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Discovery and Characterization of JADE101, an Ultra-High Affinity, Half-Life Extended Anti-APRIL Monoclonal Antibody for the Treatment of IgAN

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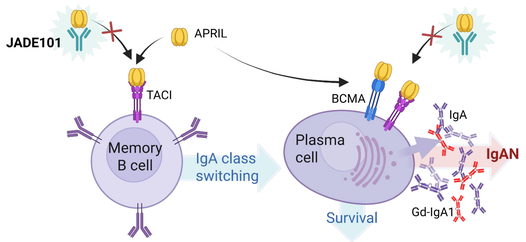
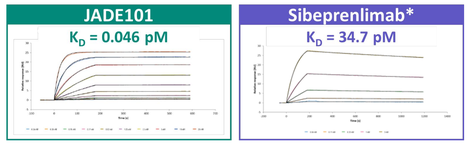
BACKGROUND

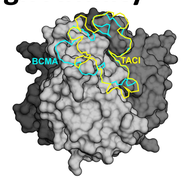
- A proliferation-inducing ligand (APRIL) plays a critical role in driving the production of pathogenic Gd-IgA1 in IgAN.
- JADE101 is a novel, fully human, neutralizing monoclonal IgG1 antibody against APRIL, specifically designed to extend half-life.



JADE101 Binds to APRIL with High Affinity

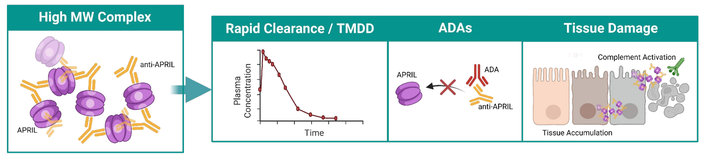


SPR binding of JADE101 or sibeprenlimab* to recombinant human APRIL



JADE101 binds a novel epitope with important functional implications

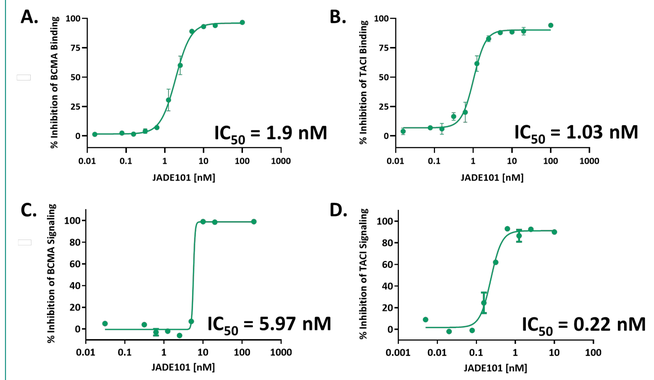
JADE101 Avoids High MW Complex Formation



- High MW complex formation can occur with mAbs binding trimeric proteins, such as APRIL.
- Avoiding high MW complexes potentially mitigates risks of immunogenicity and TMDD.

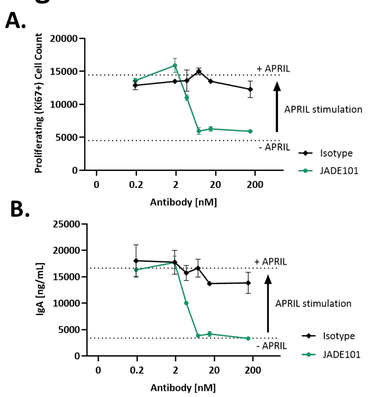
MW = molecular weight, TMDD = target mediated drug disposition, ADA = anti-drug antibodies

JADE101 Blocks Binding Of APRIL To BCMA and TACI, Inhibiting APRIL-Mediated Signaling



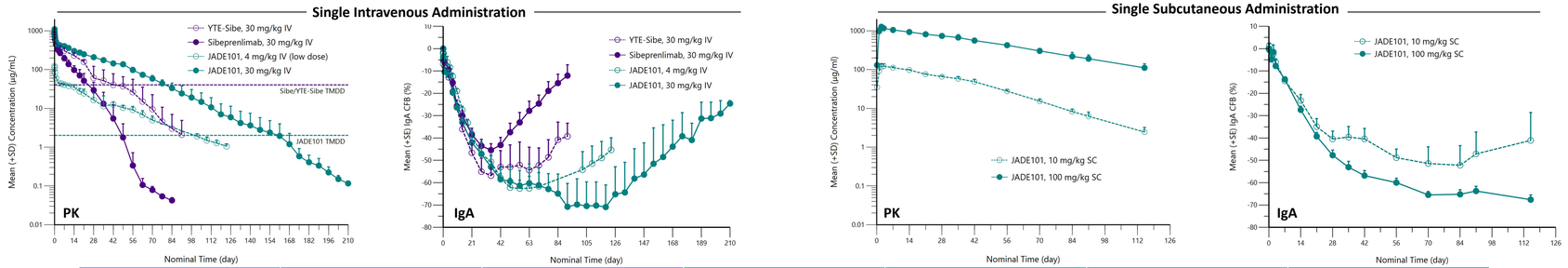
BCMA (A) and TACI (B) binding to APRIL was assessed using competitive ELISA. Inhibition of receptor signaling was assessed by stimulating NFκB luciferase reporter cells expressing BCMA (C) or TACI (D) with recombinant APRIL in the presence of JADE101.

JADE101 Inhibits Human Plasma Cell Proliferation and IgA Production *In Vitro*



B cells from healthy human donors were cultured with CpG-ODN, IL-15 and transferrin +/- APRIL for 7 days. Proliferating cells were identified by Ki67 expression using flow cytometry (A). IgA in supernatant was measured by ELISA (B).

JADE101 Exhibits an Extended Half-Life in NHP, Mitigates TMDD and Results in Deep and Prolonged IgA Reductions



Parameter (units)	Sibeprenlimab* (30 mg/kg IV)	YTE-Sibe* (30 mg/kg IV)	JADE101 (4 mg/kg IV)	JADE101 (30 mg/kg IV)	JADE101 (10 mg/kg SC)	JADE101 (100 mg/kg SC)
$t_{1/2}$ (day)	7.24 (27.9)	15.7 (23.4)	21.4 (6.59)	26.9 (5.88)	26.6 (19.6)	32.7 (12.9)
CL or CL/F (mL/day)	23.5 (30.4)	11.3 (11.7)	9.28 (13.5)	5.98 (9.52)	7.71 (28.8)	5.81 (5.35)
V_z or V_z/F (mL)	245 (15.6)	256 (20.2)	287 (6.91)	232 (6.98)	296 (33.2)	274 (18.3)
F_{abs} (%)	NC	NC	NC	NC	78.8 (58.8-106)	105 (78.0-140)

*Sibeprenlimab generated from publicly available sequence. YTE-Sibe was engineered on the IgG1 framework. PK parameters presented as geometric mean (CV%) with the exception of F_{abs} where geometric least squares mean ratios (95% CI). Confirmed ADA+ samples excluded.

CONCLUSIONS

- JADE101 binds APRIL with high affinity and potently inhibits APRIL-mediated signaling through BCMA and TACI reducing plasma cell proliferation and IgA production *in vitro.*
- JADE101 exhibits an extended pharmacokinetic half-life, significantly attenuates the impact of TMDD, and mediates deep, sustained IgA reductions in NHP.
- JADE101 is a potentially disease-modifying treatment for IgAN with the goal of providing a convenient, infrequent dosing schedule to reduce patient burden.

QUESTIONS? EMAIL: INFO@JADEBIOSCIENCES.COM