ABSTRACT

Previously we reported that the combination of anti-PD1 and β-alethine completely stopped cancer growth in a syngeneic mouse melanoma model even under conditions when neither of the drugs had statistically significant effects as a single agent. In order to further examine this dramatic result, we extended the studies, evaluated immune parameters and tested if long-term immunity to re-challenge occurred.

Surprisingly, three low doses of anti-PD1, spread over 8 days, were sufficient to allow concurrent and continuing weekly dosing of β-alethine to not only halt tumor growth, but to reverse X. The established melanomas regressed over the subsequent 4-6 weeks. Even more striking was that the short course of anti-PD1, which failed to reduce cancer growth as a single therapy, altered the immune system such that subsequent treatment with β-alethine was effective. β-alethine therapy, beginning eight days after the conclusion of anti-PD1 therapy, when tumors averaged almost 30 mm, was sufficient to cause at least stabilization of cancer in all animals and complete response (no palpable tumor on repeat measurement) in the majority of animals. Statistical comparisons of all animals receiving combination therapy (either concurrently or sequentially) with controls resulted in significant differences using ANOVA for tumor size (p < 0.05) in a 2x3 squared test for tumor presence (p < 0.0005).

No toxicity was noted in treated animals. This is consistent with previous animal and IGF toxicity studies and the complete human Phase III trial. The human trial showed that β-alethine, as a single agent, caused no drug-related side effects and lead to shrinkage or stabilization in all patients with lymphoma who were not able to receive standard chemotherapy.

The final result of re-challenging the mice with the original Cloudman melanoma at a higher dose than the initial cancer inoculation level will be presented.

CONCLUSIONS

- Combination checkpoint inhibitor therapy: Anti-PD1 and β-alethine lead to complete responses of melanoma in a syngeneic mouse model
- 88% of CRs resisted re-challenge.
- P-aldithine (β) is a small molecule drug that:  
  - Targets checkpoint receptors
  - Synergizes with anti-PD1
- Complete response (CR) is the typical (90%) response to combination therapy.

FUTURE DIRECTIONS PARTNERSHIPS

Clinical sites and corporate partners are sought for the next stages. Preliminary collaborations are also solicited. FET@Findcure.org