Therapeutic Drug Monitoring in Crohn's Disease Patients, a Comparison Between Homogeneous Mobility Shift Assay and Point of Care Method

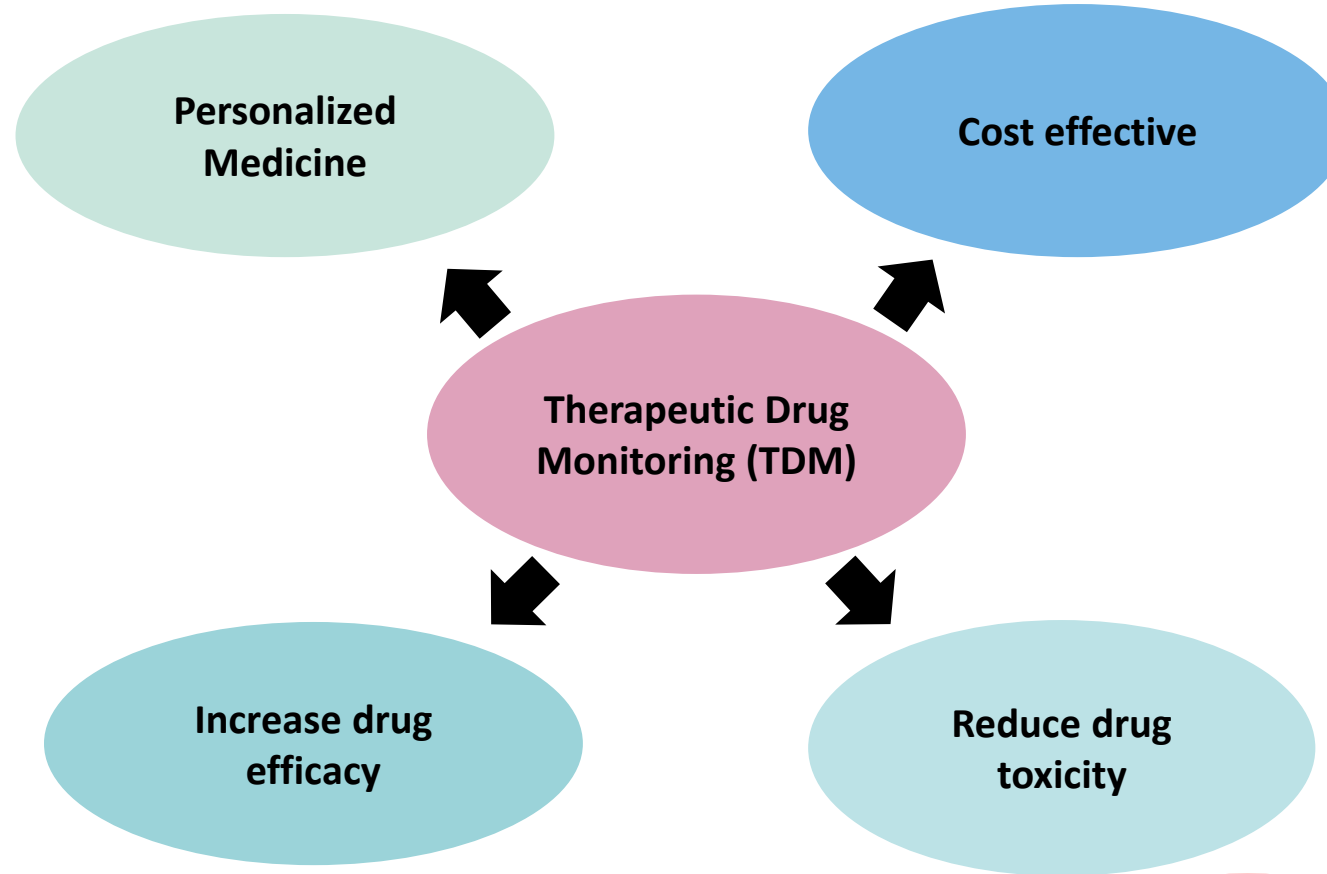**Maria Giulia Demarzo**

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Introduction (I)

Personalized Medicine

Cost effective

Therapeutic Drug Monitoring (TDM)

