group was with cancer of sigmoid colon and rectum and the other with tumor originating from cecum to descending colon. It is more suitable for them to compare baseline characteristics between patients who did and did
not receive bevacizumab in different subgroup. If significant improvement on survival was found in patients who received bevacizumab than those who did not in the subgroup with sigmoid colon and rectum cancer, but not in subgroup with tumor originating from the cecum to the descending colon, it may be possible to make their present conclusions when results was further confirmed in multivariate analyses.

Patients included in the clinical trials were mostly with tumor located in colon, and bevacizumab was proved to improve clinical outcome for MCRC [3–5]. Thereby, it is hard to claim benefit of bevacizumab occurred more in rectal cancer than in colon cancer. Though Cunningham et al. [5] carried out subgroup analyses in their study with results showing the hazard ratio (HR) of progression for rectal, rectal + colon cancer, and colon-only cancer was 0.41, 0.22, and 0.67, respectively. We do not think the comparison of HR for different tumor location by Boisen et al. [2] was meaningful since unbalanced baseline characteristics existed greatly between groups. Before tumor location is adopted as marker for use of bevacizumab, more evidence is warranted.

K. Y. You & Y. H. Gao*

Department of Radiation Oncology, State Key Laboratory of Oncology in Southern China, Sun Yat-sen University Cancer Center, Guangzhou, China (*Email: gaoyh69@sina.cn)

disclosure

The authors have declared no conflicts of interest.

references


doi: 10.1093/annonc/mdt569

Published online 12 January 2014