

# The NEW ENGLAND JOURNAL of MEDICINE

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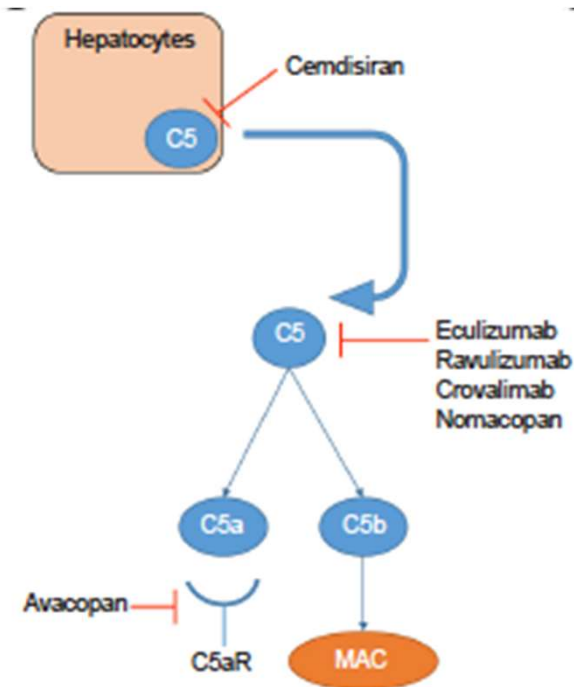
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## Avacopan for the Treatment of ANCA-Associated Vasculitis

Could avacopan replace glucocorticosteroids tapering regimen in AAV?

Avacopan : antagoniste du récepteur C5a



# ADVOCATE

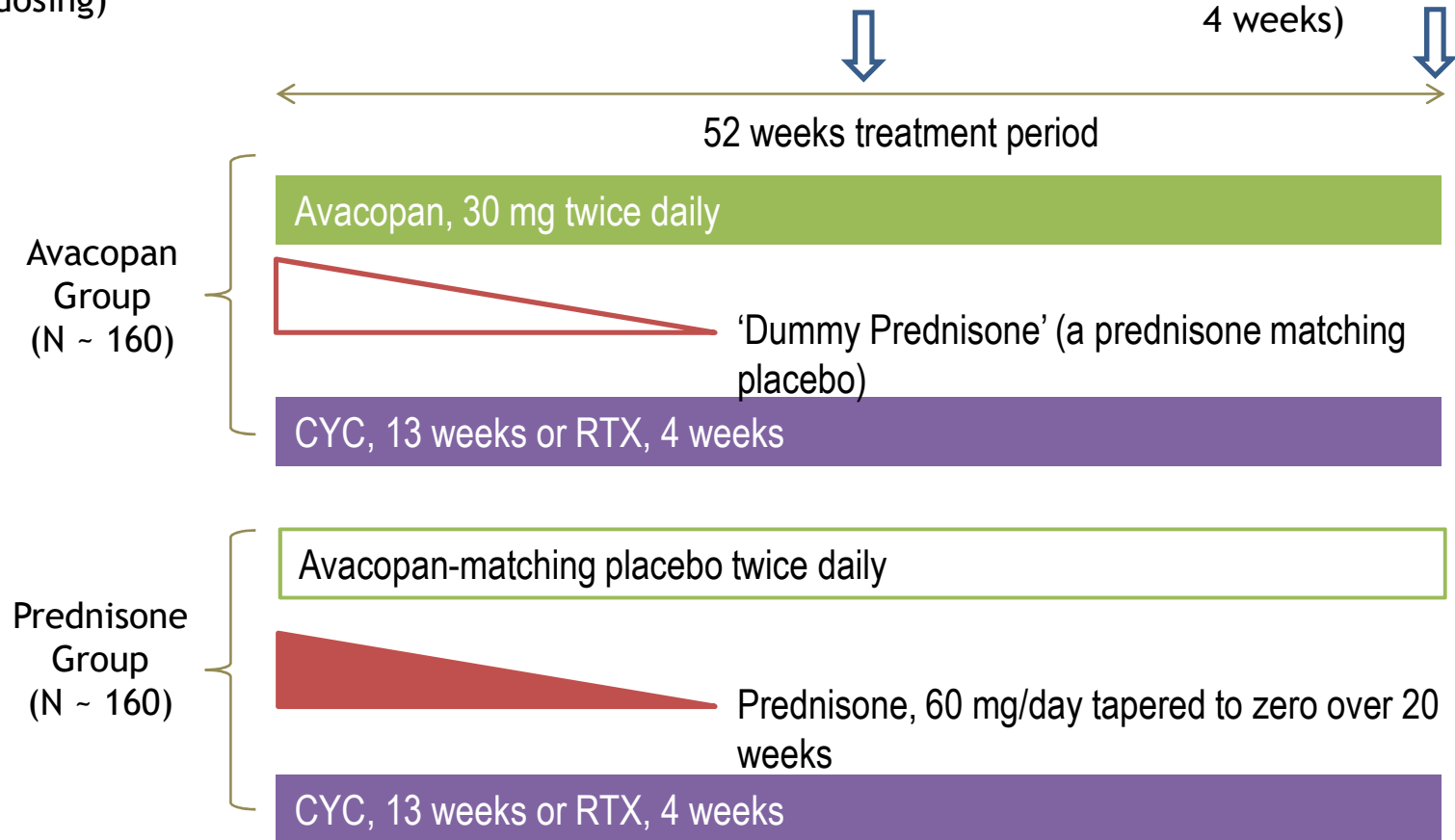
Randomized, double-blind, double-dummy, active-controlled trial  
in patients with new or relapsing AAV