Increase drug efficacy

Reduce drug toxicity

Proactive TDM

Reactive TDM

Yanai H, et al. Clin Gastroenterol Hepatol 2015
Steenholldt C et al Inflam Bowel Disease, 2017
Vande Casteele N. et al Gastroenterology 2015;148:1320–1329

Introduction (II)

Use of Therapeutic Drug Monitoring (TDM) for anti-TNF agents

		ELISA	HMSA
1.	**Execution Time**	4-6 h	
2.	**Phase**	Solid	Liquid
3.	**Accuracy for measuring anti TNFα serum concentrations**	...itative	High
4.	**Accuracy for detecting antibodies**	Drug sensitive/tolerant	High/quantitative
5.	**Antibodies inconclusive**	Positive	Negative
6.	**Aspecific interferences**	High	Low
7.	**Antibodies type**	IgG	Different subtypes and subclasses

TIME CONSUMING

Wang SL et al, J immunol Methods, 2012
Van Stappen T et al, Drug Test Anal, 2017

Point of care

15-20 min

Aim

The aim of our study was to:

- evaluate the capability of POC to discriminate between IBD relapse and remission;

- evaluate the concordance of drug TL measured with POC and HMSA.

Patients and methods

- Crohn's disease patients (n=46)

  200 infliximab serum samples

  200 adalimumab serum samples

- Blood samples were drawn at standardized points during anti-TNF treatment (2, 6, and every 8 weeks) or at loss of response

- Serum samples previously assessed with HMSA were analyzed with point of care

- Disease activity was assesses using HBI

- HMSA (Prometheus Inc, San Diego, California, USA)

- Quantum Blue® (Buhlman Laboratories AG, Schnenbuch, Switzerland)

Results (I)

|		Whole Population (n 46, 100%)	ADA patients (n 25, 54.3%)	IFX patients (n21, 45.7%)
Gender (male)	n (%)	28, 60.1	16, 64	12, 57.1
Age (years)	median (range)	39 (19-60)	39 (19-66)	39 (21-69)
Age<40 at diagnosis,	n (%)	38, 82.6	22, 88	16, 76.2
BMI	median (range)	23 (17-33)	23 (17-33)	24 (17-30)
FU (weeks)	median (range)	83 (16-144)	90 (48-144)	80 (16-138)
Disease duration (years)	median (range)	4.5 (1-22)	6 (1-22)	4 (1-20)
Montreal Classification **Behaviour**				
B1		18, 39	9, 36	9,43
B2		18, 39	10, 40	8,38
B3	n (%)	10, 22	6, 24	4,19
Location				
L1		27,59	16, 64	11,52
L2		5, 11	2, 8	3, 14
L3		14, 30	7, 28	7, 34
Perianal disease	n (%)	8, 17	4, 16	4, 19
Smoking status				
Past- smokers		11, 24	6,24	5, 24
Active smokers	n (%)	27, 59	13,52	14, 67
No smokers		8, 17	6, 24	2, 9
Previous surgery	n (%)	17, 37	10, 40	7, 33

Results (II)

