UEG Week Virtual 2021

Oral ABX464 QD is efficacious and safe during phase 2b induction and maintenance treatment of ulcerative colitis patients

Presented by: **Prof. Séverine Vermeire, M.D., Ph.D.**
Head of the IBD Center at the University Hospitals Leuven, Belgium

Abivax late-breaking abstract authors:
Vermeire, S., Sandborn, W., Gineste, P., Tilg, H., Danese, S., Kempinski, R., Tulassay, Z., Nitcheu, J., Biguenet, S., Ehrlich, H. J., Steens, J. M., Sands, B. E.

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Disclosure of potential conflicts of interests

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Introduction

- **There is still a big need for alternative treatment options to treat patients with UC**
- **ABX464 is a first-in-class Small molecule**, administered as **once-daily oral capsule**
- **Novel mechanism of action:** Selective upregulation of anti-inflammatory microRNA, miR-124[1]
- **Good safety profile** after administration to >**850 patients and volunteers, also in HIV and RA**
- **Short- and long-term anti-inflammatory effect were identified in a** phase 2a study in UC[2]

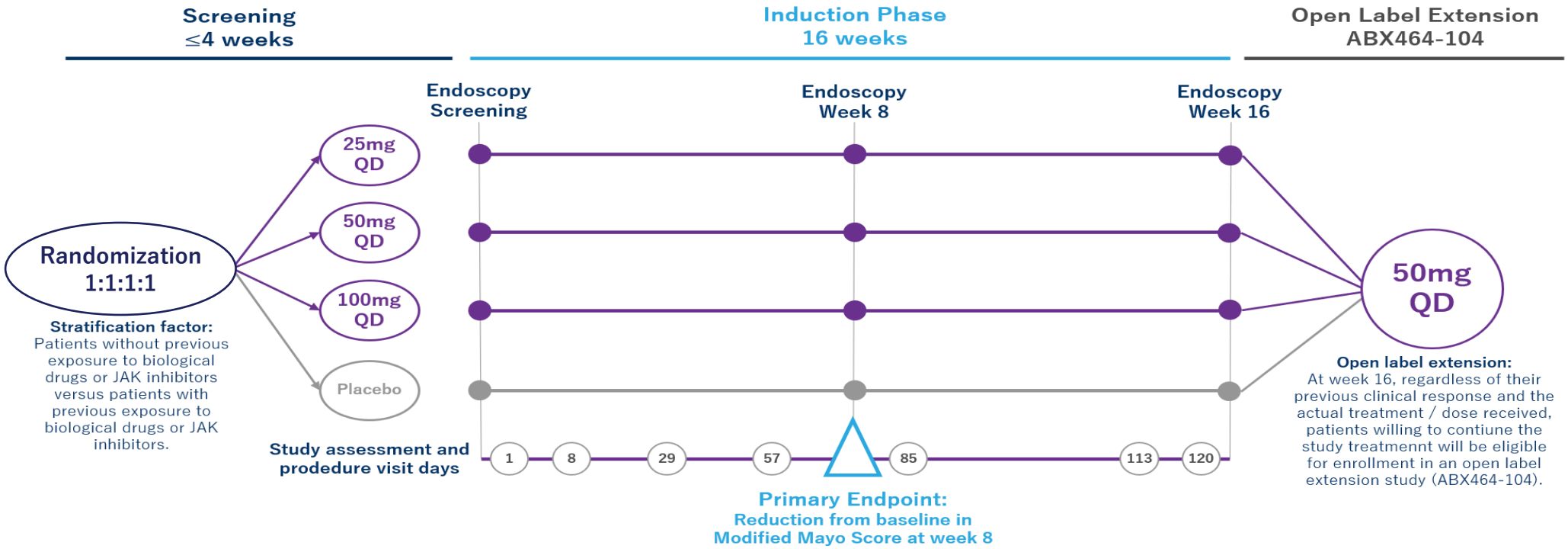
1. **Tazi J et al Drug Discov Today 2021; 26:1030-1039**
2. **Vermeire s et al Gastroenterology 2021; 160:2595-2598**

Aim and study design

A **randomized**, **double-blind**, **placebo-controlled** phase 2b induction study in **patients** with **moderate to severe UC** was conducted to evaluate the **efficacy and safety** of **3 daily doses of ABX464** (25, 50 and 100mg), followed by an **open label maintenance** (50mg QD).

