Pr Noémie Jourde-Chiche – Aix-Marseille Univ & APHM Nephrology

Conflict of interest statement

- ✓ NOVARTIS: conference & expertise & congress
- ✓ VIFOR: conference & expertise & congress
- ✓ GSK: conference & expertise
- ✓ ASTRA-ZENECA: teaching & expertise
- ✓ ROCHE: expertise & research grant pending

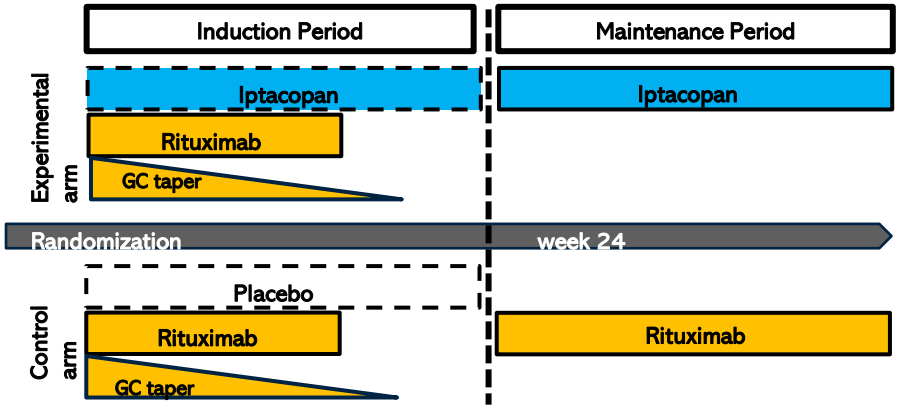
- ✓ Groupe Français d'Etude des Vascularites (GFEV)
- ✓ Groupe Coopératif sur le Lupus Rénal (GCLR)

Iptacopan – Oral Complement Factor B inhibitor

- ✓ **Paroxysmal nocturnal hemoglobinuria:** 2024 EMA approval
- ✓ **C3 glomerulonephritis: 2025 EMA approval native & KTR** – Phase 3 APPEAR positive
- ❑ Active lupus nephritis: in development
- ❑ Active ANCA-associated vasculitis: in development

Iptacopan vs Placebo in ANCA-Associated Vasculitis – Phase 2 – Novartis

- Objective: To evaluate the efficacy and safety of iptacopan in combination with RTX induction therapy for the treatment of newly diagnosed or relapsed patients with active GPA or MPA
- Number of patients expected: 78 adult patients (inclusions end in August 2026)
- Design: Multicenter, randomized, controlled Phase 2 study; induction period double blinded, maintenance period open label
- Primary endpoint: Sustained remission through Week 48
  - ✓ complete remission at Week 24
  - ✓ without major relapse up to Week 48