ADA TL HMSA vs POC (Week 14)
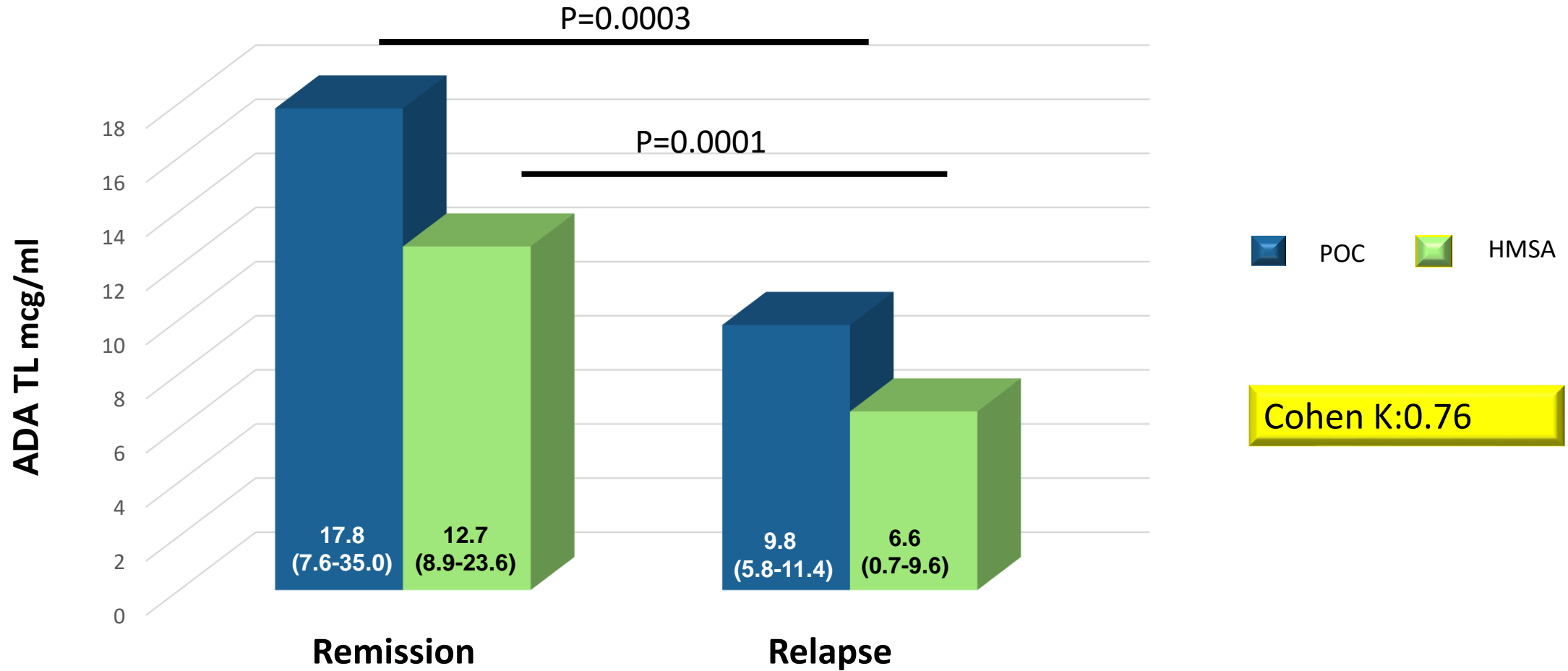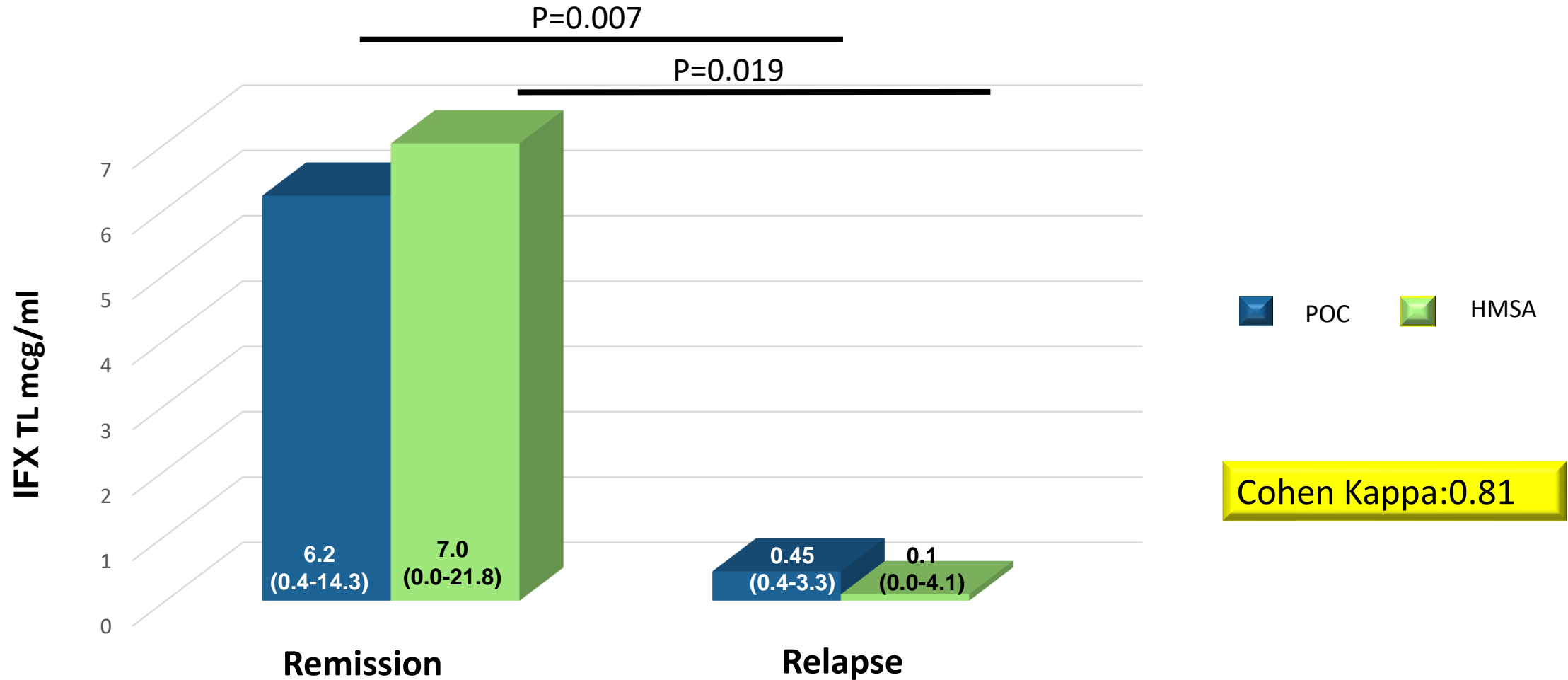
Results (III)
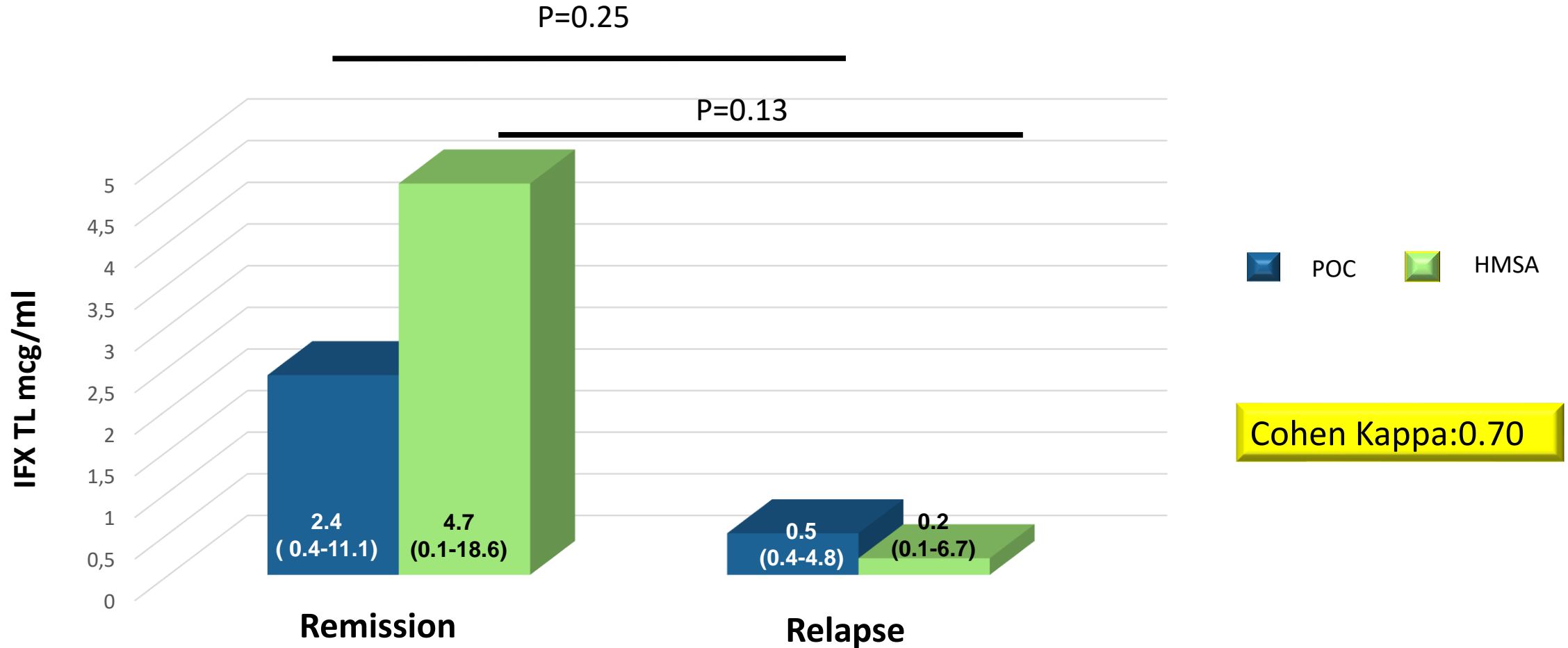