Study design:
ABX464 phase 2b clinical study in patients with moderate-to-severe ulcerative colitis

- 254 patients in 15 countries in Europe, US and Canada (130 study sites)
- Moderate-to-severe active UC (Modified Mayo Score 5-9)
- Central reading of endoscopies



Primary and secondary endpoints

Primary endpoint

Reduction from baseline in Modified Mayo Score at week 8

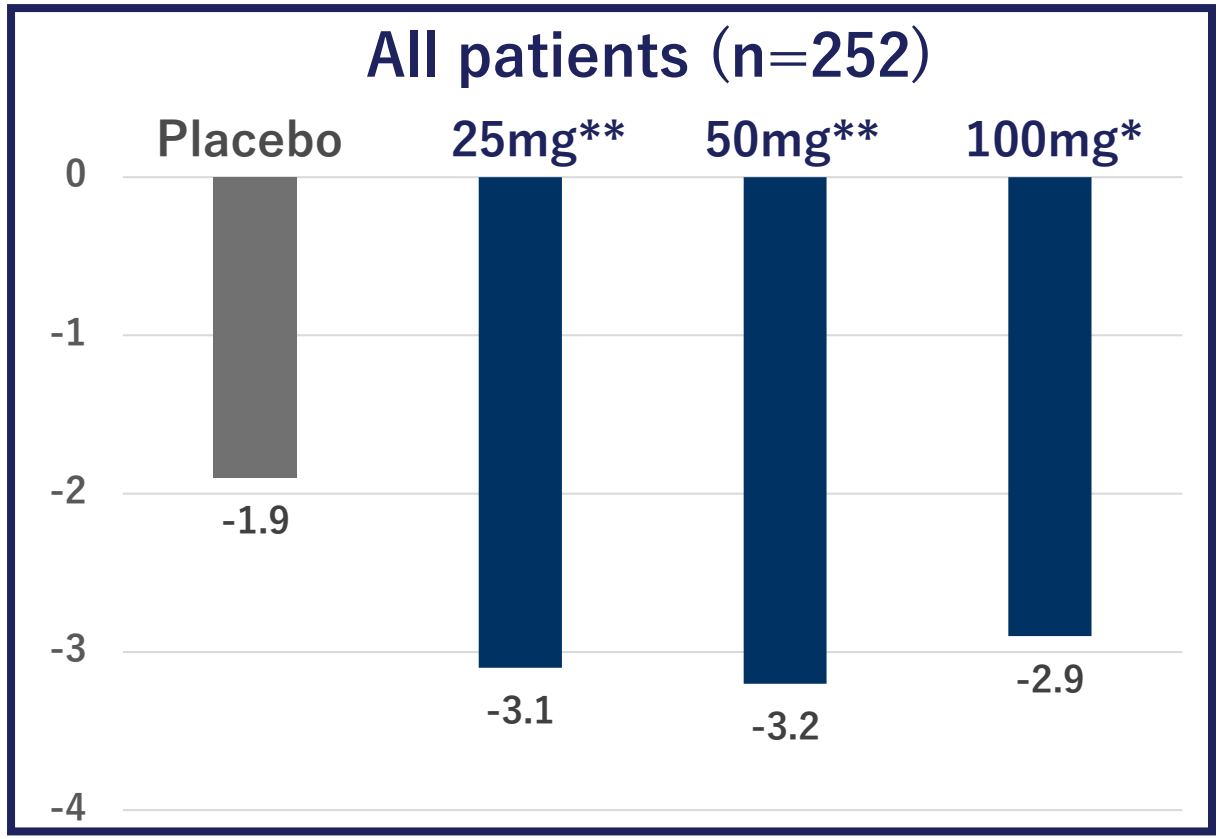
Key secondary endpoints

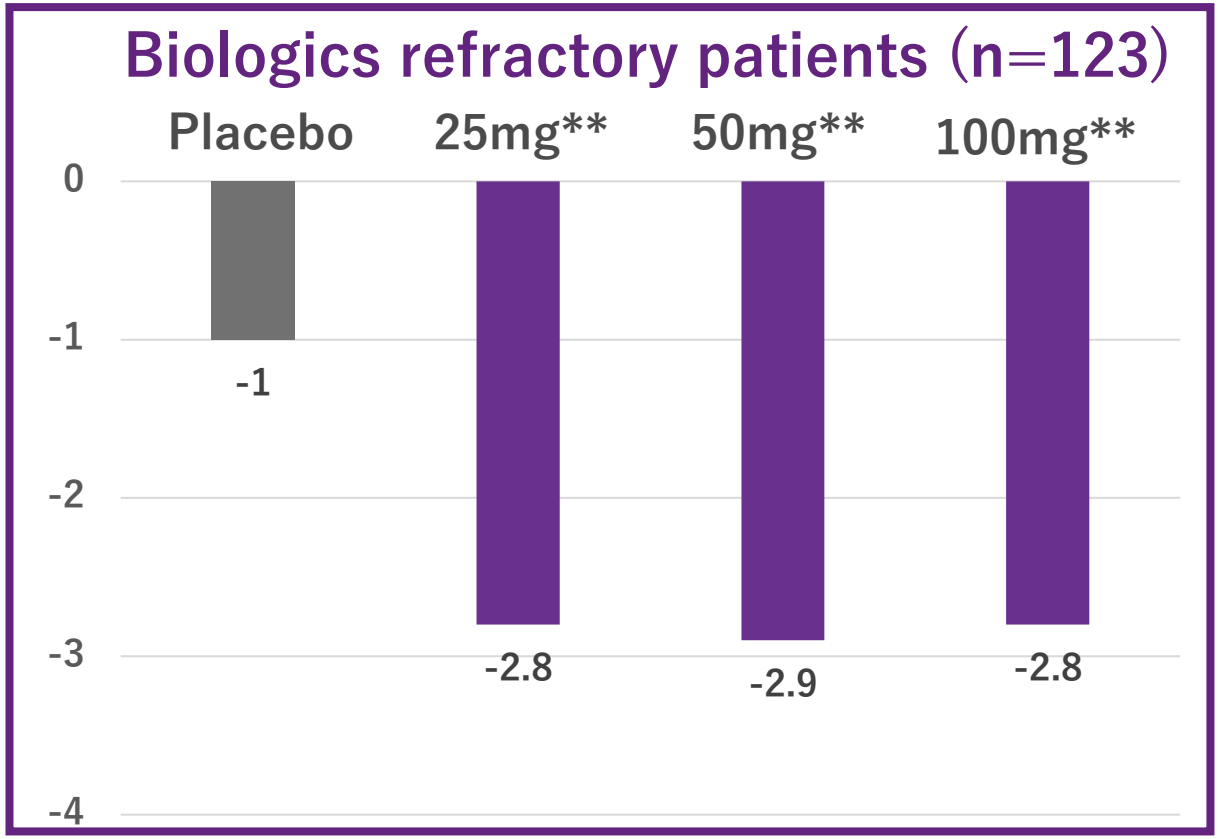
1. **Number and rate of patients in clinical remission** (stool frequency subscore (SFS) ≤1, rectal bleeding subscore (RBS) of 0 and endoscopic subscore ≤1)
2. **Number and rate of patients with clinical response** (decrease from baseline in the Modified Mayo Score ≥2 points and ≥30 percent from baseline, plus a decrease in RBS ≥1 or an absolute RBS ≤1)
3. **Number and rate of patients with endoscopic improvement** (endoscopic subscore ≤1)
4. **Reduction relative to baseline in partial Modified Mayo Score**
5. **Reduction relative to baseline in fecal calprotectin**
6. **Reduction relative to baseline in Robarts Histopathology Index**

