European Crohn's and Colitis Organisation

Efficacy and safety of tacrolimus in ulcerative colitis: a nationwide, multicentric study from GETECCU

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GETECCU

Disclosures

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Background

- Tacrolimus is a calcineurin inhibitor
  - Blocking transcription of IL-2 in T lymphocytes
  - Solid organ transplantation
- Tacrolimus has been successfully used in moderate-severe or refractory ulcerative colitis (UC)
- Colectomy rate ranges between 15 – 35%
- Evidence for its use in UC in clinical practice still remains limited

Aim

To evaluate the clinical efficacy and safety of tacrolimus in ulcerative colitis in clinical practice in Spain

Methods

- Multicentric and retrospective study
- All consecutive patients receiving tacrolimus from 1999 to 2017
- Patient and disease characteristics, treatment history, tacrolimus treatment, concomitant drugs, new immunosuppressive therapy, hospital admissions and surgery
- Partial Mayo score
- REDCap online database
- Approved by the Local Ethics Committee

Outcomes

- Clinical efficacy at 3 months
  - Clinical remission: Partial Mayo score ≤2
  - Clinical response: At least 30% reduction in partial Mayo score
  - Physician Global Assessment (PGA)
- All adverse events

Demographics

- **58 patients** were identified and included in the final analysis

Patients	Frequency, n (%)
Sex, female	23 (40)
Age, years	40.2 (12.3)
Disease duration, months	67.7 (33-135)
E1/E2/E3	2/33/**65%**
Baseline CRP, mg/dL	8.8 (4.7-14)
Partial Mayo score	5.6 (2.1)
Perianal disease	3 (5)
Mayo endoscopic subscore	1: 4% 2: 36% 3: 61%

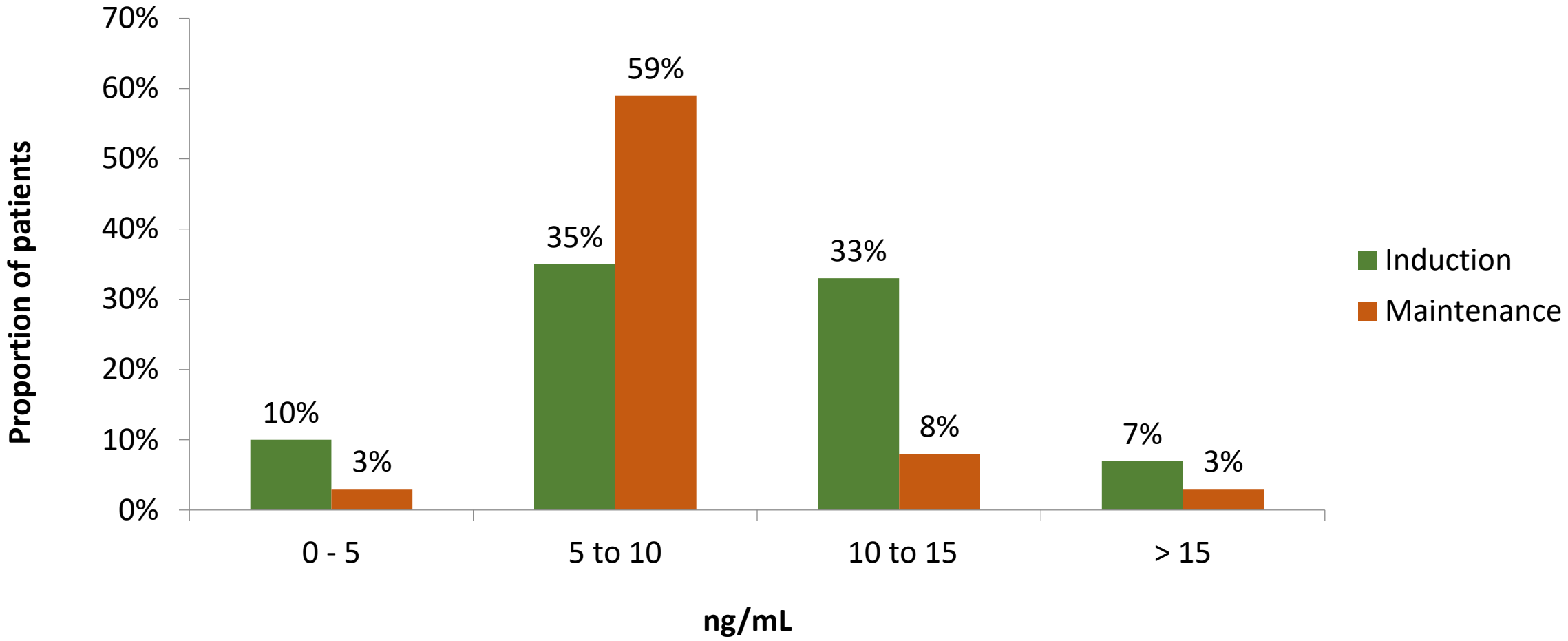
Previous treatments	Frequency, n (%)
Mesalazine	52 (89)
Steroids	48 (82)
Thiopurines	45 (78)
Methotrexate	5 (9)
Anti-TNF agents	**41 (71)**
≥ 2 anti-TNF	**25 (43)**
Vedolizumab	13 (22)