ADA TL HMSA vs POC (End of FU)
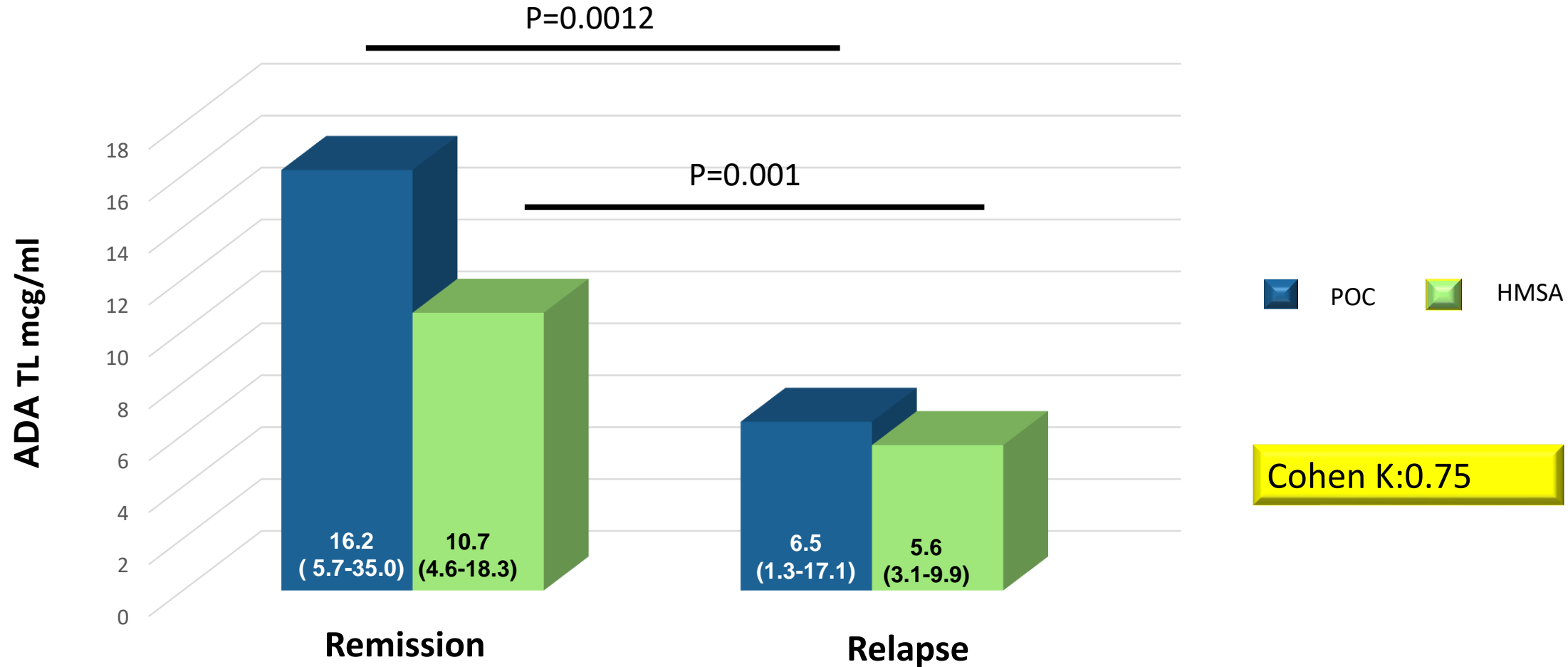
Results (IV)