Phase 2b: Baseline characteristics

		100mg	50mg	25 mg	Placebo
		(N=64)	(N=63)	(N=61)	(N=64)
Age (years)	Mean (SD)	42.2 (12.34)	40.2 (13.94)	41.5 (14.16)	41.1 (14.43)
Male	n (%)	41 (64.1)	27 (42.9)	40 (65.6)	40 (62.5)
Modified Mayo Score (MMS)	Mean (SD)	7.0 (1.07)	7.1 (0.96)	7.1 (1.09)	7.0 (1.20)
7 to 9	n (%)	47 (73.4)	47 (74.6)	44 (72.1)	42 (65.6)
Endoscopic sub-score = 3	%	66%	75%	67%	75%
Duration of disease (years)	Mean (SD)	7.77 (7.291)	8.22 (7.785)	7.35 (6.848)	8.82 (6.783)
Fecal Calprotectin (µg/g)	Median	1623	1671	1743	1558
Previous exposure to biologics/Tofacitinib	n (%)	32 (50.0)	30 (47.6)	30 (49.2)	31 (48.4)
TNF-α	n (%)	31 (48.4)	25 (39.7)	25 (41.0)	27 (42.2)
Vedolizumab	n (%)	20 (31.3)	20 (31.7)	19 (31.1)	22 (34.4)
Tofacitinib	n (%)	13 (20.3)	12 (19.0)	10 (16.4)	12 (18.8)
Concomitant UC Medication					
Corticosteroids	n (%)	37 (57.8)	33 (52.4)	32 (52.5)	29 (45.3)
Immunosuppressants	n (%)	6 (9.4)	9 (14.3)	10 (16.4)	10 (15.6)

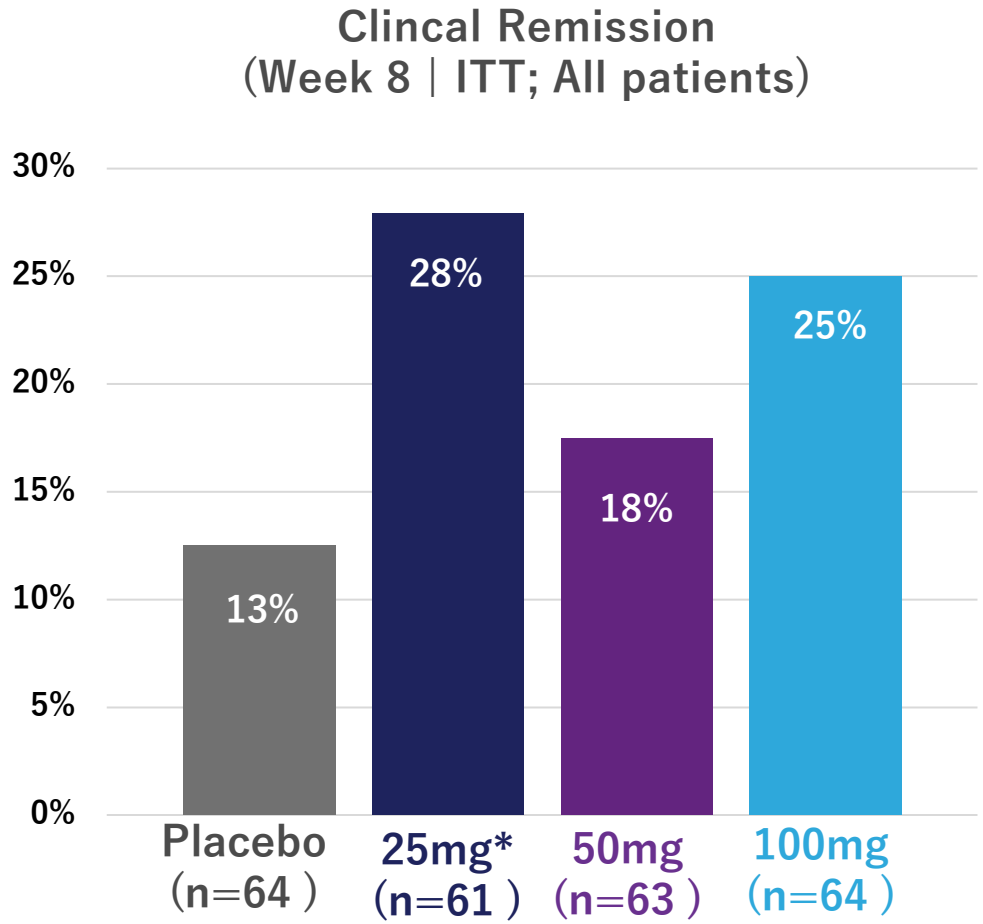
Primary endpoint: Mean change from baseline in Modified Mayo Score