Tacrolimus therapy

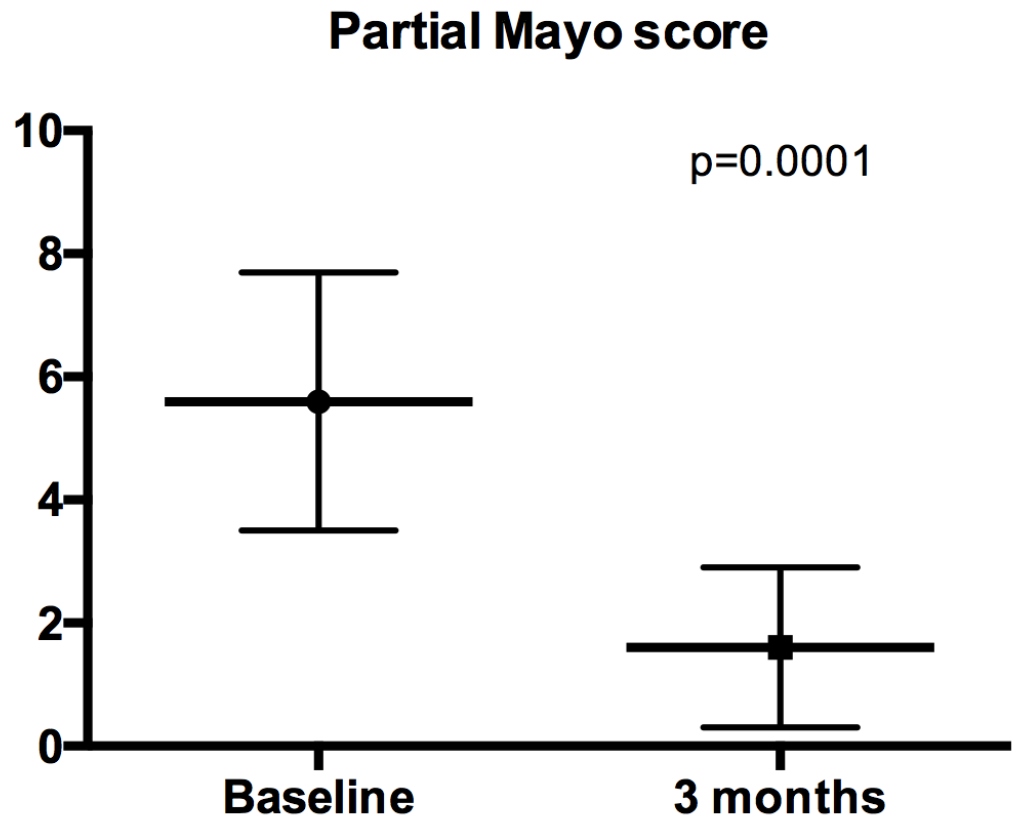
Indication	Frequency, n (%)
Steroid-dependence	32 (55)
Steroid-refractory	17 (29)
Refractory to medical therapy	3 (5)
Pouchitis	3 (5)
Perianal disease	2 (3)

