Emerging Insights on the Association of Tumor Molecular Phenotype with Clinical Benefit in Metastatic Colorectal Cancer (mCRC) Subjects Treated with AB928 + Modified FOLFOX-6

Ashahla R. Udyavali1, Michael Cecchini1, Daniel DiCesare2, Sean Chis1, Lisa Seid1, Kristian Zhang1, Stephen W. Young3, Amy E. Anderson3, Kimberlin Y. Gerick3, Matthew J. Walters4, Houston N. Gilbert5, Cheng Qiu2, Juan Jia2, and William Greenberg5

1Arcus Biosciences, Inc., 3900 Point Elden Way, Hayward, CA, USA; 2Yale University, New Haven, CT, USA; 3University of California, San Francisco, CA; 4Emory University, Atlanta, GA; 5University of Texas MD Anderson Cancer Center, Houston, TX

Overviews

AB928 is an orally bioavailable and selective dual agonist of adenosine A2A and A1 receptor, specifically designed to block the immunosuppressive effects associated with high adenosine concentration within the tumor microenvironment. It is a novel, selective, and orally bioavailable agonist of the adenosine A1 (A1) and A2A (A2A) receptors with a low binding affinity for the A2B (A2B) receptor.

CLINICAL ACTIVITY

As of Data Cutoff (DCC), October 16, 2020, the study was evaluable on a total of 44 subjects: 15 subjects without prior therapy in the metastatic setting (L+) and 29 subjects with prior line of therapy (L-) for a total of 16 subjects with prior therapy (L+ L-) from the study. The safety profile was unchanged since our most recent update.

In the L+ setting, objective responses were seen in 8/15 (53.3%) patients (4 PR, 4 CR, 1 PD), in addition to 3 SD (2L). In the L- setting, PR was seen in 6/29 (20.7%; 3 PR, 3 CR, 0 PD, 0 SD). The median DCR in the L- setting was 70% (95% CI: 57%, 81%), while the median DCR in the L+ setting was 63% (95% CI: 48%, 75%). The proportion of subjects with DCR exceeding the 10th percentile for DCC was 70% (95% CI: 60%, 79%) in the L- setting, compared with 63% (95% CI: 48%, 75%) in the L+ setting.

For the purposes of biomarker analysis, we defined clinical criteria for L- as either CR, PR, or SD in a study population (10% criterion). For L+, we aggregated patients into those obtaining partial clinical outcomes (PR or SD or PD CT+ +4 months, n=7) from this group and those benefiting from treatment (PR or SD or PD CT+ +4 months).

Biomarker Trends

Tumor CDD3 mRNA and protein levels are associated with better clinical outcome, while soluble A373 protein is inversely associated with clinical benefit in 3L+ mCRC (ARC-3)

Figure 2. Baseline soluble CDD3 (CDD3) in serum and tumor CDD3 gene/protein measurements in 3L+ mCRC patients

Figure 3. Adenosine gene signatures in 1L external cohort and 3L-ARC-3 patients

Figure 4. Tumor Mutation Burden (TMB) in 3L+ mCRC patients

Tumor Mutation Burden (TMB) is associated with better clinical outcome in 3L+ mCRC

Case Study of 3L+ mCRC Patient

Immune activation is observed in 3L+ KRAS-mutant patient with longest T6 (>11 months)

Figure 5. Evidence of CDD3 expression, immune infiltration and activation in 3L+ patient with durable clinical benefit (SD)

Table: Case Study of 3L+ mCRC Patient

<table>
<thead>
<tr>
<th>Patient Characteristics</th>
<th>Treatment</th>
<th>Clinical Status</th>
<th>Tumor Mutation Burden (TMB)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>59</td>
<td></td>
<td>15.4</td>
</tr>
<tr>
<td>Sex</td>
<td>Male</td>
<td></td>
<td></td>
</tr>
<tr>
<td>KRAS Mutation Status</td>
<td>Wild Type</td>
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</tbody>
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CONCLUSIONS

- In the L+ setting, objective responses were seen in 8/15 subjects (53.3%; 4 CR, 4 PR, 2 PD, 1 SD) in addition to 3 SD (2L). In the L- setting, PR was seen in 6/29 (20.7%; 3 CR, 3 PR, 0 PD, 0 SD). The median DCR in the L- setting was 70% (95% CI: 60%, 79%) from this group and those benefiting from treatment (PR or SD or PD CT+ +4 months).

- Arcus and Corvus adenosine gene signatures are associated with worse outcomes in 3L+ mCRC patients treated with AB928 + modified FOLFOX-6.

- In our 3L+ mCRC cohort, adenosine signature appears to correlate with higher levels of myeloid cell infiltration, a prognostic negative factor.

- Case biomarkers, particularly TMB and CDD3 expression, may offer the opportunity for patient selection in future studies of AB928 + modified FOLFOX-6 in advanced mCRC.