27-MAR-2018

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MAINEPSAN

MAINTENANCE OF REMISSION USING EXTENDED ADMINISTRATION OF PREDNISONE IN SYSTEMIC ANCA-ASSOCIATED VASCULITIS

A PROSPECTIVE, MULTICENTRIC, RANDOMIZED, CONTROLLED, DOUBLE-BLIND TRIAL

Investigator: Pr LEGA Jean Christophe (HCL)

Scientific Investigator: Dr PUECHAL Xavier (AP-HP)

Groupe Français d'Etude des Vascularites

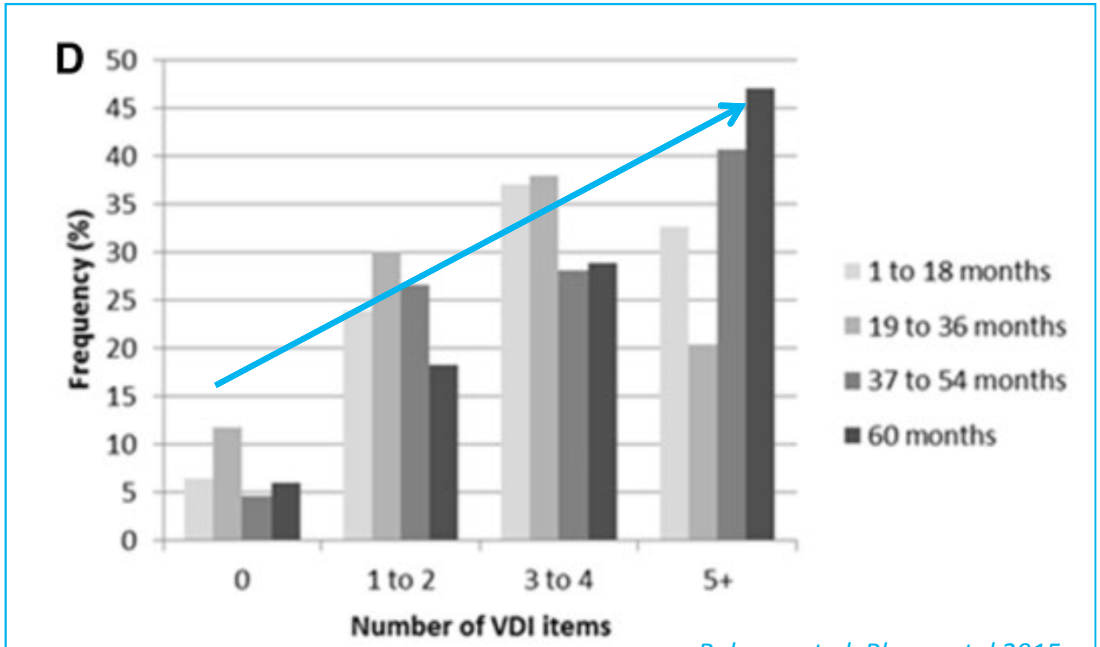
Corticosteroids in ANCA associated vasculitis

- **Discrepancies in corticosteroids use between USA and EU**
  - **USA**: withdrawal at 6-12 months post-flare
  - **France**: withdrawal at 12-18 months post-flare

