Apellis

Status ongoing: stop inclusion

S-nummer: S65698 Phase 3 study
Principal Investigator: prof. dr. Kathleen Claes

Title: A phase 3, randomized, placebo-controlled, double-blinded, multicenter study to evaluate the efficacy and safety of pegcetacoplan in patients with c3 glomerulopathy or immune-complex membranoproliferative glomerulonephritis.

Purpose and rationale: To assess the efficacy of twice-weekly subcutaneous doses of pegcetacoplan compared with that of placebo in patients with primary C3 glomerulopathy (C3G) or immune-complex membranoproliferative glomerulonephritis (IC-MPGN) on the basis of a reduction in proteinuria.

Primary endpoint: The log-transformed ratio of uPCR at week 26 compared to baseline.

Medication/treatment: Pegcetacoplan (inhibitor of C3 and its fragment, C3b). All adult participants (regardless of weight), and adolescent participants who weigh at least 50 kg, will receive 20-mL (or 1080 mg) SC infusions of pegcetacoplan or matching volumes of placebo twice weekly. Followed by a switch to an open label period after 26 weeks, meaning that all participants will be treated with pegcetacoplan twice weekly.

Duration of study: Approximately 70 week, consisting of 4 parts: Part 1: 10-week screening period; Part 2: 26-week randomized controlled period; Part 3: 26-week open-label period; Part 4: 8-week follow-up period. In total consisting of 19 visits.

Key inclusion criteria:
- Male or female subject ≥18 years old
- Diagnosis of primary C3G or IC-MPGN
- Evidence of active renal disease (At least 2+ C3c staining on the baseline renal biopsy)
- No more than 50% global glomerulosclerosis or interstitial fibrosis on the baseline biopsy
- ≥1 g/day of proteinuria (24-hour urine) and uPCR ≥1000 mg/g (first morning void)
- eGFR ≥30 mL/min/1.73 m²
- Stable regimen for C3G/IC-MPGN treatment:
    a. ACE inhibitor, ARB and/or SGLT2i stable and optimized for at least 12 weeks
    b. Stable doses of other medications that can affect proteinuria for at least 12 weeks

Key exclusion criteria:
- Improving renal disease in the 8 weeks prior to screening (>30% increase in eGFR or >50% decrease in proteinuria)
- C3G/IC-MPGN secondary to another condition
- Diagnosis of HIV, hepatitis B, or hepatitis C infection or a severe infection requiring IV antibiotic therapy within 14 days prior to first dose
- Body weight >100 kg
- History of meningococcal disease
- Absolute neutrophil count <1000 cells/mm³
- Use of rituximab, belimumab, or any approved or investigational anticomplement therapy