ABX464 is safe and efficacious in a proof of concept study in Ulcerative Colitis patients

S. Vermeire, X. Hébuterne, P. Napora, M. Wisniewska-Jarosinska, G. Kiss, A. Bourreille, Z. Przemysław, J. Nitcheu, P. Gineste, ***J.-M. Steens****, H. Ehrlich*

DDW San Diego May 21, 2019

abivax

Disclosures

GSK shareholder

ABIVAX employee and shareholder options

Background

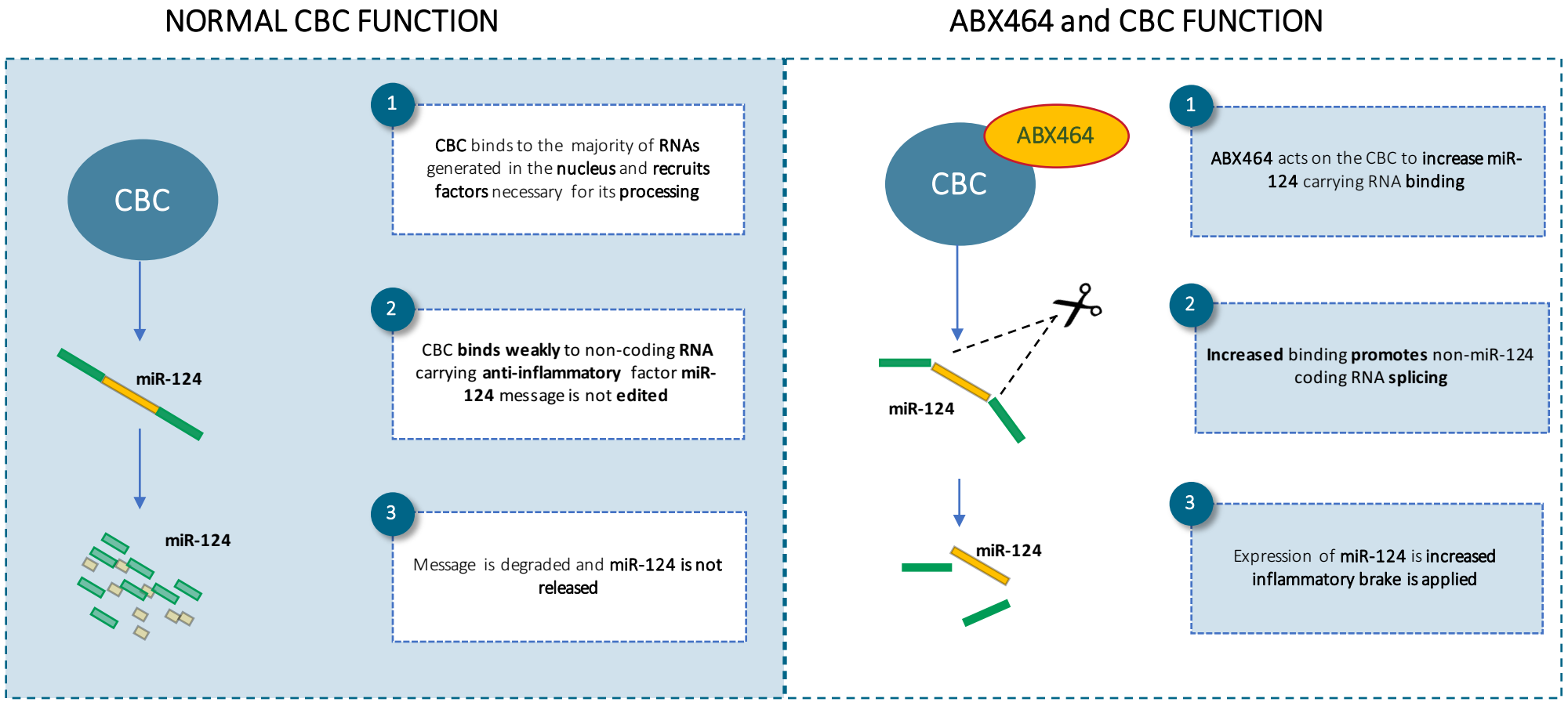
Despite the availability of new drugs, there is still a high unmet medical need for patients suffering from Ulcerative Colitis and Crohn's Disease

ABX464

- Is a small molecule administered as an oral capsule
- Has antiretroviral properties, reduces total HIV-DNA and was studied in more than 180 subjects in HIV program (1,2)
- Has potent anti-inflammatory properties impacting the expression of miR-124 (3,4)

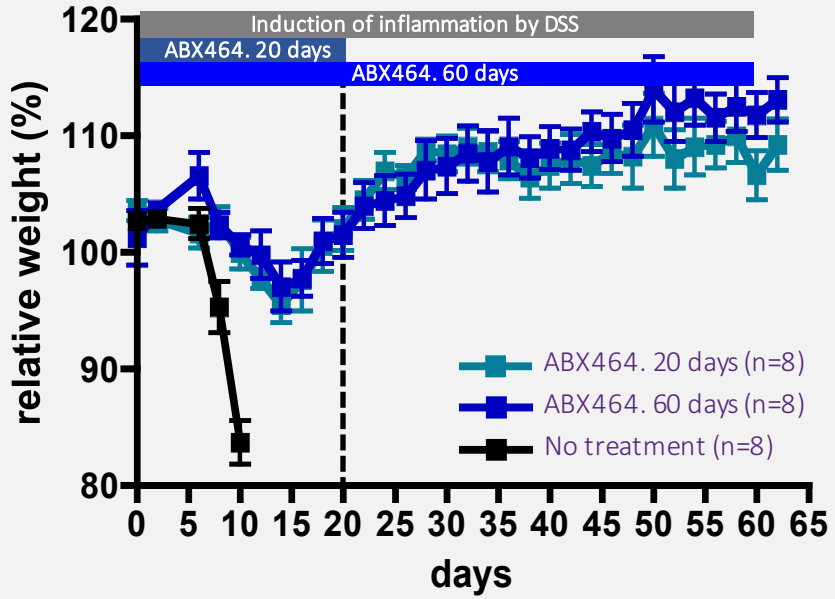
1 Steens et al, Antimicrob Agents Chemother 61:e00545-17
*2 Rutsaert et al, Journal of Virus Eradication 2018; **5**: e1–e13*
3 Chebli et al, Nature Scientific Reports | 7: 4860 (2017)
4 Vautrin et al., Nature Scientific Reports 9 (2019)