IFX TL HMSA vs POC (Week 14)
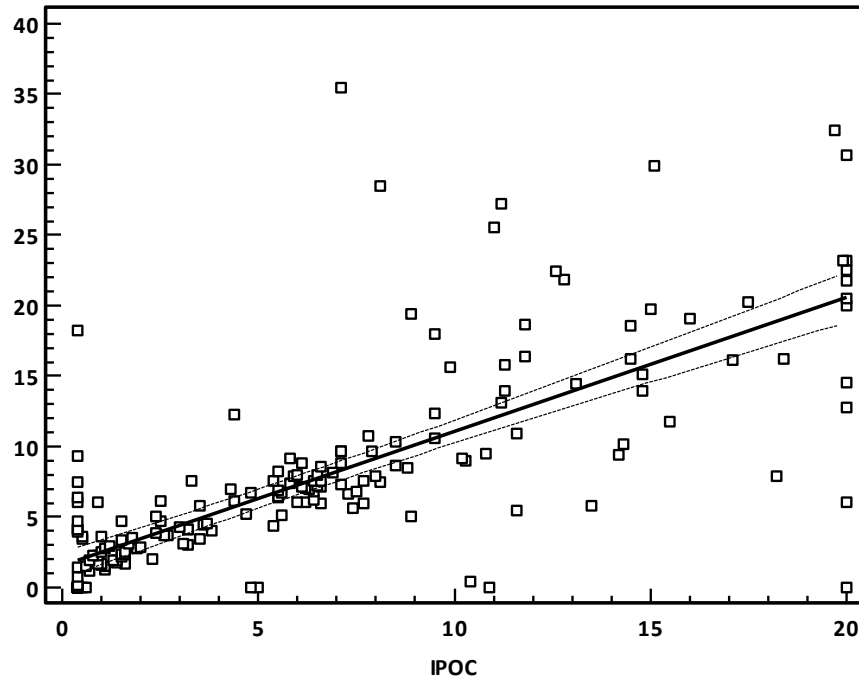
Results (V)

