BUDOPRUTUG FOR MINIMAL CHANGE DISEASE (MCD): A CASE STUDY OF DURABLE RESPONSE AND POTENTIAL DISEASE MODIFICATION VIA CD19+ B-CELL DEPLETION

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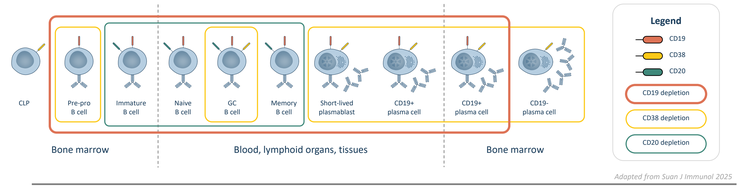
INTRODUCTION

MINIMAL CHANGE DISEASE (MCD)

- MCD, an immune-mediated podocytopathy, is an important cause of primary nephrotic syndrome.
- Complications of MCD arise from glomerular damage and extensive proteinuria[1] and can include debilitating edema, thromboembolic disease, hypovolemia, infections, hyperlipidemia or acute kidney injury.[2]
- In ~50% of adults, treatment is associated with frequent relapses and/or steroid-dependent disease[3]; primary morbidity is often related to treatment.[4]

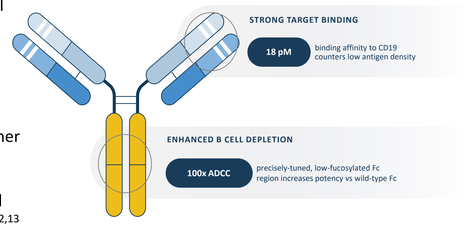
RATIONALE FOR TARGETING CD19 IN MCD

- Increasing evidence suggests that MCD is an autoimmune disease driven by pathogenic B cells that produce autoantibodies.
- Up to 70% of patients with active MCD have autoantibodies to nephrin, a key component of the glomerular slit diaphragm,[5-7] and the remaining patients are likely to have other circulating immune factors.[8]
- Because autoantibodies are produced by pathogenic B cells, there is a clear rationale for investigating steroid-sparing, B-cell-targeted agents in patients with MCD.
- Rituximab, a CD20 antibody, has demonstrated clinical benefit in MCD patients,[2,9,10] supporting the utility of B-cell depleting agents in patients with MCD.
- CD19 targeting has the potential to provide broader B-cell depletion compared to CD20 targeting, since CD19 is expressed from the early pro-B stage through maturation and differentiation to plasmablasts and certain plasma cells, including autoantibody-producing cells.[11]



BUDOPRUTUG: Highly Potent CD19 mAb Engineered for Enhanced B-Cell Depletion

- Budoprutug (TNT119) is an investigational anti-CD19 mAb bioengineered with picomolar binding affinity for CD19 and a low-fucosylated Fc region for enhanced ADCC.
- In an early clinical study in patients with primary membranous nephropathy, another autoantibody-related glomerular disease, budoprutug demonstrated rapid and sustained B-cell depletion, immunological remission, and resolution of proteinuria.[12,13]



CASE DESCRIPTION

PRESENTATION

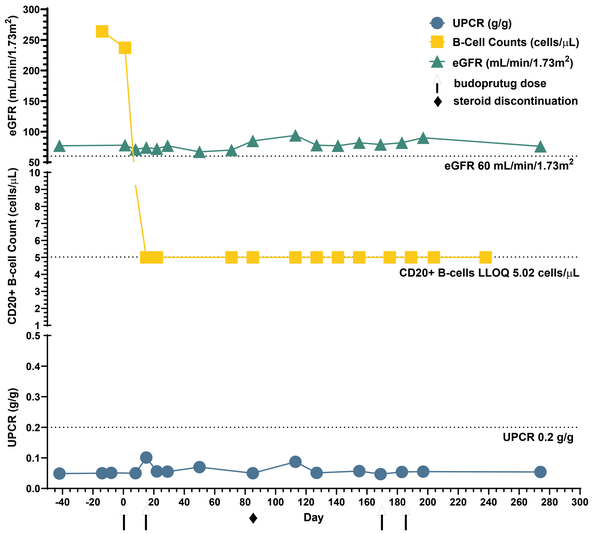
- 56-year-old white female with MCD diagnosed in 2006 upon kidney biopsy.
- For over 16 years, the patient's disease course was characterized by frequent relapses following steroid therapy-induced remission.
- In 2022, the patient was enrolled in study NCT05441826, a Phase 2 trial evaluating the efficacy and safety of budoprutug in adults with MCD or FSGS.*
- Most recent treatment prior to enrollment was a 6-month steroid course, with remission that lasted ~1 month after steroid discontinuation.
- At enrollment, the patient was in complete remission while on a prednisone taper (baseline dose 7.5 mg/day): no edema, UPCR 0.05 g/g, eGFR 78 mL/min/1.73 m^2, serum albumin 4.5 g/dL, and peripheral CD20$^+$ B-cell count 238 cells/µL.