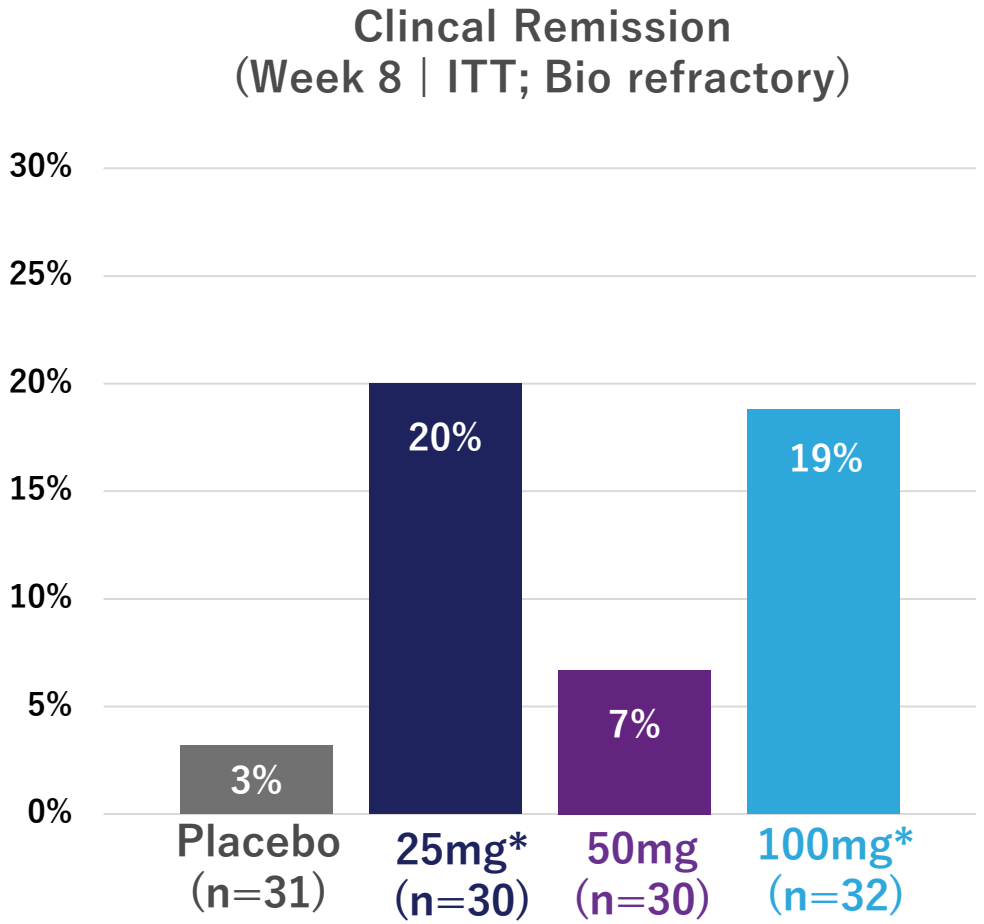


*p-values of <0.01 versus placebo (ANCOVA)
**p-values of <0.001 versus placebo (ANCOVA)

Phase 2b top-line week 8 efficacy results (ITT): Secondary endpoints



*p-values of <0.05 versus placebo using a likelihood ratio chi-square test but not according to the predefined Mantel-Haenszel Chi Square test (p=0.06 to 0.08)