ABX464 - Proposed mechanism of action

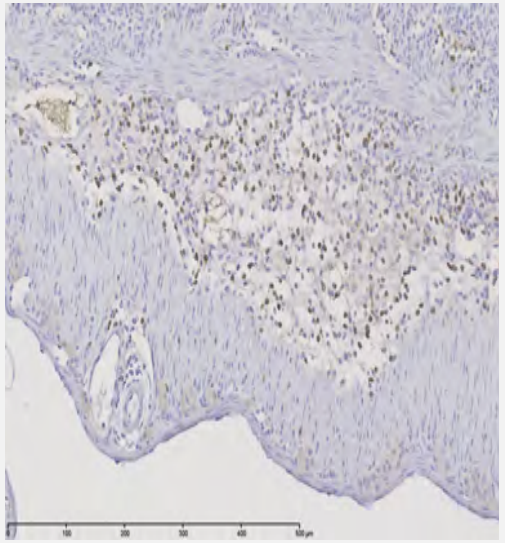


ABX464 showed efficacy in DSS Mice Model*

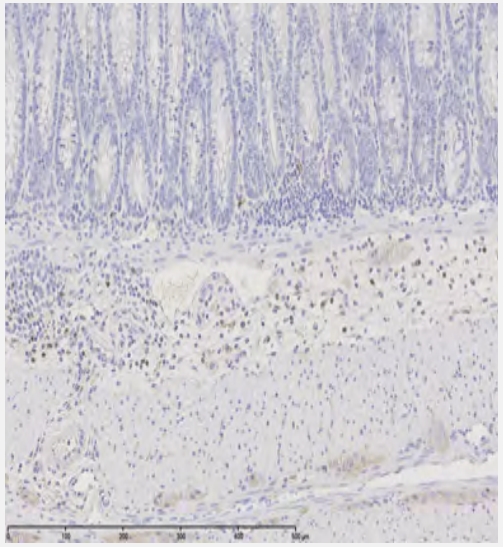
ABX464 protects mice from death in the DSS mouse model



DSS without treatment leads to intestinal damage



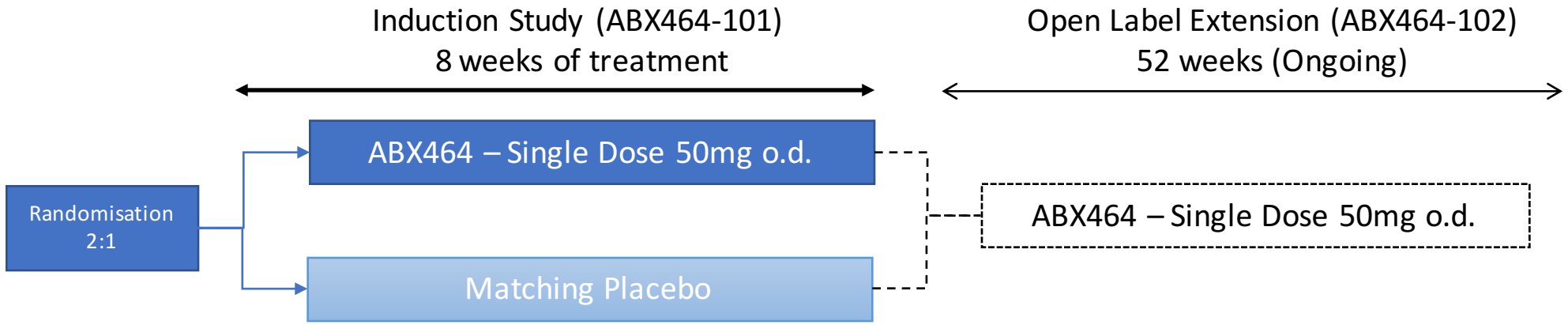
ABX464 protects intestinal Structure



*Chebli et al, Nature Scientific Reports 7: 4860 (2017)