TREATMENT

- 4 doses of IV budoprutug: 100 mg on Days 1 and 15, and 200 mg on Days 169 and 183
- Maintained on protocolized prednisone taper that ended on Day 85 of the study

*NCT05441826 was terminated on May 3, 2023 by the original Sponsor (Valenza Bio, then ACELYRIN, Inc.) for business reasons. Primary objectives were efficacy (UPCR <0.5 g/g), safety and tolerability. Three patients were screened and one was enrolled. For more information, please scan the QR code below to access the clinicaltrials.gov entry. Following the study termination, the patient continued to be followed in her HCP's office.

OUTCOMES



Scan QR code to download the poster

SAFETY:

- The patient had 1 TEAE (unrelated to study drug) of right axillary nodule on Day 155, which resolved on Day 189 without intervention.
- There were no infusion-related reactions, no events of hypogammaglobulinemia, and no anti-drug antibodies were detected.

B-CELL DEPLETION:

- CD20$^+$ B-cell counts decreased to <LLOQ (5.02 cells/µL) on Day 15 (September 23, 2022) and stayed <LLOQ (5.02 cells/µL) for the duration of the study (Day 274).
  - B-cell reconstitution (reappearance of detectable circulating CD20$^+$ B cells) was documented 24 months after Day 1, in September of 2024.

EFFICACY:

- UPCR ranged from 0.04-0.10 g/g (normal range <0.2 g/g); serum albumin also remained in the normal range with values from 4.4-4.6 g/dL during the observation period.
- eGFR remained stable and ranged from 67-94 mL/min/1.73 m^2.
- No edema was observed.

SUMMARY:

- **The patient remained asymptomatic, in complete remission, and steroid-free, with UPCR <0.2 g/g and eGFR >60 mL/min/1.73 m^2 until a relapse occurred three years after the first dose of budoprutug and one year after B-cell reconstitution.**

Figure. Key parameters over time: UPCR (g/g), CD20+ B-cell count (cells/µL), eGFR (mL/min/1.73 m^2); diamond shows steroid discontinuation on Day 85; horizontal dashed lines show: ULN for UPCR (0.2 g/g), LLOQ for CD20+ B-cells (5.02 cells/µL); eGFR 60 mL/min/1.73 m^2, LL of mild to moderate kidney function

CONCLUSIONS

- This is the **first use of budoprutug in a patient with MCD**
- Four doses of budoprutug were **well tolerated in this patient, who had frequently relapsing MCD**
- After receiving budoprutug, the patient experienced a **three-year steroid-free remission**
- The patient remained in remission **one year after B-cell reconstitution, suggesting long-term disease modification**
- The results in this patient suggest **targeting CD19** may be an effective strategy for treating complicated MCD and **warrants additional study**

ADCC antibody-dependent cellular cytotoxicity; **eGFR** estimated glomerular filtration rate; **FSGS** focal segmental glomerulosclerosis; **HCP** healthcare provider; **LL** lower limit; **LLOQ** lower limit of quantification; **mAb** monoclonal antibody; **MCD** minimal change disease; **TEAE** treatment-emergent adverse event' **ULN** upper limit of normal; **UPCR** urine protein-to-creatinine ratio.

REFERENCES

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ADDITIONAL INFORMATION

NCT05441826
https://clinicaltrials.gov/study/NCT05441826

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