Essai de non infériorité  
d'avacopan vs. prednisone à S26

Two primary endpoints\*  
(Analyzed after 52 week  
dosing)

Remission at 26 weeks  
(Based on BVAS and off GC 4 weeks)

Sustained remission at 52  
weeks  
(Based on BVAS and off GC  
4 weeks)



## Non-éligible

- DFG < 15
- MP > 3 gr
- prednisone > 10 mg/j x 6 semaines

## Traitement

Avacopan 30 x 2/d ou Pbo x 52 semaines

vs.

Prednisone (60 mg) avec arrêt à S21 ou Pbo

+

CYC IV 15 mg/kg (max 1,2 g)

J0, S2, S4, S7, S10, S13 puis AZA

ou

CYC PO 2 mg/kg

ou

RITUX 375 mg/m<sup>2</sup> x 4 puis stop

## Corticothérapie en sus du protocole

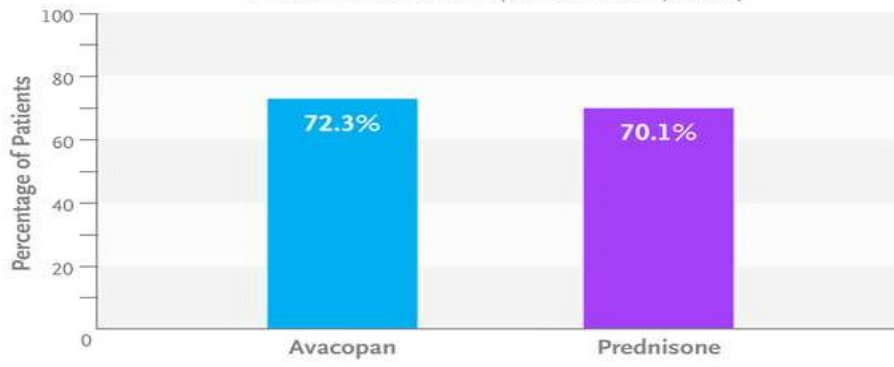
- dans les 4 premières semaines, pour contrôle initial de la maladie
- ou si résistance ou rechute