Tacrolimus	Frequency
Daily dose, mg/day Median (IQR)	7 (4.7-8.8)
Concomitant therapy	
Steroids	20 (44)
Thiopurines	8 (18)
Anti-TNF	5 (9)
Vedolizumab	6 (10)

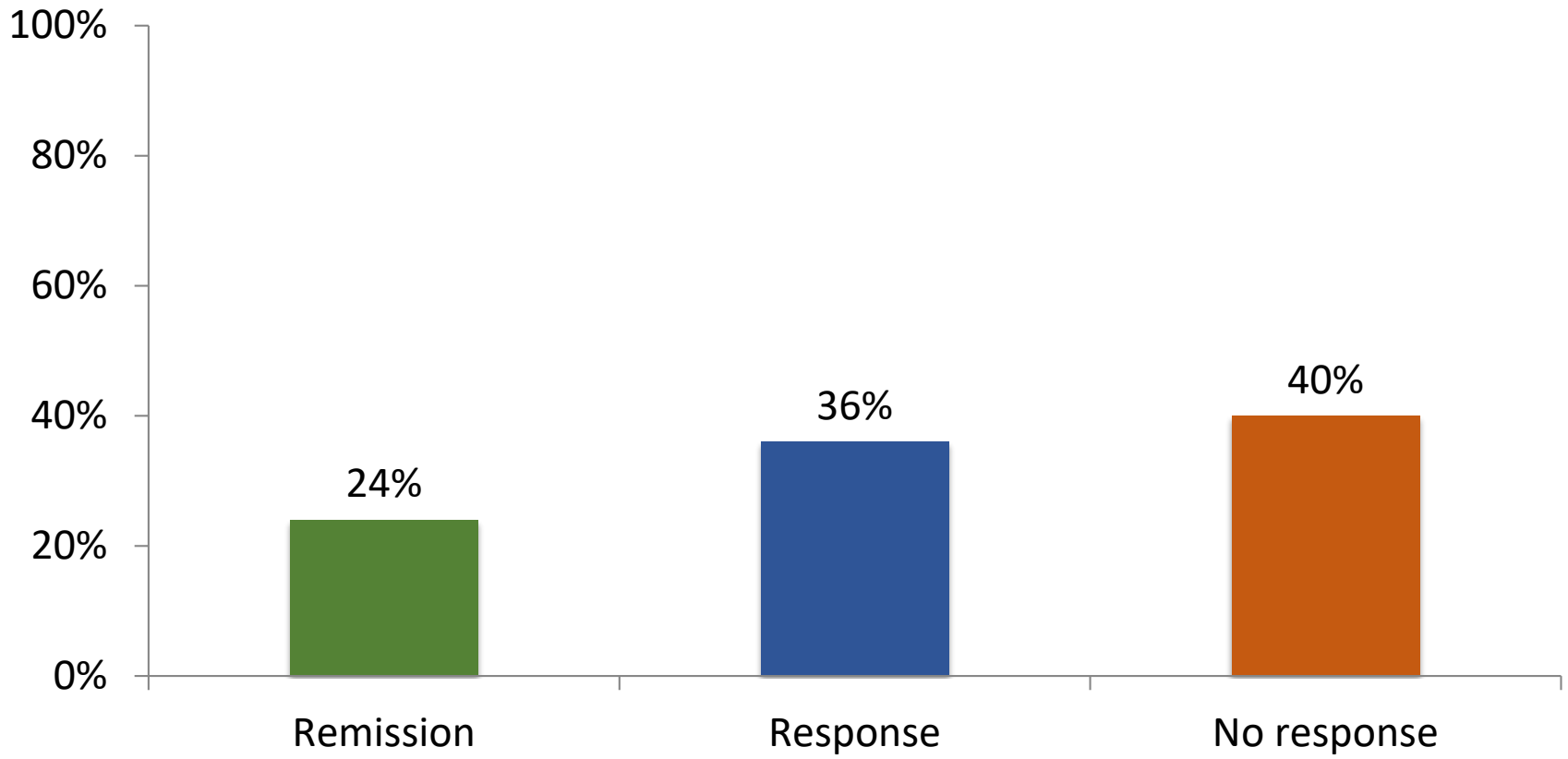
Blood drug concentrations



Clinical response at 3 months



Clinical response at 3 months (PGA)