Study Design

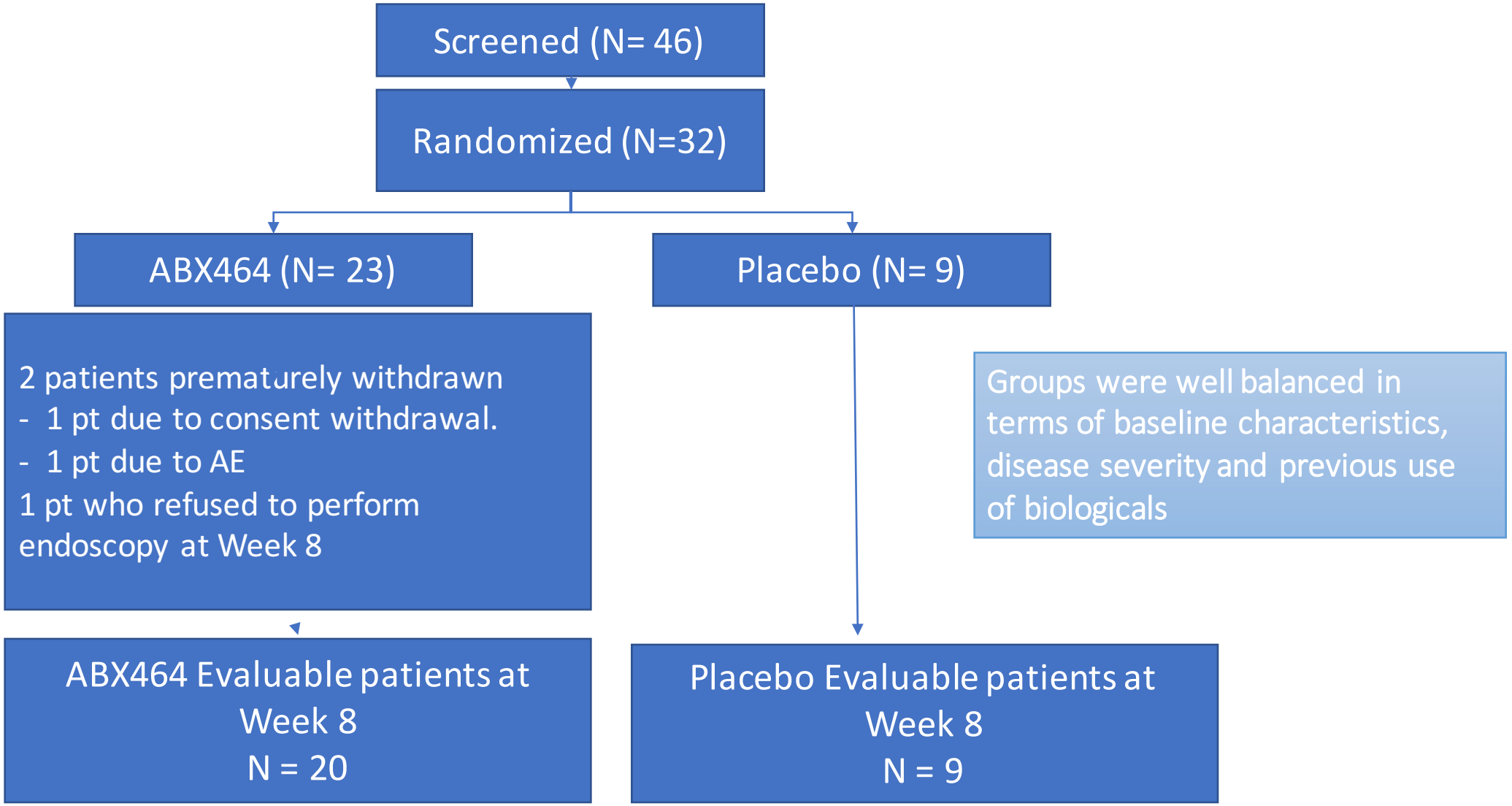
Randomized, double-blind, placebo controlled, multi-national study



- Study Population = Moderate to Severe Active UC patients who failed or were intolerant to immunomodulators, Anti-TNFα, vedolizumab and/or corticosteroids
  - Confirmed UC for at least 3 months with a Total Mayo Score of 6-12 with endoscopic sub-score of 2 or 3
  - Central reading of endoscopies

- Study Endpoints
  - Primary = Safety
  - Secondary : Mayo Score and Endoscopy, Faecal calprotectin levels , Geboes score, miRN-124 expression, microbiome, Quality of Life (SF-36) and Pharmacokinetics

Recruitment Flow



Good Safety Profile

- Very consistent with previous clinical studies
- No deaths, no malignancies, no opportunistic infections, no significant changes in the laboratory parameters including WBC
- No Serious Adverse Reaction, all AE's of mild to moderate intensity

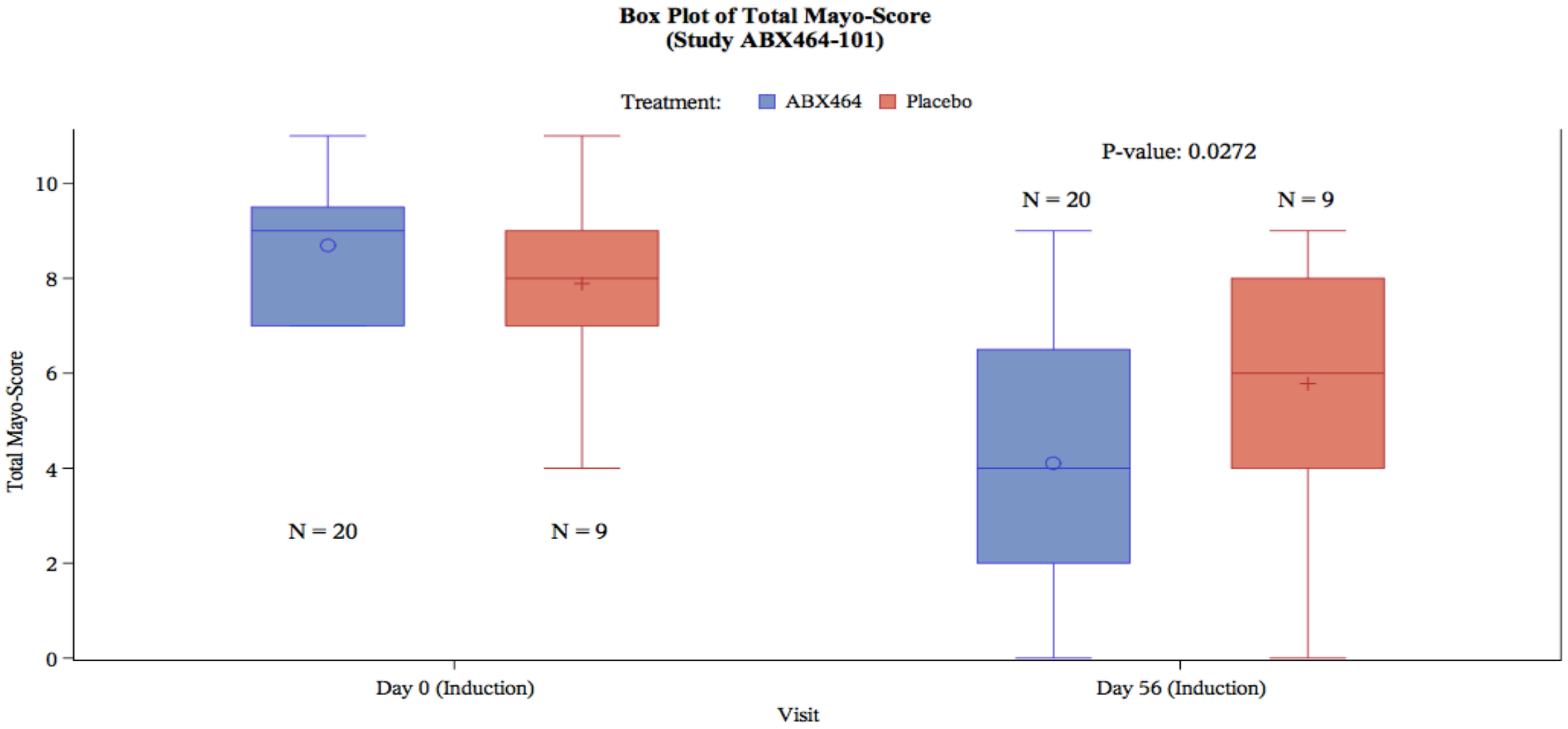
Patients with at least one Treatment Emergent Adverse Events (>15%) regardless of causality	ABX-464 (N=23)	Placebo (N=9)
	N (%)	N (%)
Any Treatment-Emergent Adverse Events	**18 (78.3%)**	**5 (55.6%)**
Gastrointestinal disorders (mainly Upper Abdominal Pain)	*8 (34.8%)*	*2 (22.2%)*
Infections and infestations	*4 (17.4%)*	*1 (11.1%)*
Nervous system disorders (mainly Headache)	*5 (21.7%)*	*0 (0.0%)*

