MM-310: An EphA2-targeted, docetaxel antibody-direceted nanotherapeutic and synergistic combination with PD-1 inhibitor

Abstract

EphA2-targeted nanotherapeutic strategies are promising approaches for cancer therapy, particularly in EphA2 overexpressing tumors. Docetaxel (DTX) is a first-line chemotherapy for a variety of tumors. The EphA2-targeted Docetaxel antibody (EphA2-scFv) is highly active in syngeneic tumor models, and represents a promising strategy for the treatment of cancer. In conclusion, the novel combination of MM-310 and an anti-PD-1 Ab in the treatment of several syngeneic tumor models. The mouse syngeneic tumor lines EMT-6, CT26, and LLC, were selected to provide a range of sensitivity to each of docetaxel and anti-PD-1, in vivo activity studies and immune phenotype analyses were performed comparing MM-310 alone to combination for the nanotherapeutic. MM-310 administration was initiated two days prior to anti-PD-1 therapy and consisted of four weekly dosed, while anti-PD-1 was dosed twice weekly for two weeks. The response to MM-310 and anti-PD-1 is nanotherapeutic among the models. MM-310 was efficacious in both anti-PD-1 and graphene nanotherapeutic therapy and was superior to each agent used alone, while anti-PD-1 was efficacious in both models. MM-310 given in combination with anti-PD-1 produces synergistic effects and demonstrates improved disease control over monotherapy with both agents. The data presented here demonstrate the potential of MM-310 as an EphA2-targeted nanotherapeutic agent that can improve the efficacy of anti-PD-1 therapy and has the potential to be used as a combination therapy with PD-1 in the treatment of cancer.

Potential benefits of taxane combination therapy

- Increased PD-1, MHC1, and antigen expression
- Increased CTL-mediated cell killing
- Decreased T-cell apoptosis
- Increased T-cell infiltration
- Decreased MDSCs and Tregs

Chemical stability

- Improved stability in liposome formulations
- Reduce antibody toxicities
- Improve immunomodulatory activity

Immunomodulatory effects of taxanes

- Increased CD8+ T cells and the ratio of CD8+ T cells to Tregs, indicating the creation of an antitumor immune response

Summary

1. The immunomodulatory effects of taxanes makes them potentially favorable combination partners for IO agents.
2. MM-310 combination with anti-PD-1 increases activity and survival in multiple murine syngeneic tumor models, including the EMT-6 model where the combination produced a 60% complete response rate.
3. MM-310 at 50 + 10 mg/kg dose significantly improves survival in vivo compared to each agent used alone. However, dose-dense delivery of docetaxel improves tumor growth inhibition, but does not have the immunomodulatory capacity of MM-310.