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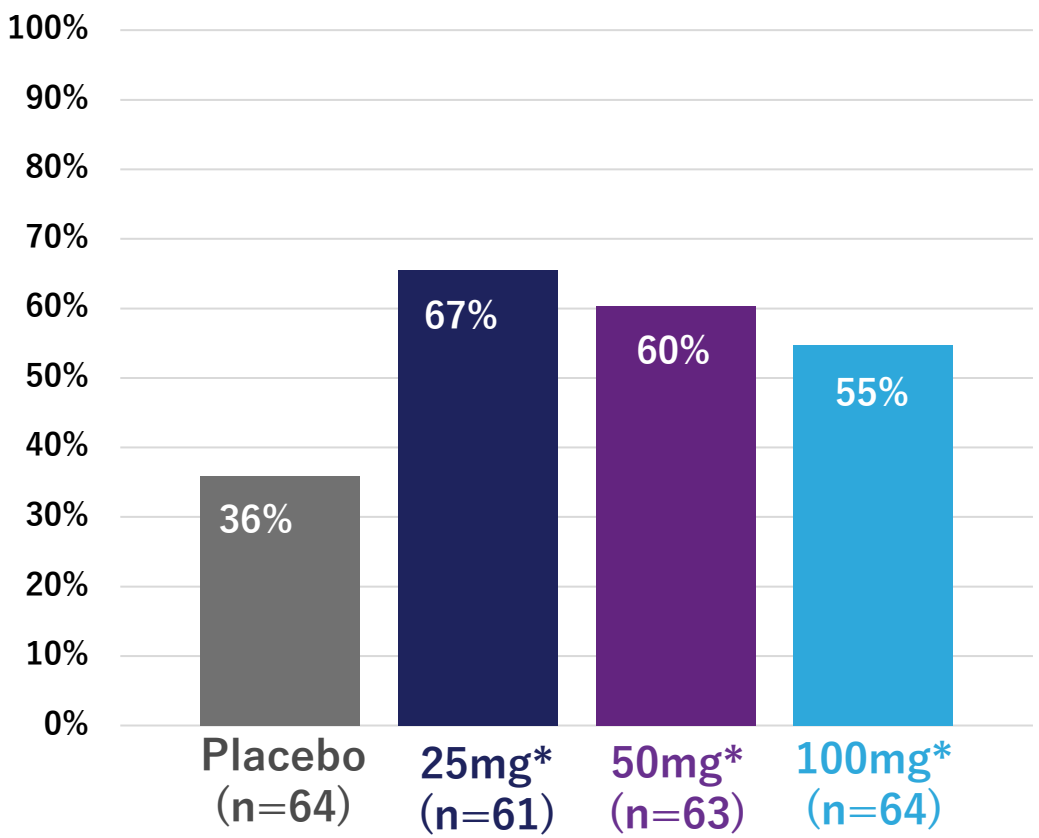
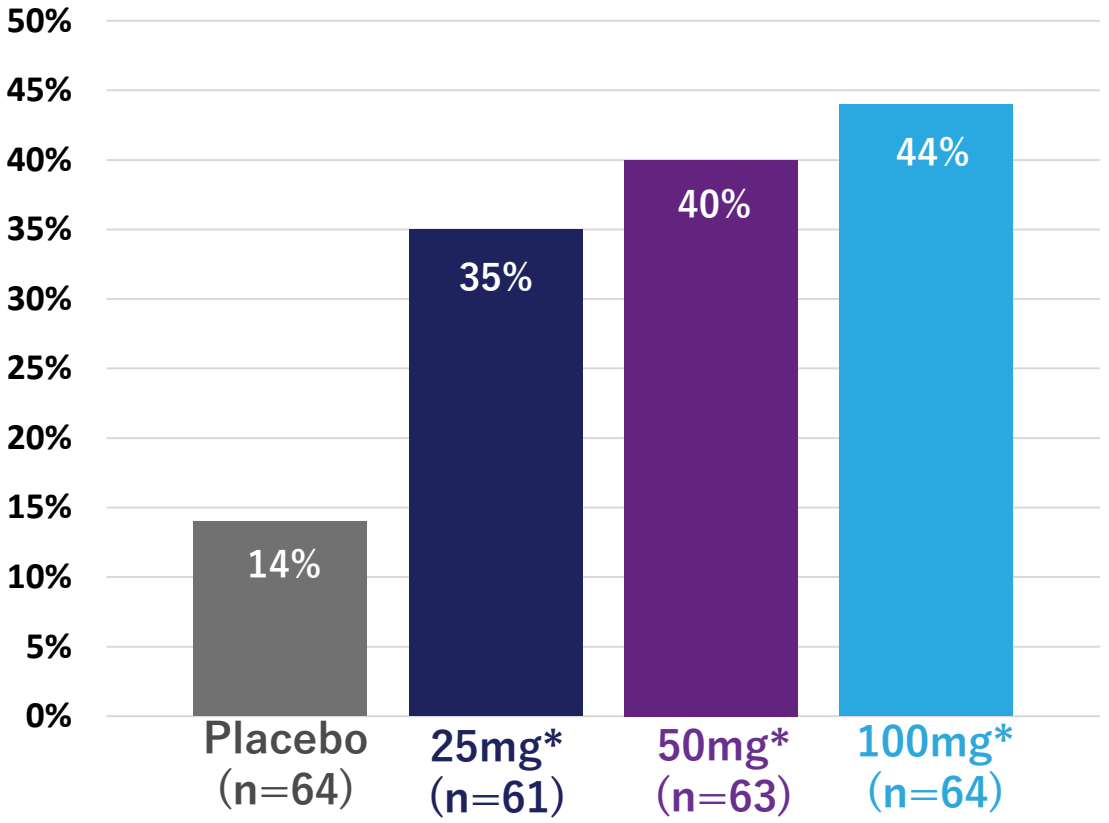
Phase 2b top-line week 8 efficacy results (ITT): Secondary endpoints