Efficacy data (Day 56)

	ABX464 (n=20/23) PP/ITT	Placebo(n=9/9) PP/ITT	p value (PP)
Clinical Remission	35% / 30%	11% / 11%	0.16
Endoscopic Improvement	50% / 43%	11% / 11%	**0.03**
Clinical response	70% / 61%	33% / 33%	0.06
Total Mayo Score Reduction	-53%	-27%	**0.03**
Partial Mayo score Reduction	-62%	-32%	**0.02**
Faecal Calprotectin decrease > 50 %	75%	50%	na
miR-124 expression in rectal biopsies (fold increase)	7.69	1.46	0.004

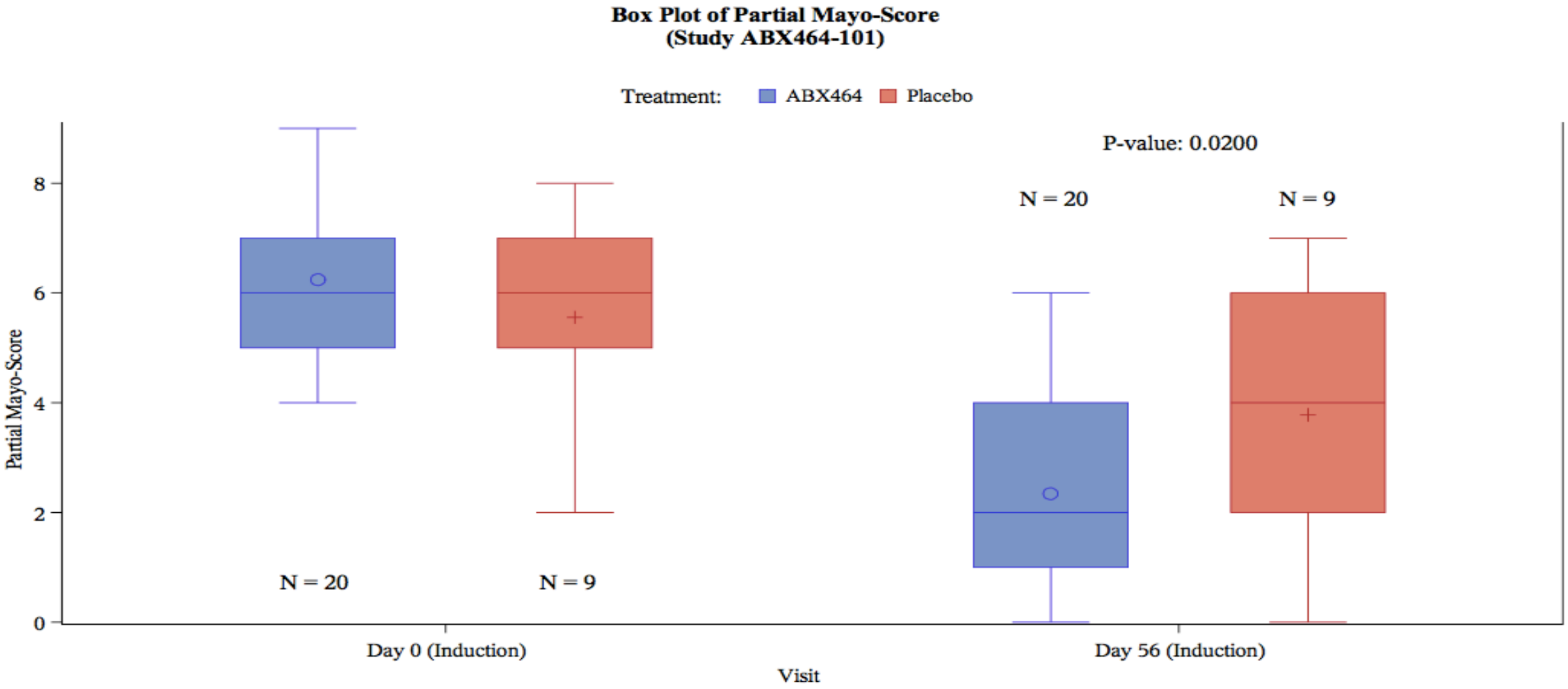
- *Clinical remission : TMS equal or lower than 2 + no sub-score >1*
- *Endoscopic improvement : Endoscopy sub-score 0 or 1*
- *Clinical response : TMS decrease of min 3 points and 30% from baseline + decrease of bleeding sub-score of min 1 point or absolute baseline of 0 or 1*

Total Mayo Score Day 0- Day 56



P-value reflects the comparison of change between Day 0 and Day 56 in active versus placebo treatment.

