Anti-Metastatic Activity of ISTH0047 – A Potent and Selective TGF-β2 Antisense Oligonucleotide - In Syngeneic Lung Metastatic Model of Mammary Carcinoma


1Isarna Therapeutics GmbH, Munich, Germany, 1,2TRAN- Translational Oncology at the University Medical Center of the Johannes Gutenberg University Mainz, Germany. 3Oncoديد, Dijon, France

Abstract
Transforming growth factor beta (TGF-β) is a potent cytokine with several biological functions such as cell proliferation, differentiation and apoptosis. The present study demonstrates the potential of ISTH0047, a TGF-β2 antisense oligonucleotide in a murine orthotopic mammary carcinoma model.

Effect of ISTH0047 on mouse primary tumor growth

Mice treated with ISTH0047 showed a decrease in tumor volume and size compared to control animals. The growth curve for ISTH0047-treated animals was significantly lower than for control animals at all time points.

Effect of ISTH0047 on lung metastasis from mouse 4T1 tumors

ISTH0047 was able to significantly reduce the number of lung metastases in mice treated with ISTH0047. The results were statistically significant at 95% confidence level.

Results

1. Upon systemic administration to orthotopic TGF-β2-seeking mouse tumors, ISTH0047 significantly decreased the number of lung metastases, whereas no effect on the primary tumor growth was observed.

2. The anti-metastatic potency of ISTH0047 on lung metastasis in this model was similar to that of anti-mouse PD-1 or anti-mouse CTLA-4 antibodies.

Conclusions

1. The potential of ISTH0047 as a novel therapeutic agent against lung metastasis in a syngeneic model was demonstrated.

2. ISTH0047 showed promising anti-metastatic activity in a syngeneic model, making it a promising candidate for further clinical development.

3. ISTH0047 may be a valuable addition to current anti-metastatic therapies.

4. Further studies are needed to evaluate the long-term effects and potential toxicity of ISTH0047.

5. Use of LNA-modified gnpers is an attractive therapeutic approach to inhibit breast cancer metastasis, for instance. However, further preclinical profiling is needed to warrant clinical investigation.