MM-401, a novel anti-TNFRII antibody that induces T cell co-stimulation, robust anti-tumor activity and immune memory
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**Abstract:** AACR-4846

Anti-TNFRII (TNFR2) has been implicated as a novel target for cancer immunotherapy. While TNFR2 has been linked to enhanced suppressive activity in regulatory T cells (Tregs) in autoimmune models, the effect of TNFR2-targeted therapy in cancer remains unexplored. We present here a novel anti-TNFRII antibody that provides a favorable therapeutic index in multiple cancer models, treatment with a murine antibody (MM-401) resulted in robust tumor activity both in vitro and in immunocompetent syngeneic tumor models targeting the TNFR2 and PD-L1. Moreover, MM-401 showed enhanced antitumor activity in combination with anti-PD-L1. MM-401 inhibited tumor growth in vivo and consisted of resistance mechanisms in comparison with anti-PD-L1 in a lung cancer model. MM-401 treatment increased the number of tumor-infiltrating T cells with increased expression of PD-1 and TIGIT, suggesting a reverse PD-1 receptor downregulation. MM-401 treatment also induced T-cell hyperplasia in vivo. This suggests a potential mechanism for the increased antitumor activity observed with MM-401. MM-401 treatment led to increased levels of cytokines, such as IL-2, IFN-γ, and TNF-alpha, which are known to be involved in anti-tumor activity. Overall, MM-401 offers promise as a potential therapeutic target for cancer immunotherapy.

**Keywords:** Anti-TNFRII, Tumor, T-cell, Immunology, Cancer therapy

**Introduction:**

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**Methods:**

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**Results:**

Anti-TNFRII (TNFR2) has been implicated as a novel target for cancer immunotherapy. While TNFR2 has been linked to enhanced suppressive activity in regulatory T cells (Tregs) in autoimmune models, the effect of TNFR2-targeted therapy in cancer remains unexplored. We present here a novel anti-TNFRII antibody that provides a favorable therapeutic index in multiple cancer models, treatment with a murine antibody (MM-401) resulted in robust tumor activity both in vitro and in immunocompetent syngeneic tumor models targeting the TNFR2 and PD-L1. Moreover, MM-401 showed enhanced antitumor activity in combination with anti-PD-L1. MM-401 inhibited tumor growth in vivo and consisted of resistance mechanisms in comparison with anti-PD-L1 in a lung cancer model. MM-401 treatment increased the number of tumor-infiltrating T cells with increased expression of PD-1 and TIGIT, suggesting a reverse PD-1 receptor downregulation. MM-401 treatment also induced T-cell hyperplasia in vivo. This suggests a potential mechanism for the increased antitumor activity observed with MM-401. MM-401 treatment led to increased levels of cytokines, such as IL-2, IFN-γ, and TNF-alpha, which are known to be involved in anti-tumor activity. Overall, MM-401 offers promise as a potential therapeutic target for cancer immunotherapy.

**Conclusion:**

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**Cross-reference:**

Future studies in the context of a novel target, TNFR2, for the treatment of cancer are warranted.