24. Arginase-2 (Arg2) inhibitor

(CRUK)

Asset Overview

Product Type	Antibody
Diseases Area	Oncology
Indication	Tumors
Current Stage	HIT to Lead
Target	Arginase 2 (Arg2)
MoA	An ARG2-specific inhibitory monoclonal antibody would restore anti-tumour immunity in cancer patients and improve overall survival
Brief Description	• Developed first-in-class inhibitory antibodies that potently and selectively inhibit arginase 2 (Arg2), using phage display technology. • Antibodies are fully human with favorable pharmacokinetics. Published May 2020 in PNAS (https://doi.org/10.1073/pnas.1919565117) • Lead molecule C0021061 has been assessed in vivo and chosen for further development (https://doi.org/10.1080/19420862.2020.1801230) • Potential indications include oncology, COPD, cystic fibrosis and atherosclerosis
Intellectual Property	WO2021032891A1
Publication	• Extensive sequence and structural evolution of Arginase 2 inhibitory antibodies enabled by an unbiased approach to affinity maturation. PNAS, (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, (2020)
Inventors	Alexandra ADDYMAN, Mark Austin, Michelle BARNARD, Vincenzo Cerundolo, Denice CHAN, Agata DIAMANDAKIS, Sebastian Fiedler, Maria Groves, Stuart HAYNES, Sarah HOLT, Lesley JENKINSON, Stephanie KESWICK, Fiona Mclaughlin, Pooja Sharma, Yoko Shibata, Louise SLATER, Jessica WHITEHOUSE, Mark D. Carr, Daniel BURSCHOWSKY, Chitra SEEWOORUTHUN

Highlights

- C0021061 shows strong and specific binding to human ARG2 and inhibits enzymatic activity
  - C0021061 inhibited the activity of THP-1 lysate derived human trimeric ARG2, with an IC50 of approximately 3 nM.
- 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.
- C0021061 is specific for human ARG2
  - Enzyme inhibition assay showing the inhibition activity of C0021061 against human (hu) or murine (mu) ARG2. NHLA and R347 were included as positive and negative controls respectively.

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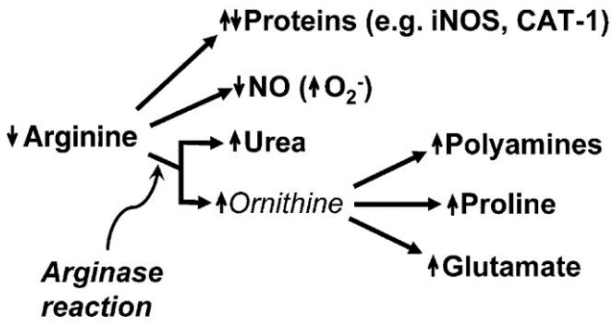
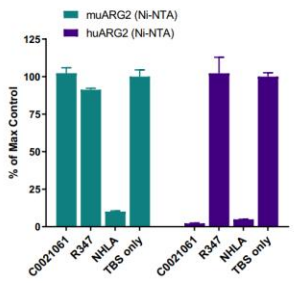
Key Data

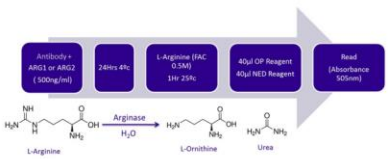
C0021061 – MECHANISM OF ACTION

- Extracellular arginase-2 is upregulated in various cancers causing reduced extracellular arginine concentration
- A reduced extracellular arginine concentration can cause reduced T-cell mediated anti tumour responses

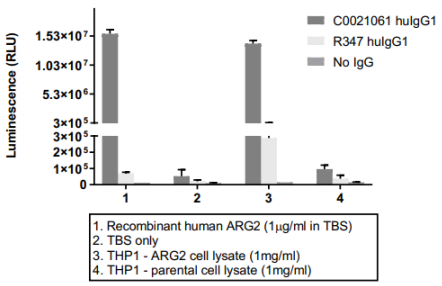


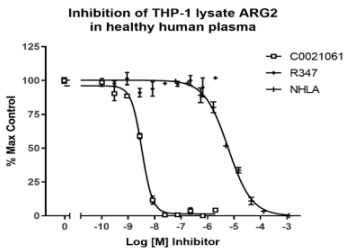
C0021061 shows strong and specific binding to human ARG2 and inhibits enzymatic activity

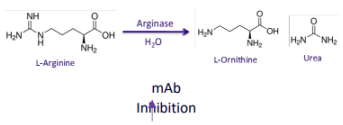




Enzyme inhibition assay showing the inhibition activity of C0021061 against human (hu) or murine (mu) ARG2. NHLA and R347 were included as positive and negative controls respectively.







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