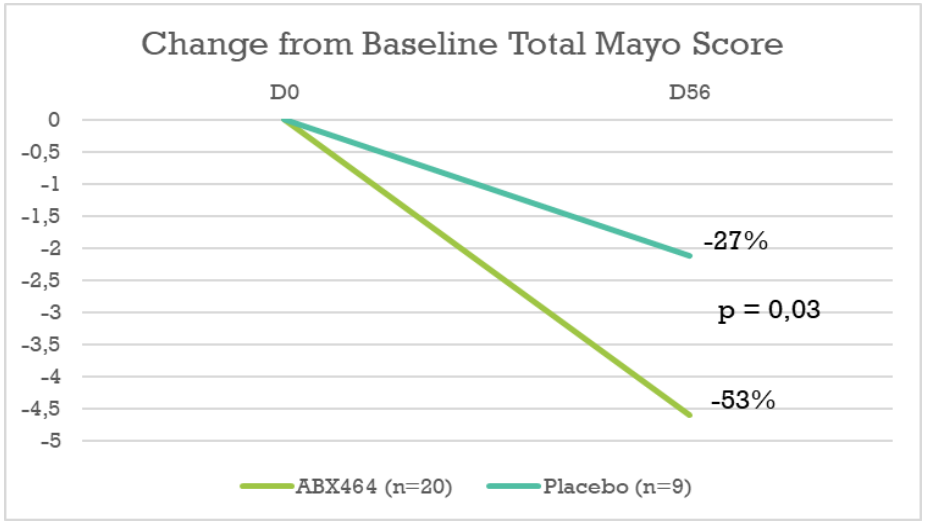
Partial Mayo Score Day 0-Day 56

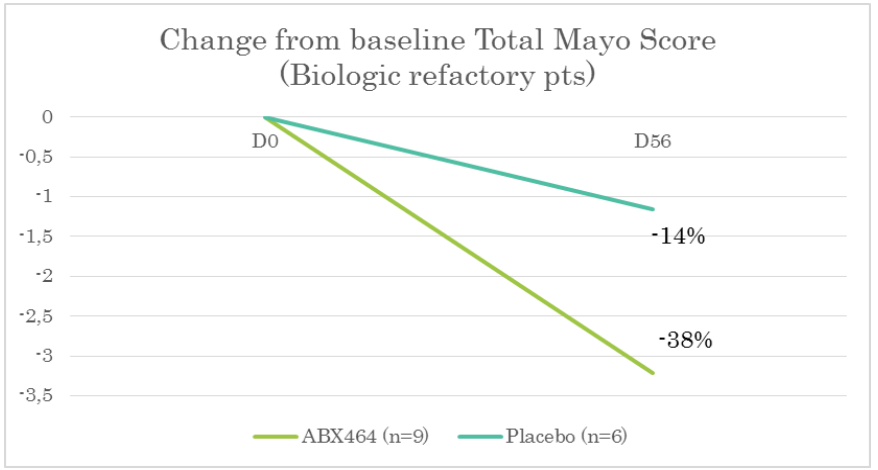


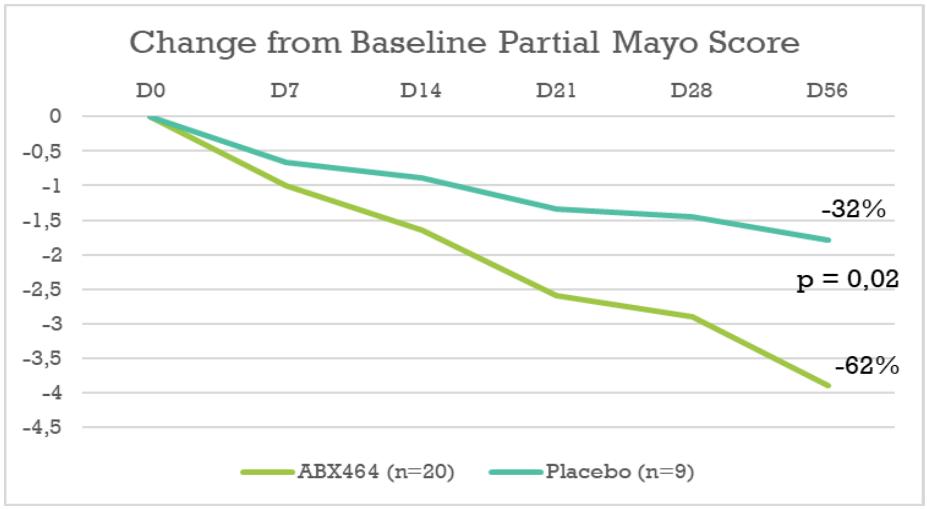
P-value reflects the comparison of change between Day 0 and Day 56 in active versus placebo treatment.

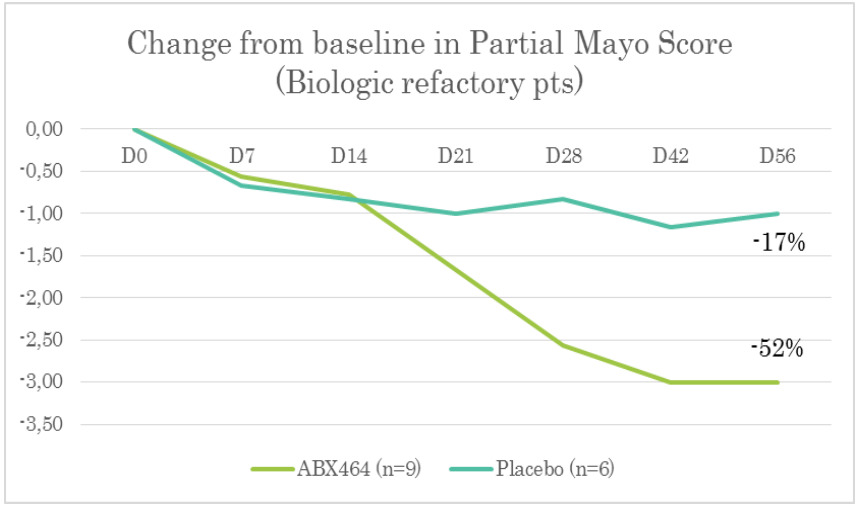
Mayo Score Results

ABX464: Fast onset of action and clinical responses in patients who failed on biologics