Diabetes: 12%

Osteoporosis: 15%

Cataracte: 8%



Robson et al. Rheumatol 2015

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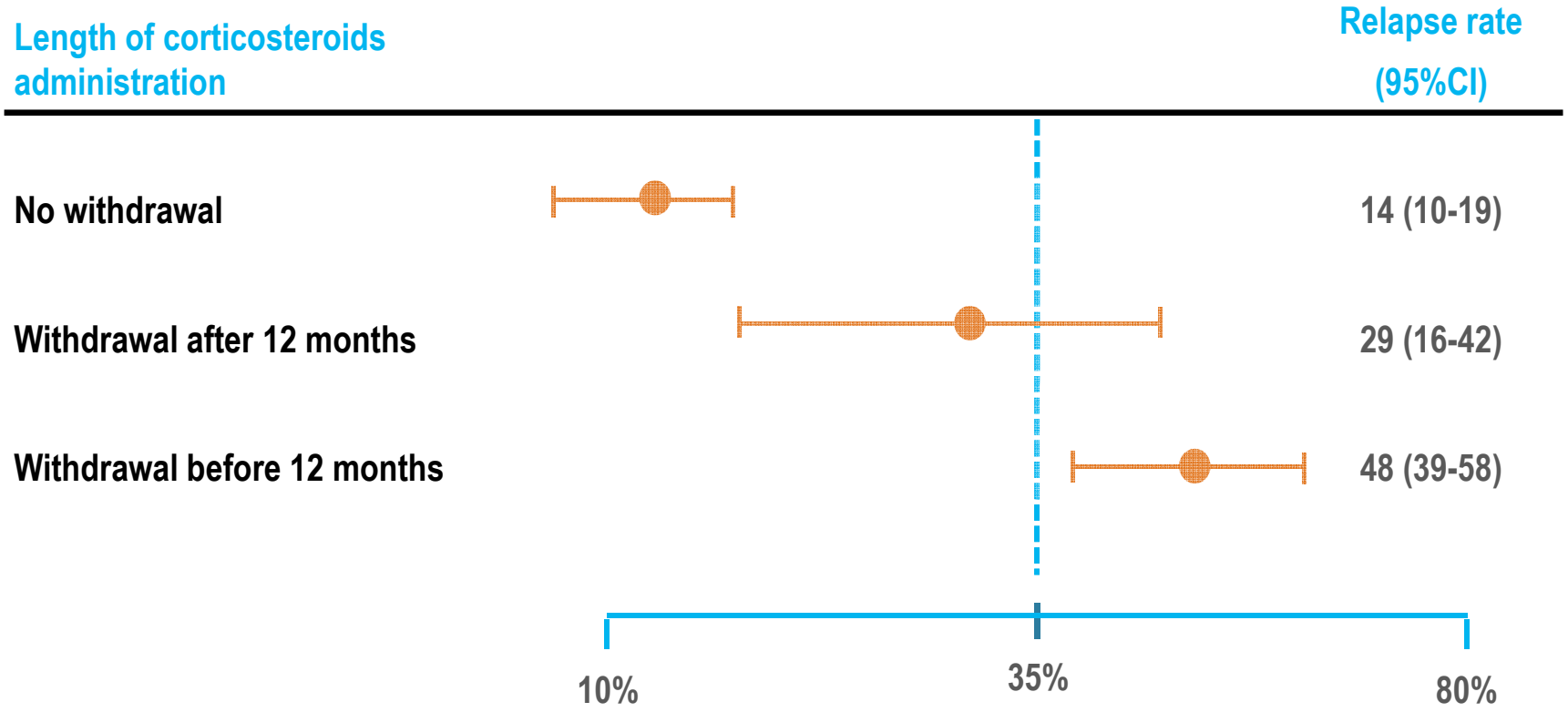


Walsh et al. Arthritis Care Research 2010

MAINEPSAN trial - Primary Objective

146 Subjects

Primary objective:

To compare **relapse-free survival** of patients continuing **low-dose prednisone treatment (5mg)** until **Week 52** (***Month 25 post-flare***) versus those who will have prednisone treatment cessation at **Week 4** (***Month 13 post-flare***) on **remission maintenance** with rituximab therapy, after achievement of remission of **GPA or MPA**, defined as in patients with GPA or MPA and who will all have received glucocorticoids for 12 months after diagnosis or last flare before inclusion.

Primary assessment criterion:

Survival of patients maintaining a **BVAS=0** at **Week 120** (***Month 42 post-flare***), with ITT analysis

MAINEPSAN trial - Inclusion Criteria

- Patients who has been informed about the study and has given his/her **written consent prior to participation in the study**,
- Patients with **newly-diagnosed or relapsing MPA or GPA** according to the ACR 1990 criteria and/or revised Chapel Hill Consensus Conference definition, independently of ANCA status,
- Patients aged of **18 years or older**,
- Patients **in remission (BVAS =0) for MPA or GPA** achieved with rituximab or cyclophosphamide or methotrexate,
- Patients who will all **have already received glucocorticoids for 12 months** after diagnosis or last flare before Day 1.
- Patients ha**ving received 500 mg pre-emptive low-dose rituximab maintenance infusions at remission achievement** (4 to 6 months after initiation of induction therapy), and 6 months after.
- Patients **receiving from 5 to 10 mg/day prednisone dose within 35 days before randomization**.