Long-term clinical response

- Tacrolimus was maintained for 5 months (IQR 2-13)
- Clinical follow-up of 22 months (IQR 13 – 57)
- 81% stopped tacrolimus
  - 75% absence or loss of response
  - 15% adverse event
- 33% underwent colectomy

Adverse events

Adverse event (AE)	Frequency, n (%)
Number of AE	20 (35)
Type of AE	
Tremor	8 (40)
Asthenia	4 (20)
Gastrointestinal intolerance	3 (15)
Acute kidney injury	2 (10)
Cramps	2 (10)
Headache	2 (10)
Paresthesia	2 (10)
Withdrawal due to AE	7 (35)

Predictors of clinical response

Variable	OR (95% CI)
Blood levels during induction <10 vs >10 ng/mL	3.8 (0.73 – 20.3)
Baseline partial Mayo score	**0.63 (0.40 – 0.97)**
Previous anti-TNF therapy	0.3 (0.06 – 1.4)

Conclusions

- Tacrolimus offers a clinical benefit in medically refractory UC cases in the short-term
- Adverse events may occur in one-third of cases, but low rate of withdrawal due to them
- One-third of the patients may need colectomy
- Long-term effectiveness and safety represent important limitations of this therapy

Young IBD Group from GETECCU

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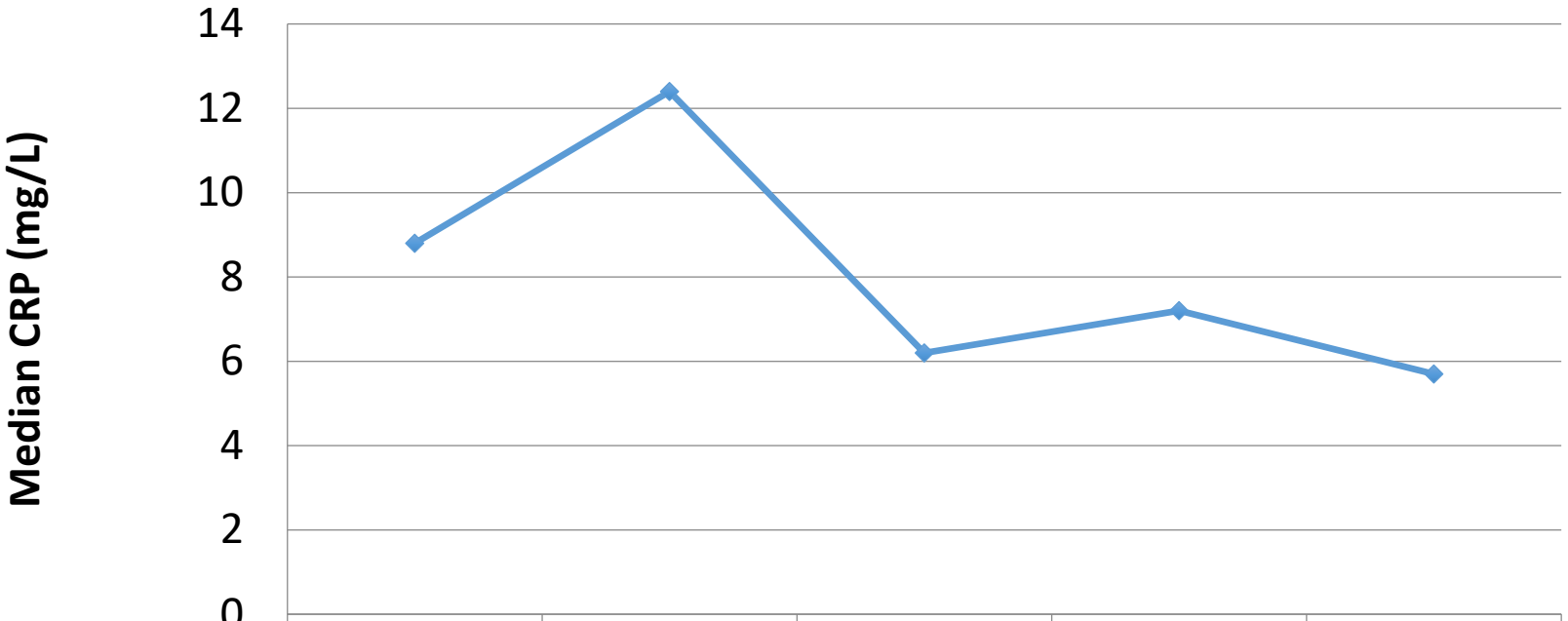
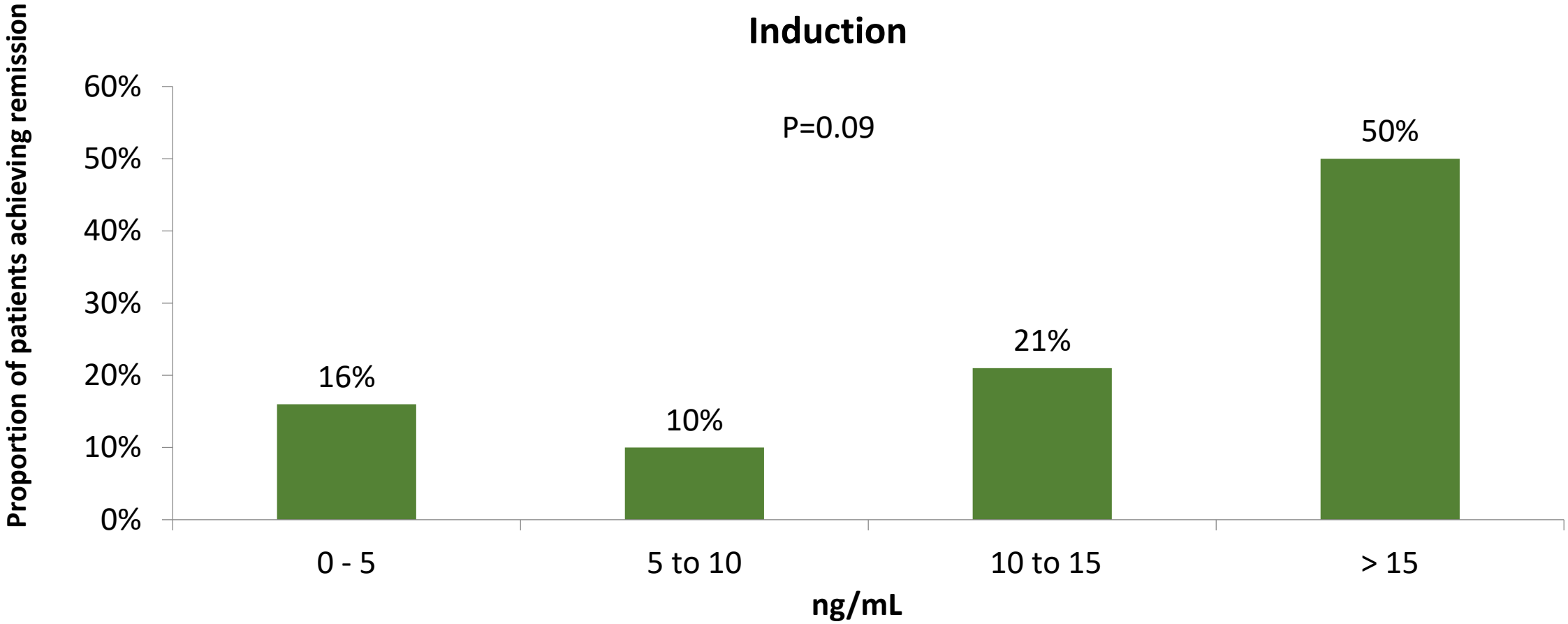
- Hospital Clinic
- Hospital de Cruces
- Hospital de Galdakao
- Hospital Sant Pau
- Hospital de Montecelo
- Hospital del Mar
- Hospital Marqués de Valdecilla
- Hospital Reina Sofía
- Hospital de Salamanca
- Hospital German Trias i Pujol
- Hospital la Paz
- Hospital Miguel Servet
- Hospital Puerta de Hierro
- Hospital de Girona
- Complejo Hospitalario de Navarra
- Hospital de la Princesa
- Hospital Son Llàtzer
- Mutua Terrassa
- Hospital Arnau de Villanova
- Hospital Clínico San Carlos