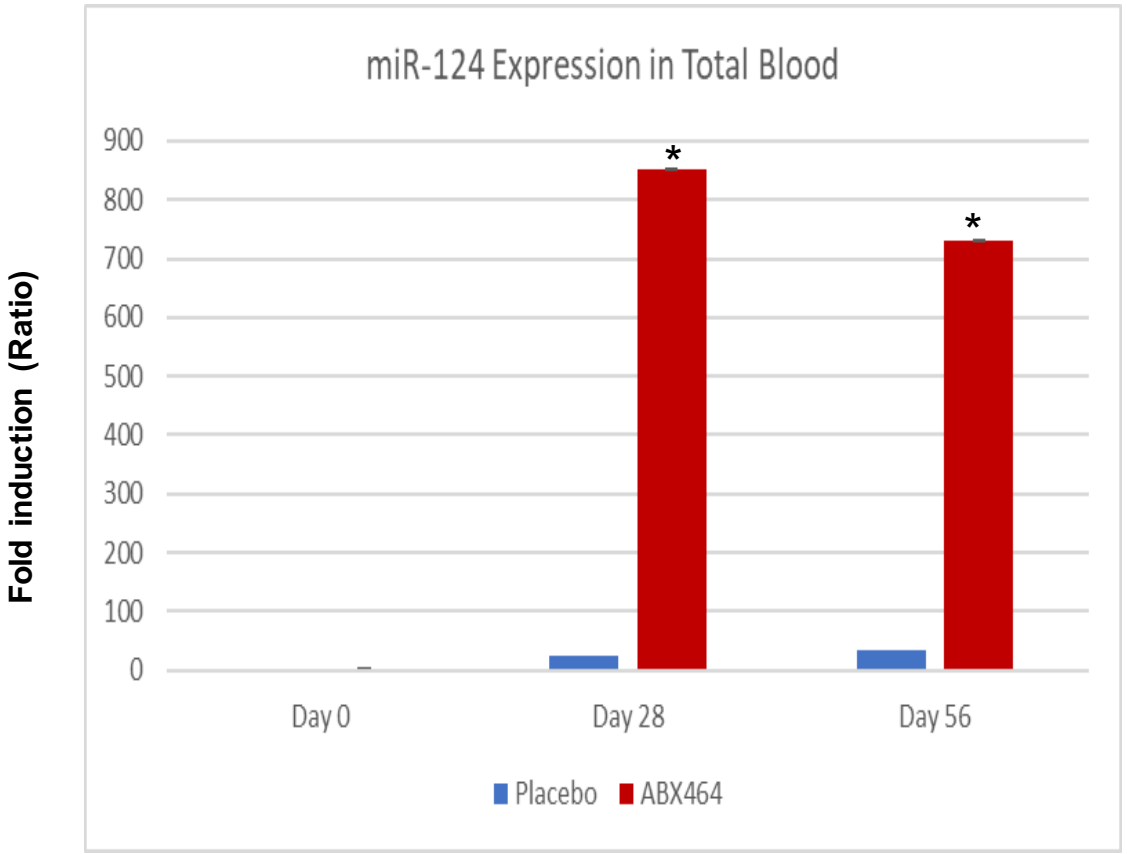


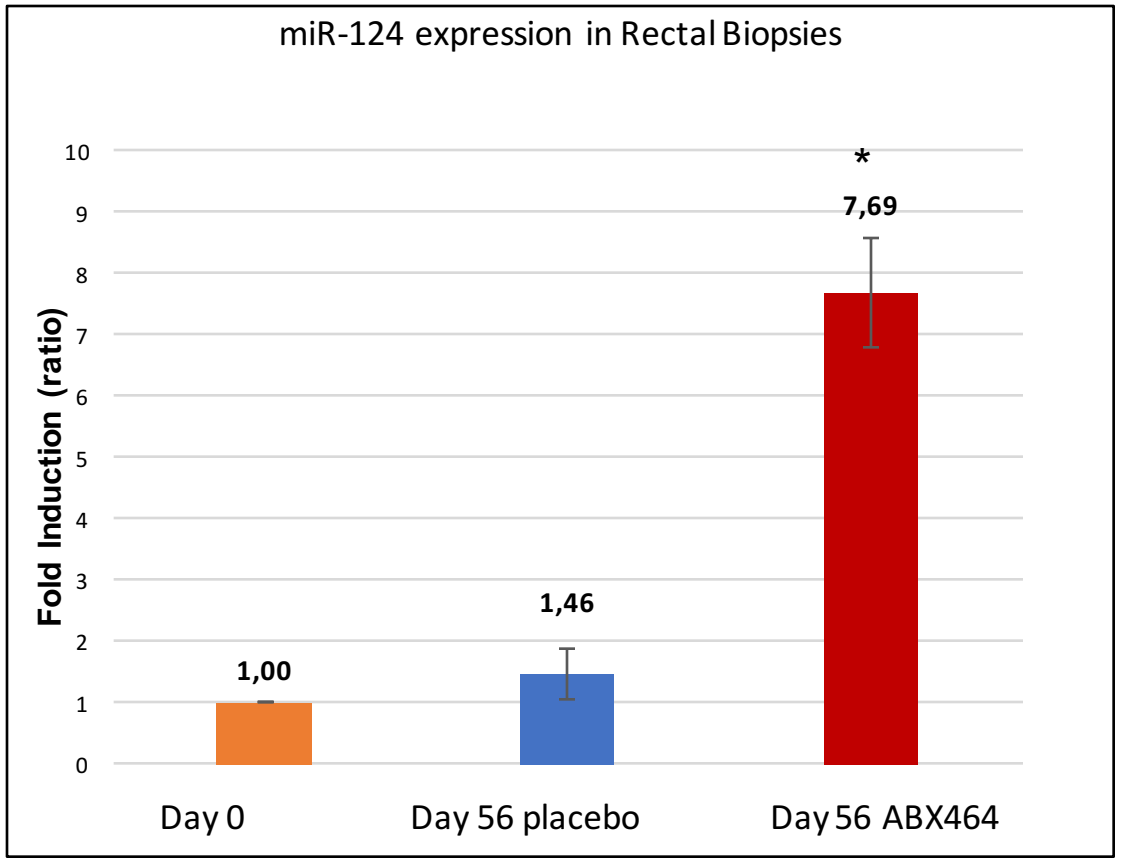




Statistically significant increase in miR-124 expression