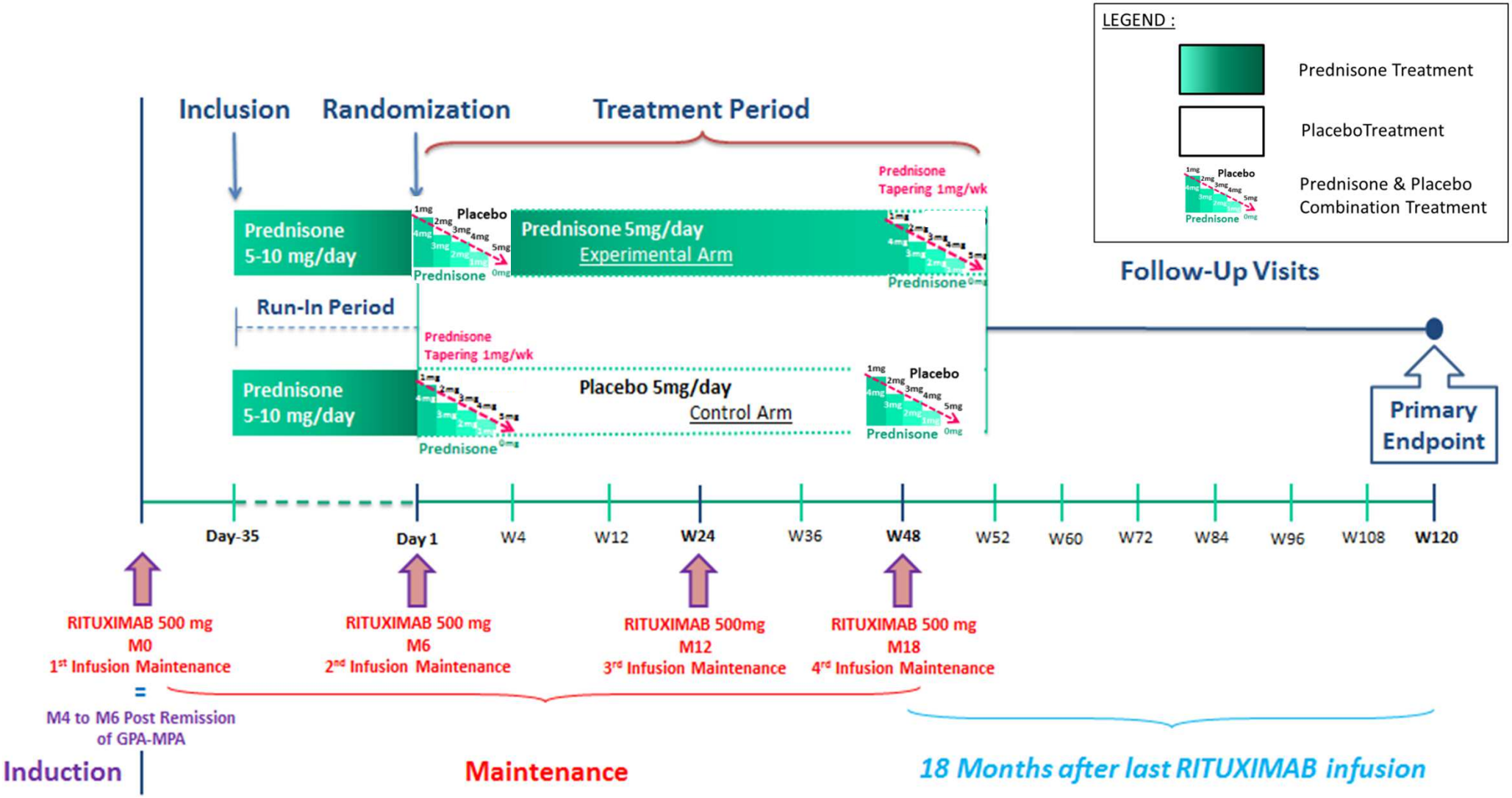
MAINEPSAN trial - Exclusion Criteria (1)