## ADVOCATE : caractéristiques à l'inclusion

	<b>Prednisone Group (N=165)</b>	<b>Avacopan Group (N=166)</b>	<b>Total (N=331)</b>
Age (years), mean $\pm$ SD	60.6 $\pm$ 14.46	61.2 $\pm$ 14.56	60.9 $\pm$ 14.49
Male/Female	53.9% / 46.1%	59.0% / 41.0%	56.5% / 43.5%
New/Relapsing	69.5% / 30.5%	69.3% / 30.7%	69.4% / 30.6%
ANCA, PR3+/MPO+	42.7% / 57.3%	43.4% / 56.6%	43.0% / 57.0%
Rituximab/Cyclophosphamide	65.2% / 34.8%	64.5% / 35.5%	64.8% / 35.2%
GPA/MPA	54.9% / 45.1%	54.8% / 45.2%	54.8% / 45.2%
BVAS, mean $\pm$ SD	16.2 $\pm$ 5.69	16.3 $\pm$ 5.87	16.2 $\pm$ 5.77
eGFR, mean SD	52.9 $\pm$ 32.67	50.7 $\pm$ 30.96	51.8 $\pm$ 31.80

### Clinical Remission at Week 26

Estimated common difference, 3.4 percentage points  
95% CI, -6.0 to 12.8  
P<0.001 for noninferiority; P=0.24 for superiority



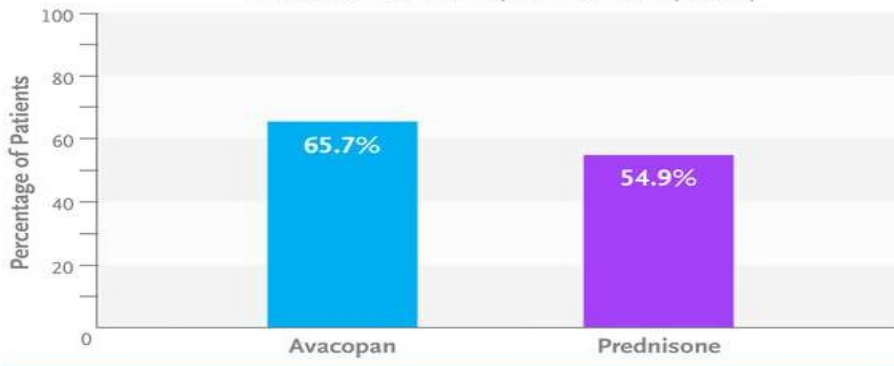
S26 : rémission clinique

- BVAS = 0

- Pas de prednisone depuis S22

### Sustained Remission at Week 52

Estimated common difference, 12.5 percentage points  
95% CI, 2.6 to 22.3  
P<0.001 for noninferiority; P=0.007 for superiority

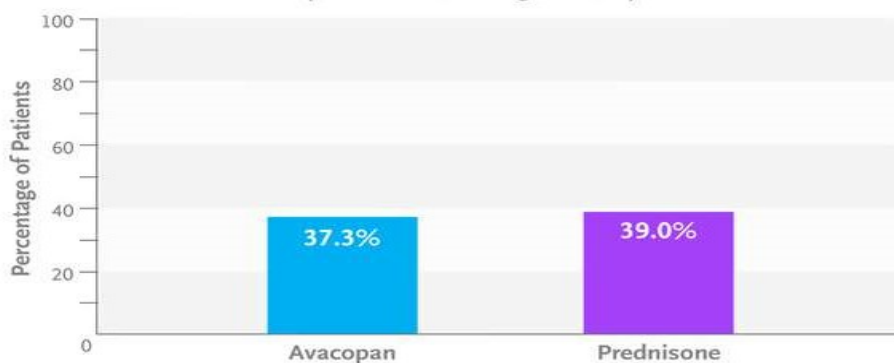


S52 : rémission prolongée

(rechute =  $\geq 1$  item BVAS majeur)

### Incidence of Serious Adverse Events

(aside from worsening vasculitis)