CRP response

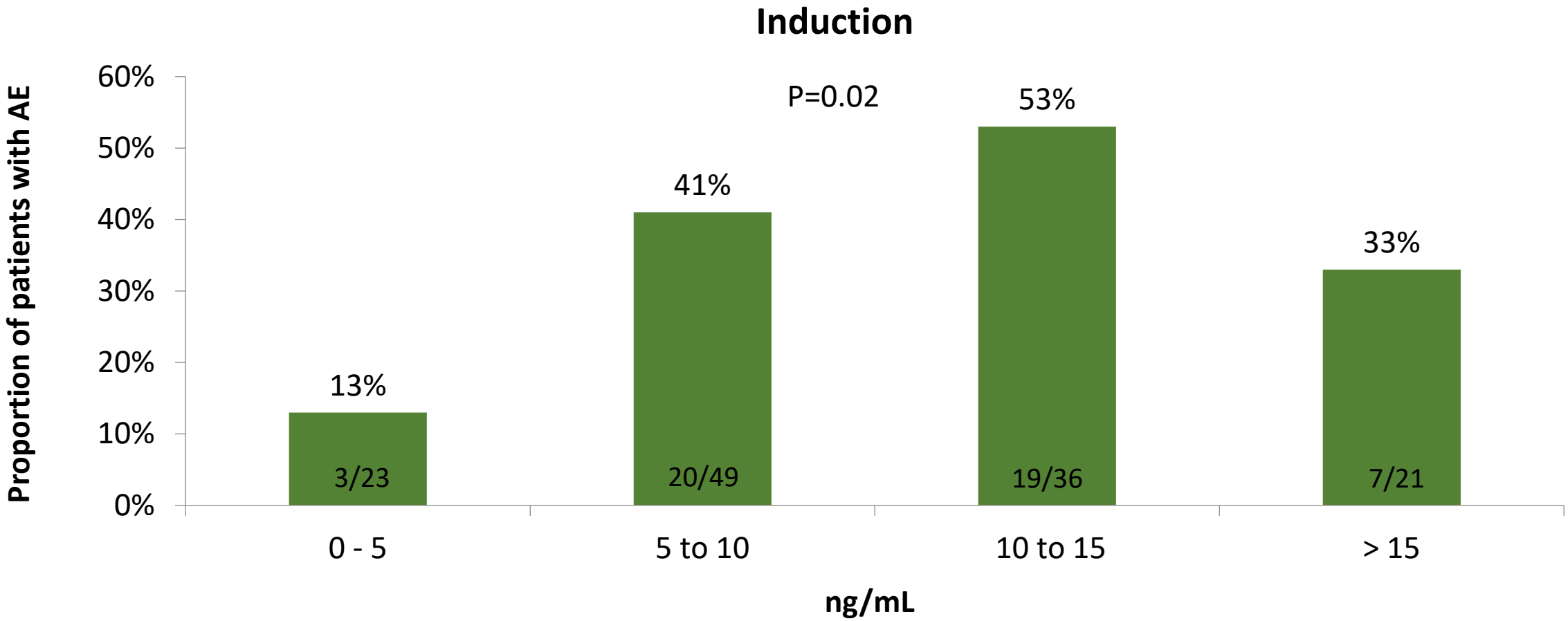


	Baseline	1 month	3 months	6 months	12 months
CRP (mg/L)	8,8	12,4	6,2	7,2	5,7

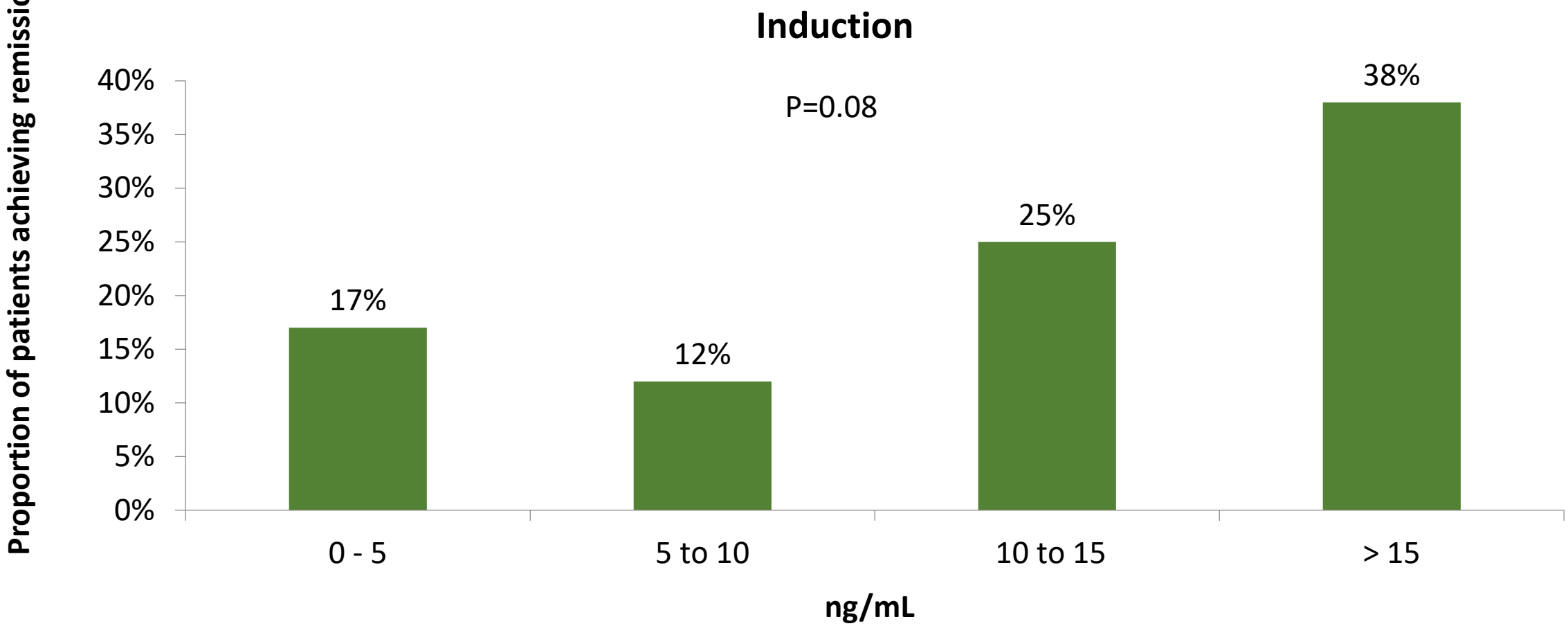
Blood drug levels and clinical remission



Adverse events and blood drug levels Ulcerative colitis and Crohn's disease



Blood drug concentrations during induction Ulcerative colitis and Crohn's disease



Endoscopic disease activity

Mayo endoscopic score	Baseline	Follow – up endoscopy	p value
0	2%	2%	0.10
1	17%	3%	
2	29%	15%	
3	48%	21%	

Median time until endoscopic follow-up of 6 months (IQR 4.2 – 9.5)