- Patients with **EGPA, or other vasculitides**, defined by the ACR criteria and/or the Chapel Hill Consensus Conference,
- Patients with vasculitis with **active disease defined as a BVAS>0**,
- Patients with **acute infections or chronic active infections** (including HIV, HBV or HCV),
- Patients with **active or recent cancer** (<5 years) or **myelodysplasia**, except basocellular carcinoma and low activity prostatic cancer controlled by hormonal treatment,
- **Pregnant women and lactation**: women of childbearing potential will have to follow an effective method of contraception for the duration of the study,
- Patients with **contraindication to rituximab use**,
- Patients with **other uncontrolled diseases**, including drug or alcohol abuse, severe psychiatric diseases, that could interfere with participation in the trial according to the protocol,

MAINEPSAN trial - Exclusion Criteria (2)

- Patients **included in other investigational therapeutic study** within the previous 3 months excepted for the PNEUMOVAS trial,
- Patients **suspected not to be observant** to the proposed treatment,
- Patients who have **white blood cell count ≤ 4000/mm^3,**
- Patients who have **platelet count ≤ 100 000/mm^3,**
- Patients who have **ALAT or ASAT level greater than 3 times the upper limit of normal**,
- Patients **unable to give written informed consent form** prior to study participation,
- Patients **under legal protection,**
- Patient **not affiliated to a social security scheme** or other social protection scheme.