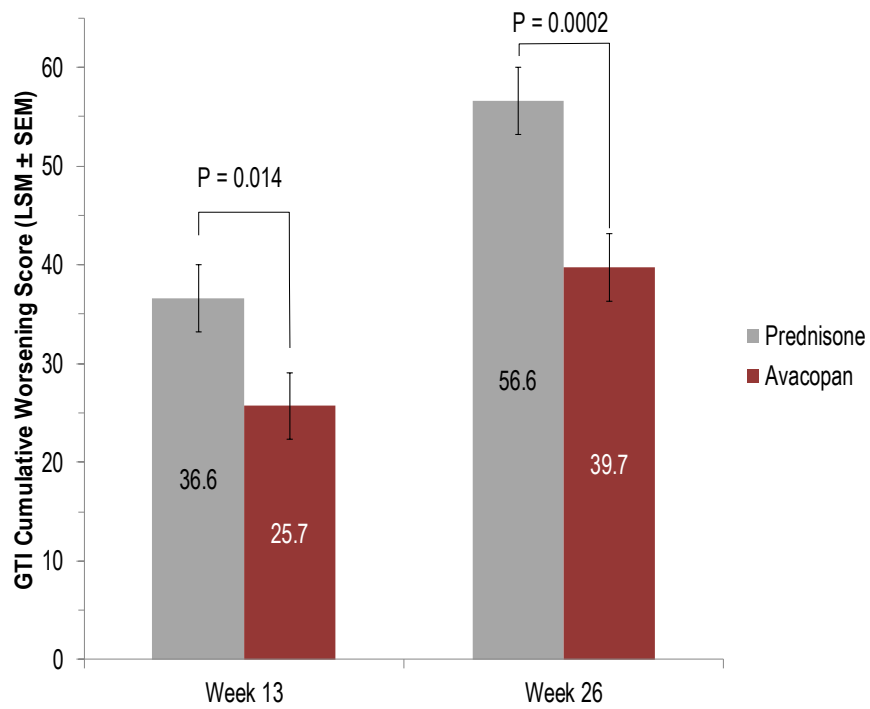


## Effets indésirables (EI)

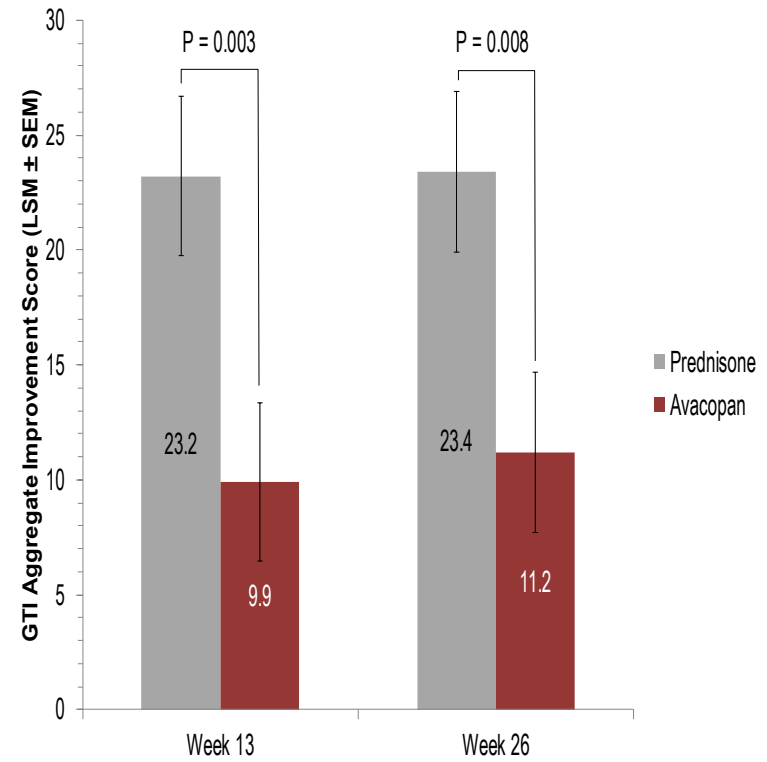
	<b>Prednisone (N=164)</b>	<b>Avacopan (N=166)</b>
<b>N. EI liés au traitement</b>	2139	1779
<b>Incidence (%) EI imputé à traitement</b>	161 (98.2)	164 (98.8)
<b>N patients avec EIG</b>	41 (25.0)	39 (23.5)
<b>N patients avec EI vitaux</b>	14 (8.5)	8 (4.8)
<b>Décès</b>	4 (2.4)	2 (1.2)
<b>N. EIG</b>	166	116
<b>Subjects incident (%), serious adverse event</b>	74 (45.1)	70 (42.2)
<b>Subjects with any serious infection</b>	31	24
<b>Décès de cause infectieuse</b>	2 (1.2)	1 (0.6)
<b>N. Patients avec EIG hépatique</b>	6 (3.7)	9 (5.4)
<b>N. Patients avec EI imputés aux corticostéroïdes</b>	132 (80.5)	110 (66.3)

