BYON422 is a pan-allelic blocking SIRPα antibody that potentiates killing of antibody-opsonized tumor cells and lacks binding to T cells

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BACKGROUND

A broad panel of tumor-targeting antibodies provides standard of care in clinical practice. For most antibodies immunological effectors, including antibody-dependent cellular cytotoxicity (ADCC) and antibody-dependent cellular phagocytosis (ADCP), critically contribute to their efficacy. In preclinical models, the CD47-SIRPα axis has been readily established as an immune checkpoint that inhibits myeloid-derived ADC and ADCP, and therefore limits efficacy of anti-tumor antibodies. Different CD47-targeting molecules are currently in clinical development. However, the ubiquitously expressed CD47 not only binds macrophages from representative donors with different SIRP1 and SIRPα variants that are present in the human population, or they also block the related SIRPβ. Since SIRPβ is pivotal for optimal T cell responses, SIRPγ inhibition might curtail durable anti-tumor immunity. We therefore set out to develop a novel and unique SIRPα-blocking antibody, BYON4228, and report its preclinical characterization.

IN VITRO BINDING

BYON4228 is a potent pan-allelic SIRPα binder

IN VITRO FUNCTIONAL ACTIVITIES

BYON4228 induces ADCP and ADCD enhancement is Fc-tail independent

REFERENCES/ OTHER

2. Sen et al. (2008) JHE 11:1364
4. Kashiwagi et al. (2013) JBC 289:10024
5. Igbal. patent application WO 2020/068752 A1
7. Hatherley et al. (2014) JBC 289:10024

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BYON4228 lacks binding to T cell-expressed SIRPs

BYON4228 and CD47 footprints projected on SIRPs

BYON4228 lacks binding to T cell-expressed SIRPs

BYON4228 blocks CD47-induced SIRPα signaling

CONCLUSIONS

• Pan-allelic: BYON4228 recognizes all allelic variants SIRPα and SIRPβ
• No binding to T cell-expressed SIRPα: leaving T cell activation and migration unimpeded
• Blocking of the CD47-SIRPα axis: BYON4228’s epitope overlaps with the CD47-binding site
• Enhancement of immune cell effector functions: induced by therapeutic anti-tumor antibodies
• Broad potential clinical applicability: cellular effector functions enhancement of all tested therapeutic antibodies, incl. trastuzumab, rituximab, daratumumab and cetuximab
• Clinical studies: planned to start in 2022