https://clinicaltrials.gov/ct2/show/NCT06388941

Iptacopan vs Placebo in ANCA-Associated Vasculitis – Phase 2 – Novartis

Inclusion

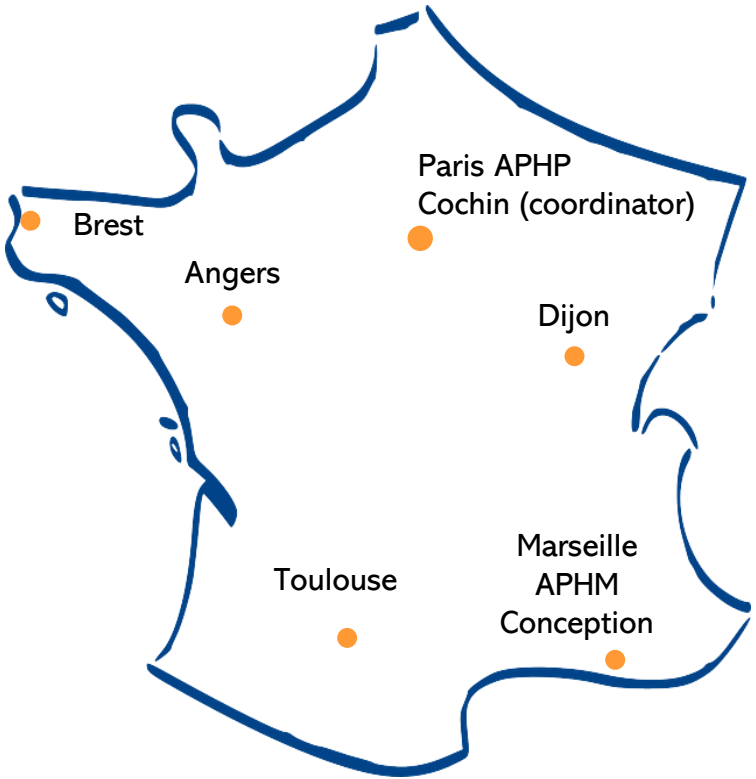
- ✓ Newly diagnosed or relapsed GPA and MPA
- ✓ Requiring treatment with RTX and corticosteroids as per investigator's judgement
- ✓ BVAS with ≥1 major item, or ≥3 minor items, or ≥2 renal items at Screening
- ✓ Positive anti-proteinase 3 (PR3) or anti-myeloperoxidase (MPO) antibodies at Screening or with history of documented evidence of a positive antibody test

Exclusion

X Other systemic disease which constitutes the primary illness
X Alveolar hemorrhage requiring invasive pulmonary ventilation support at Screening.
X Severe kidney disease defined as eGFR <15 mL/min/1.73m2, or requiring renal replacement therapy, or kidney transplant recipient
X Plasma exchange/apheresis within 12 weeks prior to Screening.

https://clinicaltrials.gov/ct2/show/NCT06388941

Iptacopan vs Placebo in ANCA-Associated Vasculitis – Phase 2 – Novartis



France : 10 patients randomized
World : 31 patients randomized

https://clinicaltrials.gov/ct2/show/NCT06388941

Iptacopan vs Placebo in Active Lupus Nephritis – Phase 2 – Novartis

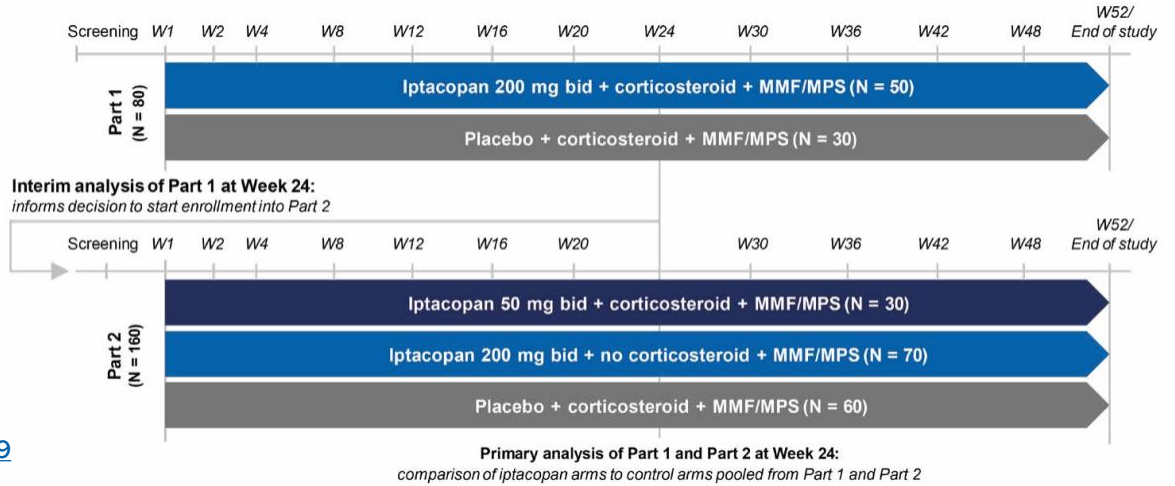
✓ Objective: To evaluate the efficacy and safety of iptacopan versus placebo, in combination with standard treatment (SoC) with or without corticosteroids, in patients with active lupus nephritis (III or IV, +/- V).

