ABSTRACT

Extracellular adenosine in the tumor microenvironment is known to play a significant role in tumor immune evasion and promote tumor growth and metastasis (Ohia, 2016). We defined the receptor(s) required for mediating the effect of adenosine on immune cells within the tumor microenvironment and report the characterization of a novel immune-oncology-dedicated adenosine receptor 2A antagonist that functions in the high adenosine concentration found in tumors. Our main findings are as follows:

1. The receptor(s) required for mediating the effect of adenosine on immune cells in the tumor microenvironment were identified

2. A novel adenosine A2A receptor antagonist was discovered

3. The antagonist is selective for the A2A receptor and, when used as a therapeutic, shows efficacy in tumor-bearing murine models

DEVELOPMENT OF ADENOSINE-RICH TUMOR MODELS

adenosine receptor antagonist

SIGNALING IN IMMUNE CELLS

Parameter

iTeos A2A antagonist

Potency (IC50: IC50)

< 1 nM

Potency in high adenosine (uM: IC50)

< 50 nM

Selectivity vs other adenosine receptors

> 100-fold vs hA1 receptor

> 100-fold vs hA2B receptor

CNS penetration

No

These results suggest that iTeos’ new generation of A2A receptor antagonists, designed to be selective in the adenosine-rich tumor microenvironment, may offer a new therapeutic opportunity in Immuno- Oncology.

CONCLUSIONS

iTeos A2A antagonist is a novel, best-in-class A2A antagonist designed for Immuno-Oncology.

iTeos A2A antagonist is specifically designed to address the tumor microenvironment challenges.

- Potent in high intratumoral adenosine concentration
- Limited CNS penetration

iTeos A2A antagonist fully rescues adenosine-driven T cell immunosuppression