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Table 1. Result summary of PA-018 therapeutic responses and toxicities

Table 1. The therapies used include DNA synthesis inhibitors (5-FU, oxaliplatin), a DNA alkylating agent (cisplatin), a DNA intercalating agent (etoposide), a topoisomerase inhibitor (oxaliplatin), an EGFR inhibitor (erlotinib), a c-MET inhibitor (crizotinib) and an angiojenic inhibitor (bevacizumab). Tumor growth was continually observed after treatment regimen ceased in order to determine time-to-endpoint (TTE) and difference between TTE medians (T). Body weight (BW) nadir was shown as percent change and deaths were divided into treatment-related deaths (TR) and non-treatment related deaths (NTR).

Our group was presented with a highly motivated patient who enrolled in a personalized designed treatment based on the genetic and molecular profile of his tumor, which was cultured into primary cells and treated with a group of chemotherapeutics. Our lab also established a PACC pancreas derived xenograft (PDX) mouse model from his tumor biopsy and we have proceeded in treating mice with therapies that target specific molecules and DNA replication, in order to find effective targets.

We hypothesized that this rationally designed treatment will yield effective therapies.

Pancreatic acinar cell carcinoma; (PACC) is a unique disease that is not well understood. The disease accounts for ~1% of the pancreatic malignancies each year (3). Nevertheless PACC is a lethal disease that is likely to become metastatic to the liver or lung (4). The molecular signals that drive PACC are still a mystery, and investigators have been trying to test existing cancer treatments to find the most effective therapy. Since little is known about the disease, an understanding of the molecular components is imperative to finding a targeted therapy. Past studies have found that genes that regulate DNA repair may be mutated (5). Genomic profiling on 44 PACC patients uncovered DNA repair mutations in 45% of the patients, BRCA2 being the most common gene, followed by BRCA1 and ATM (5).

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We hypothesized that this rationally designed treatment will yield effective therapies.

Conclusions

Therapeutic responses in a novel patient-derived xenograft mouse model for rare pancreatic acinar cell carcinoma


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References

1. ibid.

2. ibid.

3. ibid.

4. ibid.

5. ibid.

6. ibid.

7. ibid.

8. ibid.

9. ibid.