MAINtenance of remission with RITuximab versus azathioprine for patients with newly-diagnosed or relapsing Eosinophilic Granulomatosis with polyangiitis.

A prospective, randomized, controlled, double-blind study.

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These therapeutic strategy in EGPA has led to good remission and survival rates.

The probability of uncontrolled disease, without maintenance therapy, was similar in patients whatever the FFS score at inclusion and remains to be improved.

- **In EGPA BP FFS=0** (only GC without maintenance):
  - M28: vasculitis flares: 28.4%
  - M28: asthma/rhinosinus leading to ↑GC or other IS: 30.2%
  giving a total of 58% patients with uncontrolled disease at M28.

- **In EGPA MP FFS ≥ 1** (GC and 6 or 12 IV CYC without maintenance),
  - M28: vasculitis flares: 29.7%
  - M28: asthma/rhinosinus leading to ↑GC or other IS: 30.5%
  giving a total of 60% patients with uncontrolled disease at M28.

=> Without maintenance therapy, relapses remain a matter of concern and uncontrolled disease at M28 is observed in 60% of patients, leading to high cumulative morbidity and damage.

• (h): As with other AAV, EGPA patients would also benefit from maintenance to avoid relapses and allow GC tapering.

• Only one trial has yet evaluated medication (MEPO) for EGPA maintenance therapy.

=> Thus, it remains unmet needs to improve the long-term outcome and to evaluate maintenance regimen in controlled studies of EGPA patients.

Main Objective

To compare RTX versus AZA maintenance therapy:

- **on duration of remission**, defined as accrued duration in weeks where BVAS=0 and prednisone dose ≤7.5 mg/day,
- in patients with relapsing or newly-diagnosed EPGA
- receiving standard of care therapy including GC therapy reduction/withdrawal.
Secondary Objectives

To investigate RTX versus AZA maintenance therapy on:

• proportion of patients remaining in remission with a BVAS=0 and prednisone dose ≤7.5 mg/day at month 28
• number and severity of vasculitis relapses and asthma/rhino-sinusal exacerbations
• time to vasculitis relapses
• time to significant asthma/rhino-sinusal exacerbations
• survival, relapse-free survival
• corticosteroid sparing effect
• safety,
• damage,
• and quality of life.
The primary endpoint is the total duration of remission over the 28 month study period, i.e.

- the accrued number of weeks where a patient remains in remission with BVAS=0 and prednisone dose $\leq 7.5$ mg/day.
MAINRITSEG: Design

RTX (500 mg) maintenance + Placebo-AZA for 24 months

Placebo-RTX + AZA 2 mg/kg/day for 24 months

Primary endpoint

accrued number of weeks where a patient remains in remission with BVAS=0 and prednisone ≤7.5 mg/day
Patients receiving RTX or placebo-RTX infusion will receive premedication including 100 mg of MP, paracetamol and dexchlorphéniramine (Polaramine©).

In accordance with standard of care, in the absence of clinical manifestations, to obtain total GC therapy duration after disease onset/flare of ~ 12 months, both groups will receive the same predefined GC tapering regimen of 1 mg/day/month, until discontinuation.
MAINRITSEG: Inclusion criteria

- Diagnosis of EGPA (ACR and/or revised Chapel Hill and/or MIRRA)
- with newly-diagnosed disease or presenting with a vasculitis flare within the past year,
- within 30-360 days following vasculitis remission (BVAS=0) achieved with an induction regimen similar to the one used in the REOVAS trial: CS seuls ou avec RTX ou CYC IV (5-10g),
- with stable GC dose for 30 days or no more (≠ < 7.5mg/day),
- independently of ANCA status,
- after oral IS cessation if started at remission.
Les patients doivent être informés le plus tôt possible de cette étude évaluant le maintien de la rémission.

Les patients peuvent être inclus en dehors de REOVAS.

Les patients peuvent être inclus et randomisés dans MAINRITSEG à la visite de M12 de REOVAS :
- A la visite précédente = J270 de REOVAS, information
- à M12, visite finale de REOVAS, si le patient est en rémission avec corticoïdes stable depuis 1 mois
- après information et recueil consentement
- soit randomisation et traitement par IV immédiat
- soit nouveau RdV dans les 30 jours pour perfusion