Total blood and Rectal tissue





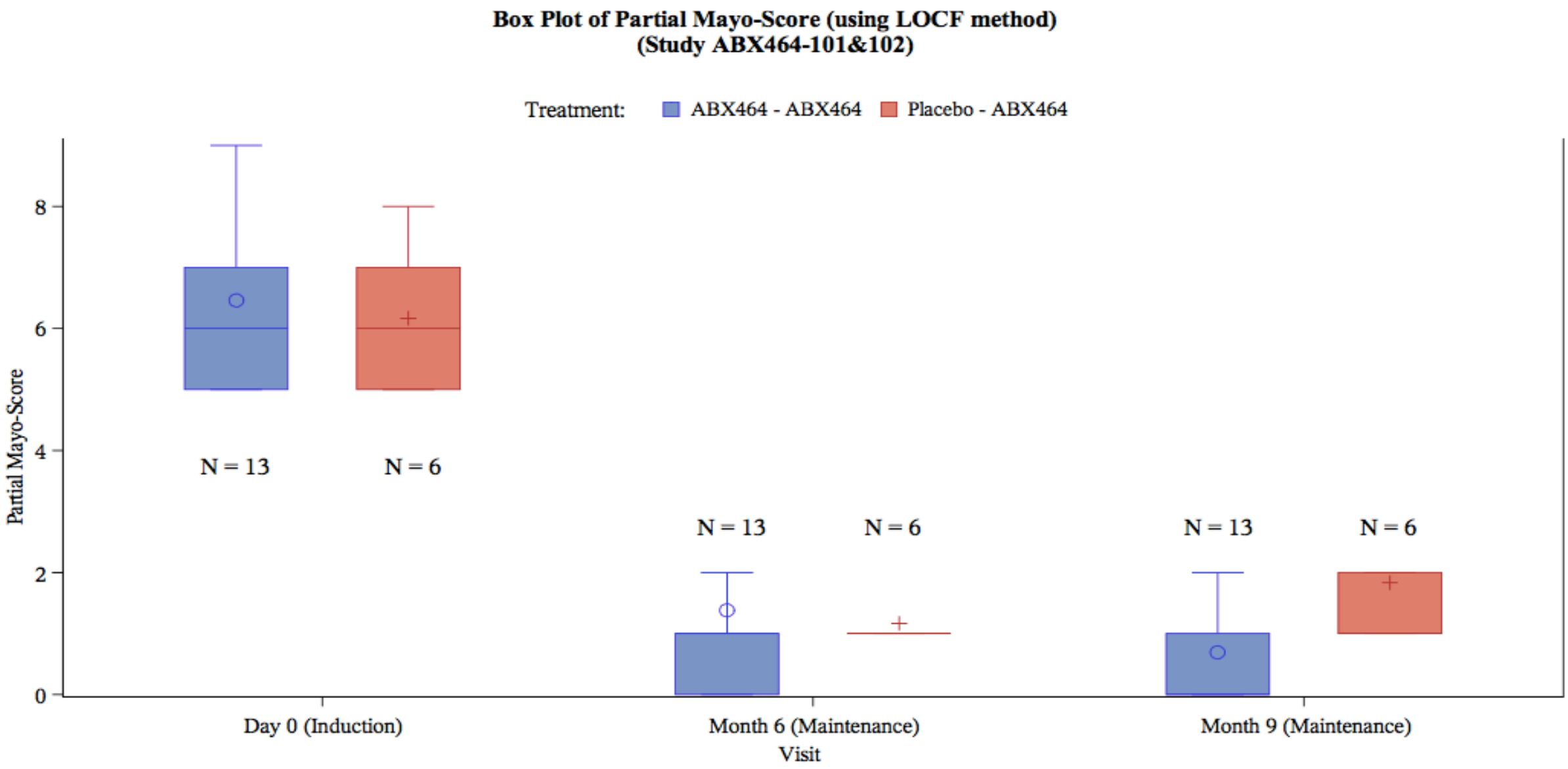
** p value < 0.05 (Treatment and time point)*