Clincal Response (Week 8 | ITT; All patients)



*p-values of <0.05 versus placebo using a likelihood ratio chi-square test

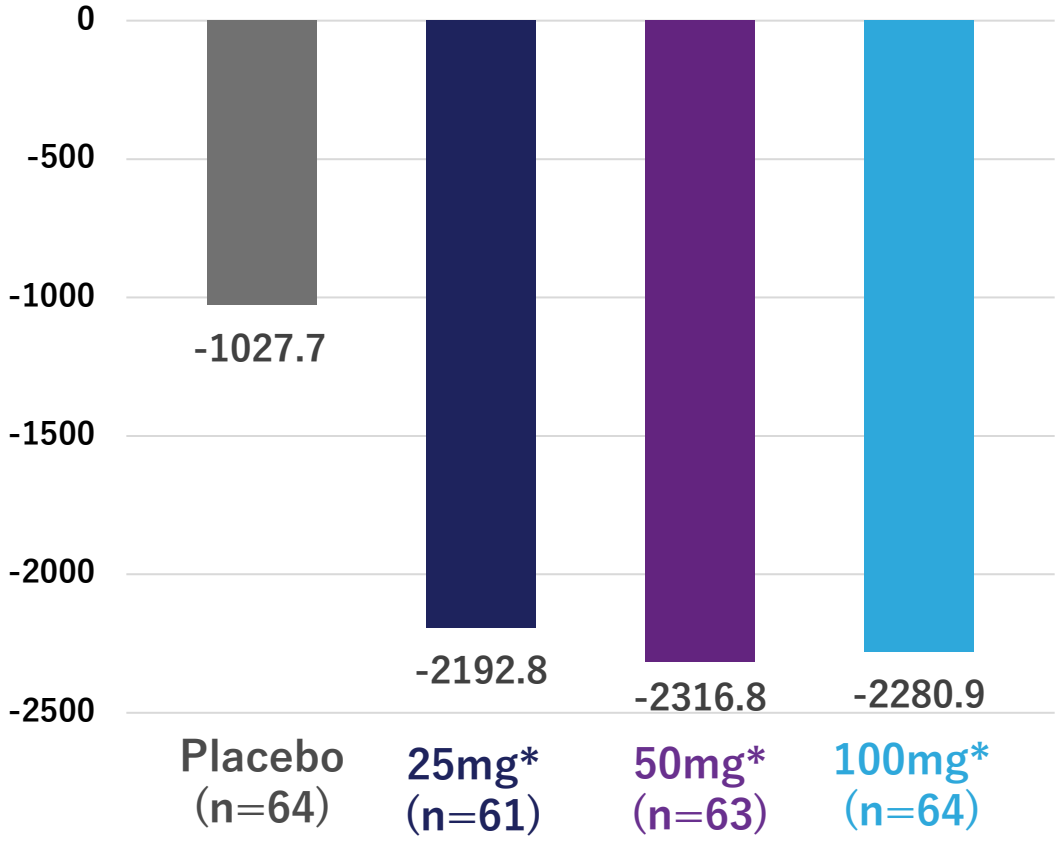
Endoscopic improvement (Week 8 | ITT; All patients)