IFX TL HMSA vs POC (End of FU)
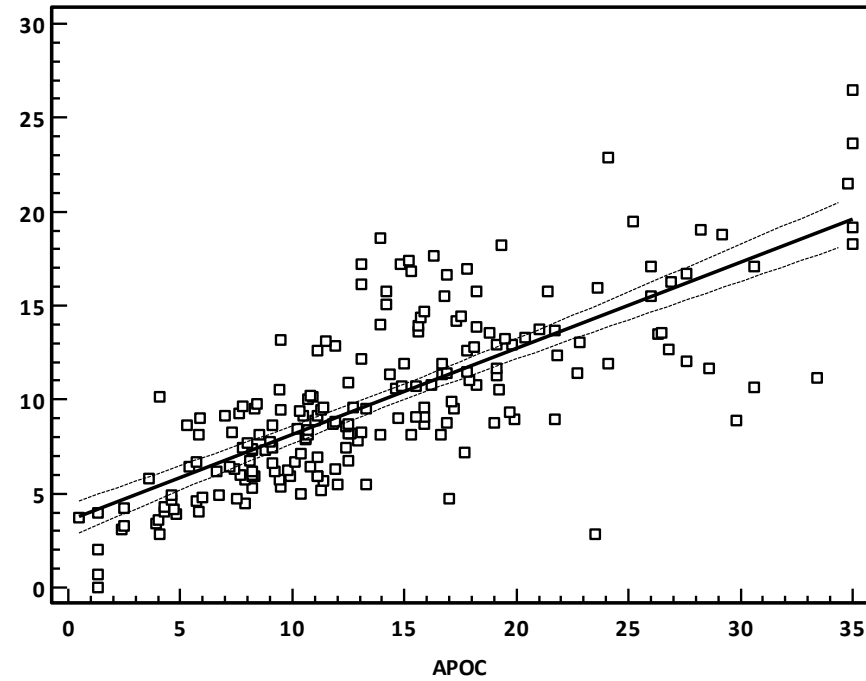
Results (VI)

