ONM-501 - A polyvalent STING agonist for oncology immunotherapy

Suxin Li1, Jian Wang1, Jonathan Wilhelm1, Qingtai Su2, Gaurav Bharadwaj3, Jason Miller2, Wei Li4, Katy Torres1, Zirong Chen2, Ruolan Han3, Tian Zhao5, Jinming Gao1,2

1Harold C. Simmons Comprehensive Cancer Center, University of Texas Southwestern Medical Center, Dallas, TX 75390
2OncoNano Medicine, Inc., Southlake, TX 76092

Introduction

The stimulator of interferon genes (STING) plays a central role in innate immune response against infection and cancer. Several cyclic di-nucleotide (CDN) and non-CDN small molecule STING agonists have demonstrated effectiveness against cancer in preclinical animal models, however their clinical trials showed limited therapeutic efficacy. ONM-501, a dual-activating STING agonist employs PC7A, a synthetic polymer that induces polyvalent STING condensation and prolongs innate immune activation, has been recently developed. ONM-501 encapsulates the endogenous STING agonist cGAMP with the PC7A micelles offering dual ‘burst’ and ‘sustained’ STING activation. The mechanism and effectiveness of intratumorally delivered ONM-501 as an immunotherapy against solid tumors has been demonstrated in preclinical models.

Schematic Illustration of ONM-501

ONM-501 mediated anti-tumor efficacy is host STING dependent

Treatment by PC7A NP and ONM-501 shows completely blocked anti-tumor efficacy in host STING KO mice with WT MC38 cells (B), but not in WT mice with both WT (A) and STING KO MC38 cells (C).

ONM-501 mediated anti-tumor efficacy is CD8 T cell dependent

Tumor growth curves were measured in wild type mice (inoculated with wild type MC38 cells) with control (A), anti-CD8 blockade (B), and with anti-CD11b blockade (C). Blockade of CD8 T cells completely abolished the anti-tumor efficacy (B) whereas blockade of NK cells showed minimal effect (C).

The pilot maximum tolerable dose studies demonstrate ONM-501 was well tolerated with no noticeable adverse effects

Summary

ONM-501 demonstrated pronounced anti-tumor efficacy in a panel of syngeneic tumor models. The anti-tumor effect was mediated by host STING and dependent on CD8+ T cells but not NK. These results support further evaluation of ONM-501 as a clinical candidate for the potential treatment of solid tumors.

References


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