**Background**

Cediranib is an oral, highly potent, vascular endothelial growth factor receptor (VEGFR) tyrosine kinase inhibitor with efficacy against both VEGF receptors and PDGFR. HORIZON I and II were pivotal, randomized, double-blind Phase II studies of cediranib in patients with metastatic colorectal cancer (mCRC).

HORIZON II (NCT00399035): Cediranib plus FOLFOX/XELOX showed a significant improvement in PFS compared with chemotherapy alone (HR 0.94, P =0.0012), but no improvement in OS versus chemotherapy alone (HR 0.92, P =0.113).

HORIZON III (NCT01818417): HORIZON III showed significant improvement in PFS compared with chemotherapy alone (HR 0.84, P =0.0016) and OS (HR 0.77, P =0.0016).

HORIZON II and III: HORIZON II and III were the first two large randomized (1:1:1) Phase III trials to compare cediranib (20 mg) with chemotherapy alone or placebo in patients with mCRC at baseline (HORIZON II) or following cediranib treatment (HORIZON III).

cediranib 20 mg (n=502) or placebo (n=358) (Figure 1).}

**Results**

For each baseline cutoff, patients were stratified into high and low subgroups of patients with a better or worse outcome following cediranib treatment compared with the overall group.

To explore potential prognostic and predictive factors for clinical outcome, a retrospective analysis of baseline levels of plasma markers, CEA, and soluble VEGF receptor 2 (sVEGFR-2) was performed.

**Medically baseline values for VEGF, sVEGFR-2 and CEA across HORIZON II and III.**

**Table 1. Subgroup populations for VEGF, sVEGFR-2 and CEA**

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>High (≥98 pg/ml)</th>
<th>Low (&lt;98 pg/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CEA</td>
<td>393 (45.7%)</td>
<td>644 (45.3%)</td>
</tr>
<tr>
<td>VEGF</td>
<td>372 (69%)</td>
<td>236 (64%)</td>
</tr>
<tr>
<td>sVEGFR2</td>
<td>531 (68%)</td>
<td>743 (64%)</td>
</tr>
</tbody>
</table>

Conclusions

- The efficacy of cediranib given as a fixed-dose oral agent was confirmed in two large randomized Phase III trials, and should be considered when selecting a treatment for patients with mCRC.

**References**