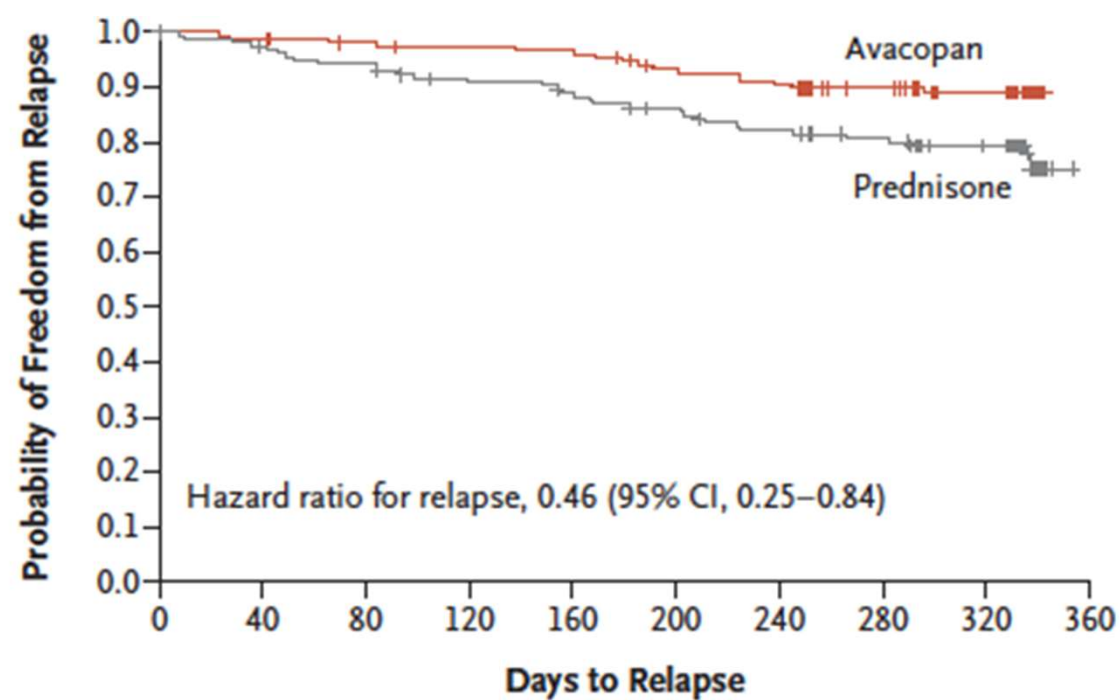
# Improvement of glucocorticoid toxicity index

- Cumulative Worsening Score



- Aggregate Improvement Score





No. at Risk										
Avacopan	158	153	149	146	145	133	129	115	92	0
Prednisone	157	151	146	137	133	126	119	111	90	0

**Figure 2.** Kaplan–Meier Plot of Time to Relapse.



## *Principaux résultats*

- Essai de non-infériorité concluant à 6 mois
- Supériorité à M12 pour rémission clinique
- Bonne tolérance

## *Réserves :*

- Arrêt complet de PDN à fin de M4
- Pas de ritux à M6
- Malades les plus sévères non inclus