KDDF
Korea Drug Development Fund

Asset #19
Cancer Research Horizons

Arginase-2 Inhibitory Antibody

Therapeutic Area	Oncology	**Indications**	Cancer
Modality	Monoclonal Antibody	**Development Stage**	Hit to Lead/Lead Optimization

Overview

Background

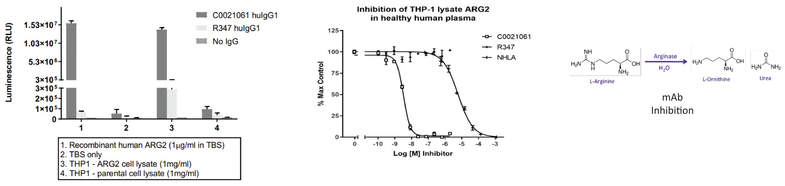
- Arginase (ARG) are metabolic enzymes responsible for arginine metabolism and play a fundamental role in the urea cycle, which provides protection against excess ammonia, while its metabolites are needed for cell proliferation
- It has been noted that the two isoforms, ARG1 and ARG2, can have effects in different disease settings. Their dysregulation has been linked to disorders associated with inflammation and immunity
- Extracellular arginase-2 is upregulated in various cancers causing reduced extracellular arginine concentration, which can cause reduced T-cell mediated anti-tumor responses

Technology Advantages

- Inventors developed a monoclonal antibody to target ARG2. It may enable both inhibition and depletion of ARG2
- An antibody that specifically targets extracellular ARG2 may alleviate concerns about toxicity and reduce the risk of unwanted adverse effects in patients resulting from the inhibition of intracellular arginase
- An antibody therapeutic may have better pharmacological properties than small molecule inhibitors

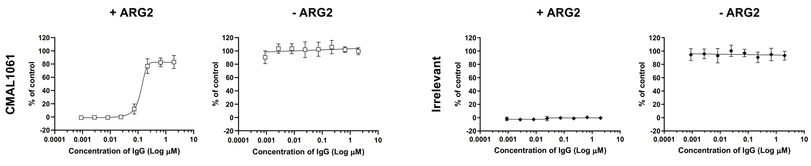
Key Data

C0021061 Shows Strong and Specific Binding to Human ARG2 and Inhibits Enzymatic Activity



Inhibition of THP-1 (human monocytic cell line derived from acute monocytic leukemia patient (AML)) derived human ARG2 activity by antibodies in the presence of human plasma. C0021061 inhibited the activity of THP-1 lysate derived human trimeric ARG2, with an IC50 of approximately 3 nM. The isotype control antibody R347 did not inhibit the activity of THP-1 lysate derived human trimeric ARG2 as expected

C0021061 Restores T Cell Proliferation in vitro



C0021061 huIgG1 can relieve ARG2-mediated suppression of T cell proliferation in vitro, whereas R347 as an isotype control showed no such effect. T cells isolated from PBMCs were incubated in the absence / presence of recombinant trimeric ARG2 (15 μg/ml) with a titration of the antibody.

IP Status & Publication(s)

Intellectual Property

Patent Number
PCT-EP2020-073579 (2020.08.21)

Patent Family
PCT, KR, US, EP, JP, CN

Publication(s)

- Austin, M., Burschowsky, D. et al. (2020). Structural and functional characterization of C0021158, a high-affinity monoclonal antibody that inhibits Arginase 2 function via a novel non-competitive mechanism of action. mAbs, 12(1).

- Chan, D. T. Y. et al. (2020). Extensive sequence and structural evolution of Arginase 2 inhibitory antibodies enabled by an unbiased approach to affinity maturation. Proceedings of the National Academy of Sciences of the United States of America, 117(29), 16949–16960.