Expanding the Therapeutic Potential of anti-PD-1 and anti-CTLA-4 Therapy with Innovative Fc Engineering and Rational Combinations for the Treatment of Solid Tumors

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Background
AGEN1181, an Fc-engineered Anti-CTLA-4 Antibody Engages Multiple Mechanisms of Action to Promote T-Cell-Mediated Antitumor Immunity

1. Ligated blockade & CD80-dependent T-cell activation
2. Diphosphorylation of intracellular regulatory T-cells (Tregs)
3. Efficacy T-cell priming and memory formation

Hypothesis: Optimizing Fc - FcγR co-engagement enhances the activity of anti-CTLA-4 antibody by increasing binding affinities to activating Fc receptors FcRv-CD16 (CD64, mouse) or FcRRIIA (CD16a, human) augment T-cell priming by increasing the quality of the immune synapse between a T-cell and an antigen presenting cell (APC).

Fcγ binding studies of studied antibodies

Table 1: Fcγ binding experiments

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<th>Fcγ Binding</th>
<th>Parental</th>
<th>FcRRIIA</th>
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<tr>
<td>Parental</td>
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<td>Fc-Engineered</td>
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AGEN1181™ has improved therapeutic potential against immunogenic tumors by enhancing Treg depletion and T cell priming

AGEN1181™ Fc-Enhanced anti-CTLA4 & PD1 triple combination with ACT and Vaccines are curative in IO refractory models

Sequential treatment with Fc-enhanced anti-CTLA-4 and PD1 promotes curative responses in combination with ACT

Concurrent treatment promotes curative responses in combination with HSC70 tumor antigen vaccine + QS-21

Conclusions
AGEN1181™-enhanced anti-CTLA-4 demonstrates superior single agent and broader IC50 & IC90 combinations activity than conventional CTLA-4 drugs

On-Going Trial
Combination of AGEN1181™ with Agens’ Balbifalmmab (anti-PD-1) is advancing in the phase II/III study (NCT03680027)

References
1. Tanne A et al. Cancer Cell 2018
2. Tanne A et al. Curr Opin Immunol 2018
3. Tanne A et al. Proc Natl Acad Sci USA 2018

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For a more detailed description, please refer to the original publication.