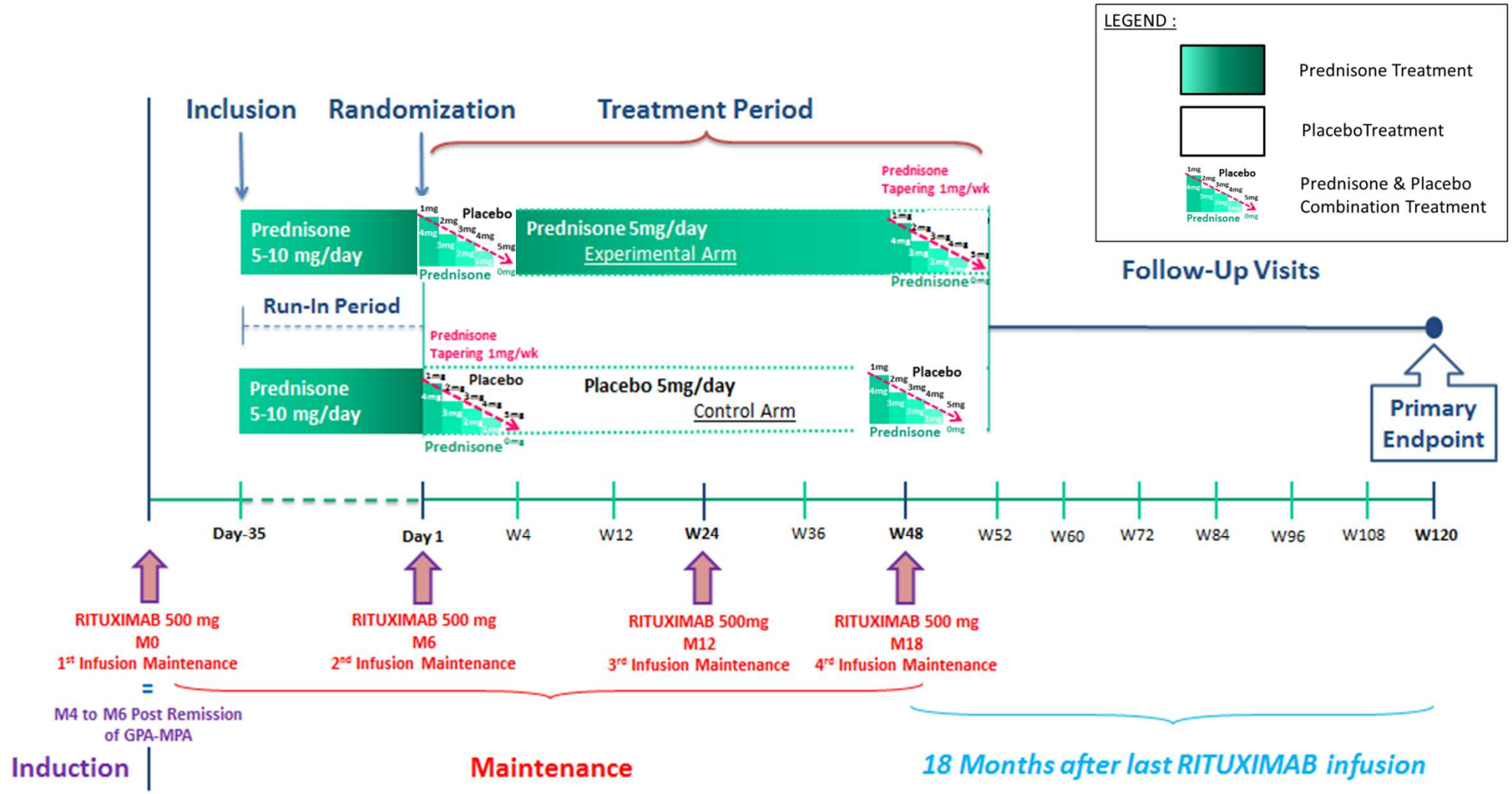
MAINEPSAN trial – Study Design



	M0 Semaine 1	M0 Semaine 2	M0 Semaine 3	M0 Semaine 4	M1 à M12	M12 Semaine 1	M12 Semaine 2	M12 Semaine 3	M12 Semaine 4
Experimental Arm	5 mg actif + placebo 4 mg	5 mg actif + placebo 3 mg	5 mg actif + placebo 2 mg	5 mg actif + placebo 1 mg	5 mg actif	4 mg actif	3 mg actif	2 mg actif	1 mg actif
	32 gélules actif 5 mg + 1 Kit « décroissance » de 4 piluliers				X 11 piluliers de 32 gélules Actif 5 mg	1 Kit « décroissance » de 4 piluliers			
	7 gélules Placebo 4 mg	7 gélules Placebo 3 mg	7 gélules Placebo 2 mg	7 gélules Placebo 1 mg		7 gélules Actif 4 mg	7 gélules Actif 3 mg	7 gélules Actif 2 mg	7 gélules Actif 1 mg

	M0 Semaine 1	M0 Semaine 2	M0 Semaine 3	M0 Semaine 4	M1 à M12	M12 Semaine 1	M12 Semaine 2	M12 Semaine 3	M12 Semaine 4
Control Arm	Placebo 5 mg + 4 mg actif	Placebo 5 mg + 3 mg actif	Placebo 5 mg + 2 mg actif	Placebo 5 mg + 1 mg actif	Placebo 5 mg	Placebo 4 mg	Placebo 3 mg	Placebo 2 mg	Placebo 1 mg
	32 gélules placebo 5 mg + 1 Kit « décroissance » de 4 piluliers				X 11 piluliers de 32 gélules placebo 5 mg	1 Kit « décroissance » de 4 piluliers			
	7 gélules actif 4 mg	7 gélules actif 3 mg	7 gélules actif 2 mg	7 gélules actif 1 mg		7 gélules Placebo 4 mg	7 gélules Placebo 3 mg	7 gélules Placebo 2 mg	7 gélules Placebo 1 mg

MAINEPSAN trial – Study Design



STRATIFICATION

- Newly diagnosed vs. relapsing vasculitis
- Anti-PR3 status (positive vs. negative) at diagnosis for newly-diagnosed vasculitis or at last relapse
- ELISA ANCA status (positive vs. negative) at inclusion (M12 after initiation of treatment)
- Methotrexate versus Rituximab or Cyclophosphamide at the diagnosis or relapse of vasculitis

MAINEPSAN trial - Calculation of Sample Size

- **146 patients**

- In regards of the MAINEPSAN results, the primary hypothesis of the trial is a relative decrease of 60% of the relapse rate at 24 months post-flare, i.e. 14% vs 34%

- Based on this hypothesis, using a bilateral test, we calculated that 140 patients would be required for the study to have 80% power to detect an absolute 20% reduction with a two-sided alpha level

Etude MAINEPSAN

Répartition géographique des 38 centres

27-MAR-2018

MAINEPSAN ACKNOWLEDGMENTS

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THANKS FOR YOUR ATTENTION

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