Abstract 166

**RAS status in circulating-tumor DNA (ctDNA) and outcomes during rechallenge treatment with anti-EGFR antibodies in metastatic colorectal cancer (mCRC)**

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**Background**

Several trials have evaluated the efficacy of rechallenge treatment with anti-EGFR antibody. In our phase II trial, JACCRO CC-08 (LUMINOUS trial) in patients with RAS-wt type HCC, the response rate was 2.5% for CC-08 and 8.3% for CC-09.

**Methods**

An exploratory analysis showed that patients with/without RAS mutations at progression: KRAS mutations at baseline had a shorter PFS than those without RAS mutations in PFS of 2.3 to 4.7 months. (log-rank test: \( P = 0.0126 \)).

**Conclusions**

The anti-EGFR antibody plus irinotecan regimen were evaluated for the primary endpoint of 3-month PFS rate in JACCRO CC-08 (NCT01961544) and JACCRO CC-09 (NCT02953649).

**Sample collection**

 Patients (325) were obtained, and the blood DNA was extracted from the plasma using QIAamp Circulating Nucleic Acid Kit (QIAGEN).

**Clinical outcomes**

<table>
<thead>
<tr>
<th>Outcome</th>
<th>JACCRO CC-08 (N=34)</th>
<th>JACCRO CC-09 (N=34)</th>
<th>Current study (N=15)</th>
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<tbody>
<tr>
<td>Median PFS, mo</td>
<td>1.0 (95%CI 0.7-1.3)</td>
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<td>Disease control rate (%)</td>
<td>21.2% (95%CI 10.4-31.0)</td>
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**Summary**

RAS mutations were detected in ctDNA at the baseline in 8 out of 10 patients.

All patients had mutations in RAS codon 12 and codon 61 but was almost at RAS codon 61 simultaneously. We investigated an association between RAS status and outcome of patients with baseline and median OS (HR*; 1.0 vs. 1.37; 95%CI 1.28-1.58). We found that the hazard rate was significantly higher in patients with high RAS mutation in baseline ctDNA.

**Conclusion**

Our study demonstrated that RAS status in ctDNA using QIAGEN BEAMING technology predicts survival of rechallenge treatment with anti-EGFR antibody in mCRC patients. This data can support the application of ctDNA monitoring into clinical practice.