✓ Number of patients expected: 240 adult patients

✓ Design: Adaptive, Randomized, Double-blind, Dose Exploration, Parallel Group, Placebo Controlled, Multicenter Phase 2 Trial

Part 1 : proof of concept (N = 80)

Part 2 : exploratory (N = 160)



https://clinicaltrials.gov/ct2/show/NCT05268289

Iptacopan vs Placebo in Active Lupus Nephritis – Phase 2 – Novartis

Inclusion

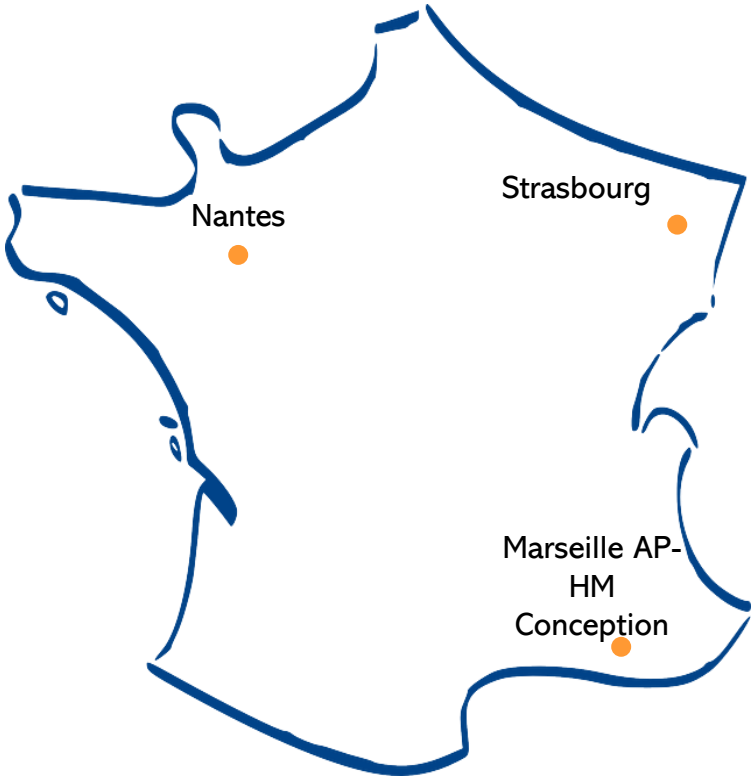
- ✓ Unequivocally positive ANA and/or anti-dsDNA upon selection
- ✓ Class III/IV +/- V active lupus nephritis (biopsy < 3 months)
- ✓ Active renal disease at screening, requiring corticosteroids + MMF
- ✓ eGFR >= 30 ml/min/1.73 m2
- ✓ Vaccinations : Neisseria meningitidis, Streptococcus pneumoniae and Haemophilus influenzae
- ✓ Supportive care :
  - ✓ antimalarials unless contraindicated
  - ✓ ACEi/ARB at the maximum daily dose approved locally or maximally tolerated dose
- ✓ First presentation or relapse of lupus nephritis

Exclusion

- ✗ RPGN (50% decrease in eGFR within 3 months prior to selection)
- ✗ IF/TA or glomerulosclerosis > 50%
- ✗ Induction by CYP or treatment with CNI =< 3 months prior to selection
- ✗ Corticosteroids >15 mg/day on average in the previous 4 weeks
- ✗ Corticosteroids > 30 mg/day on average in the previous week
- ✗ Corticosteroids > 5 mg/day for indication other than lupus
- ✗ Corticosteroids cumulative dose >1000 mg i.v. methylprednisolone in the 2 weeks prior to inclusion

https://clinicaltrials.gov/ct2/show/NCT05268289

Iptacopan vs Placebo in Active Lupus Nephritis – Phase 2 – Novartis



France : 2 patients randomized
World : 65 patients randomized

https://clinicaltrials.gov/ct2/show/NCT05624749