Correlation HMSA vs POC

IFX

ADA

r= 0.76

p< 0.0001
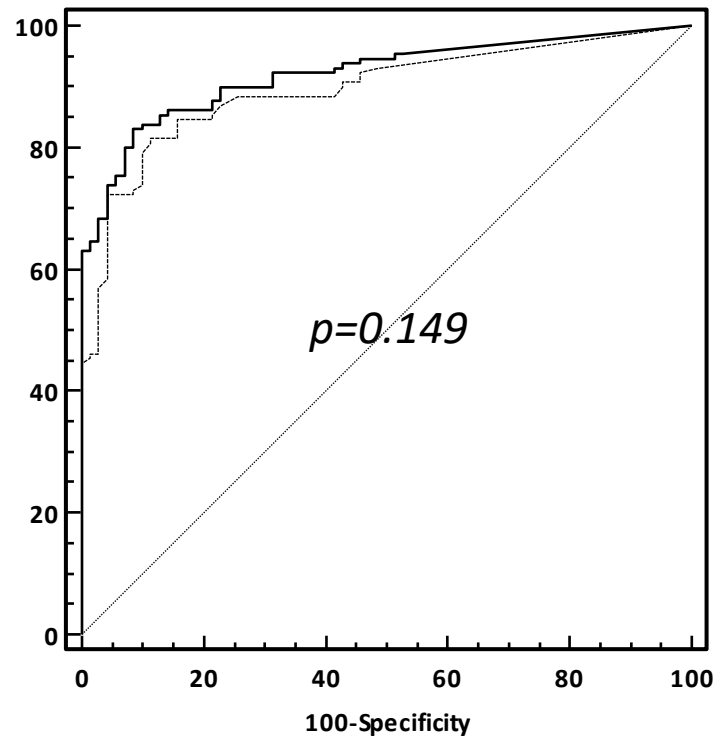
95% CI = 0.690-0.810

r= 0.75

p< 0.0001

95% CI = 0.688-0.809

Results (VII)

ROC Curve HMSA vs POC

IFX

$p=0.149$

I-HMSA
I-POC

POC C_{index} = 0.895 95% CI (0.845-0.934)

HMSA C_{index} = 0.921 95%CI (0.874- 0.954)

ADA

$p=0.197$

A-HMSA
A-POC
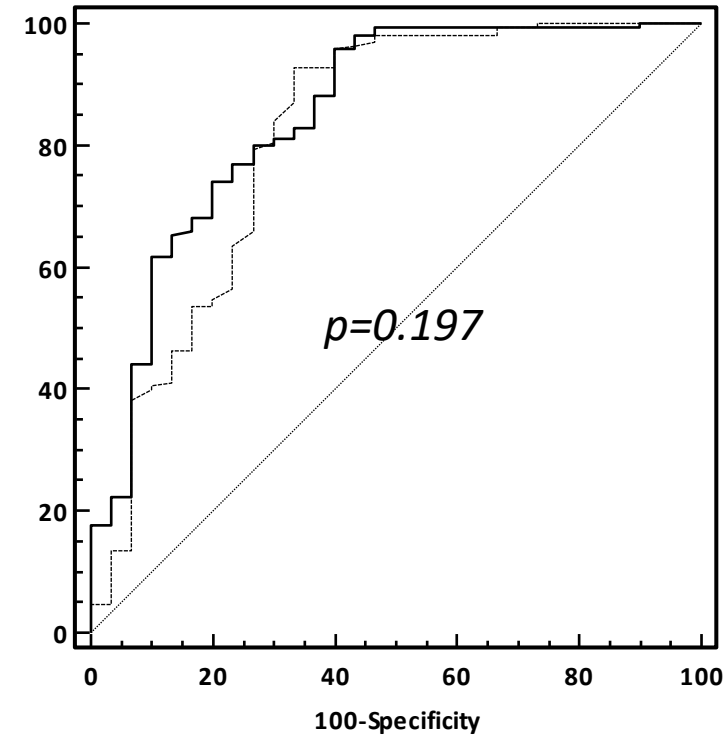
POC C_{index} = 0.850 95% CI (0.756-0.868)

HMSA C_{index} = 0.817 95%CI (0.793- 0.896)

Conclusions

Both POC and HMSA are TL tests able to differentiate relapse and remission in IBD patients

The association between anti-TNF TL and disease status (remission/relapse) was better in ADA-treated patients rather than patients treated with IFX

Good concordance, correlation and accuracy between HMSA and POC

Anti-drug antibody concentrations while available on HMSA were not available on POC. This would limit the identification of anti-TNF non-responders on the POC test if a percentage of those were anti-drug antibody positive.