Maintenance Phase: 6 and 9-months interim analysis

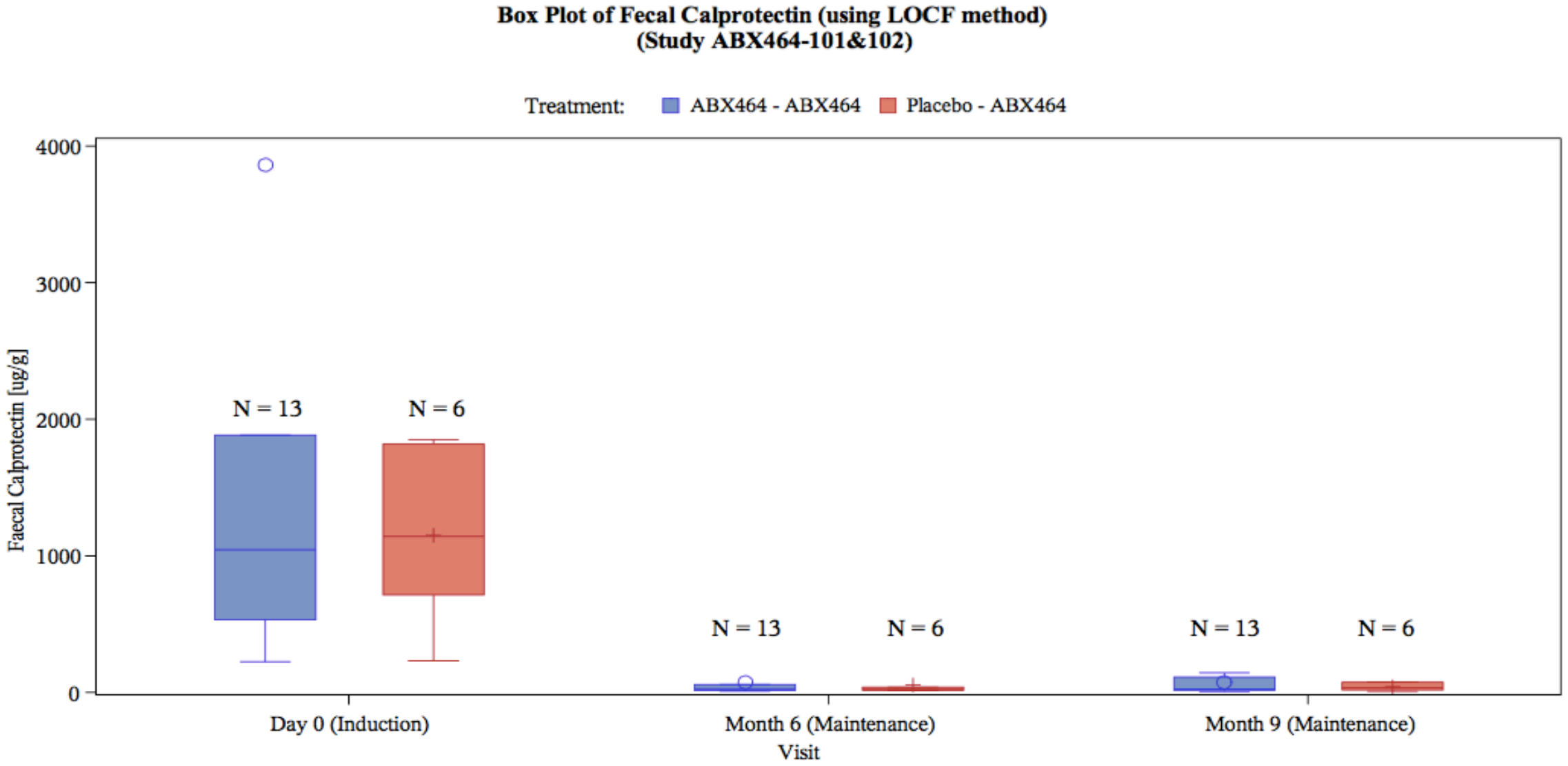
- 22/23 patients including 7 patients initially on placebo enrolled in the induction phase (2 countries did not grant regulatory clearance because of lack of efficacy data at the time of submission)
- 3 patients dropped out
  - One Lack of Efficacy at M1, initially on ABX464
  - One due to subject's decision despite clinical response at M4, initially on ABX464
  - One due to TEAE (Headache, grade 2, drug related according to PI) occurring 4 months after first dosing at M5, initially on placebo
- All other 19 patients ongoing
- As of May 20, 2019 the cumulative exposure is the following;

Mean (Days)	**415**
Median (Days)	401
Max (Dasy)	537
Min (Days)	321

Maintenance Phase : 6 and 9 Months interim analysis Partial Mayo Score



Maintenance Phase : 6 and 9 Months interim analysis Faecal Calprotectin



Maintenance Phase : 9 Months interim analysis

- At 9 months, all 19 patients were still in study
- From these 19 patients, 18 patients have clinical response :
  - 7 patients (6 initially on ABX464, 1 initially on PLO) were in clinical remission at the end of the 8 weeks induction phase. After 2 months maintenance, clinical remission was confirmed in all 7 patients and they all continued to have clinical response at month 9. Endoscopy is planned at month 12.
  - 12 patients (7 initially on ABX464, 5 initially on PLO) were not in clinical remission but 6 had clinical response at the end of the 8 weeks induction phase. After 2 months maintenance, 6 patients had endoscopic improvement and 11 patients have clinical response at month 9. Endoscopy is planned at month 12.
- Calprotectine levels normalised from median 1044 µg/g at baseline to 23,5 µg/g at Month 9.

Conclusions

- New mechanism of action ORAL drug ABX464
- Promising preclinical data in IBD model
- Good Safety and tolerability of ABX464 in UC patients and HIV program in more than 200 subjects treated (No Serious Adverse Reactions, no severe infections, no lymphopenia, no neutropenia)
- Confirmed preliminary efficacy in Phase 2a UC study
  - All endpoints favorable to ABX464
  - Fast onset of action
- Durability of effect :
  - Maintenance 6-month interim data
    - Partial Mayo Score continued to decrease
    - Faecal Calprotectin levels went down to values approaching normal values
  - Maintenance 9-months data confirm safety ad durability

ABX464 next steps

- Phase 2b study protocol in 232 patients with moderate to severe ulcerative colitis was submitted to regulatory agencies in first countries
  - Approved in Canada and first EU countries
  - Study open to recruitment of new sites

- Phase 2a studies are being submitted in Rheumatoid Arthritis and Crohn's disease

Acknowledgements

- Patients and investigators

COUNTRY	PRINCIPAL INVESTIGATOR	INSTITUTION
BELGIUM	**Prof. Sévérine Vermeire**	University Hospitals Leuven
FRANCE	**Prof. Xavier Hebuterne**	CHU de Nice - Hôpital Archet 2
	Dr Arnaud Boureille	CHU de Nantes - Hôtel Dieu
POLAND	**Dr Robert Petryka**	NZOZ ViVamed
	Dr Piotr Napora	Piotr Napora Centrum Badań Klinicznych Lekarze Sp.p.
	Dr Zając Przemysław	KO-Med
	Dr Maria Wisniewska-Jarosinska	SANTA FAMILIA, Centrum Badań, Profilaktyki i Leczenia
GERMANY	**Prof. Tanja Kuehbacher**	Asklepios Westklinikum Hamburg
HUNGARY	**Prof. Zsolt Tulassay**	Semmelweis Egyetem
	Dr Gyula G. Kiss	Vasútegészségügyi Nonprofit Közhasznú Kft
	Dr József Pauer	DRC Gyógyszervizsgáló Központ Kft.
AUSTRIA	**Prof. Herbert Tilg**	Univ.-Klinik für Innere Medizin I