*p-values of <0.05 versus placebo using a likelihood ratio chi-square test

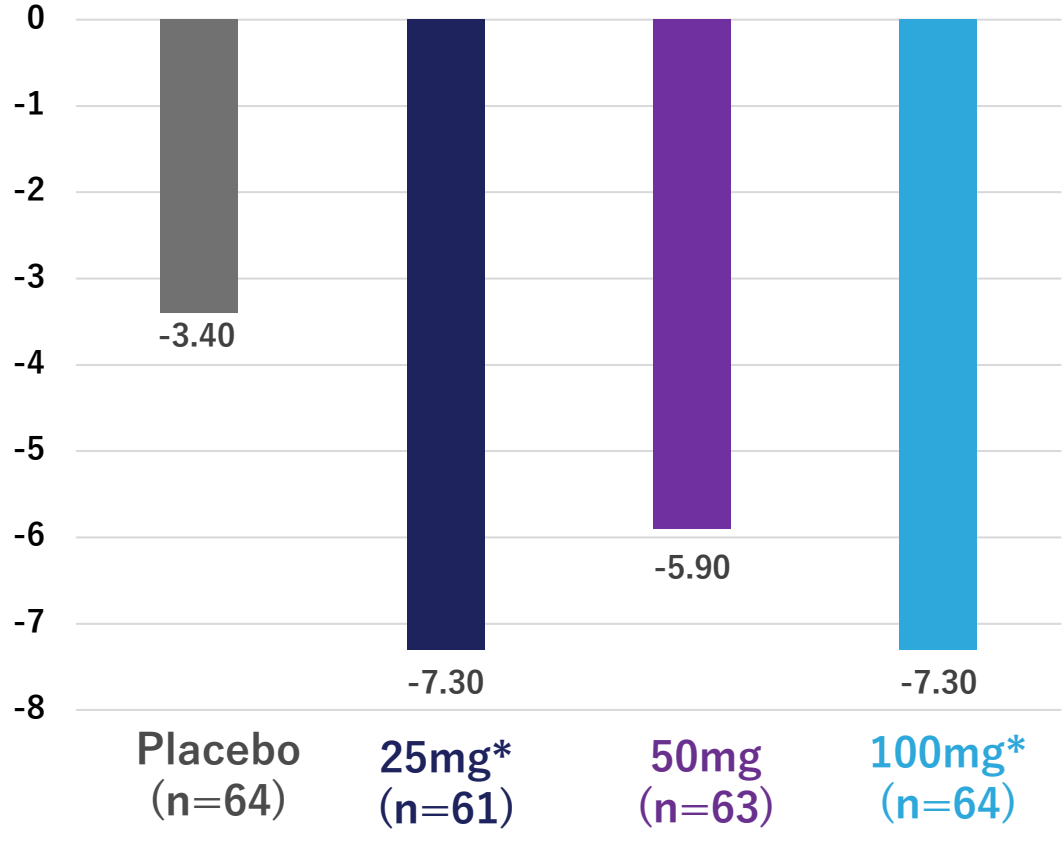
Secondary endpoints: Fecal calprotectin and Robarts Histopathology Index

Mean Change from baseline in Fecal calprotectin (µg/g)



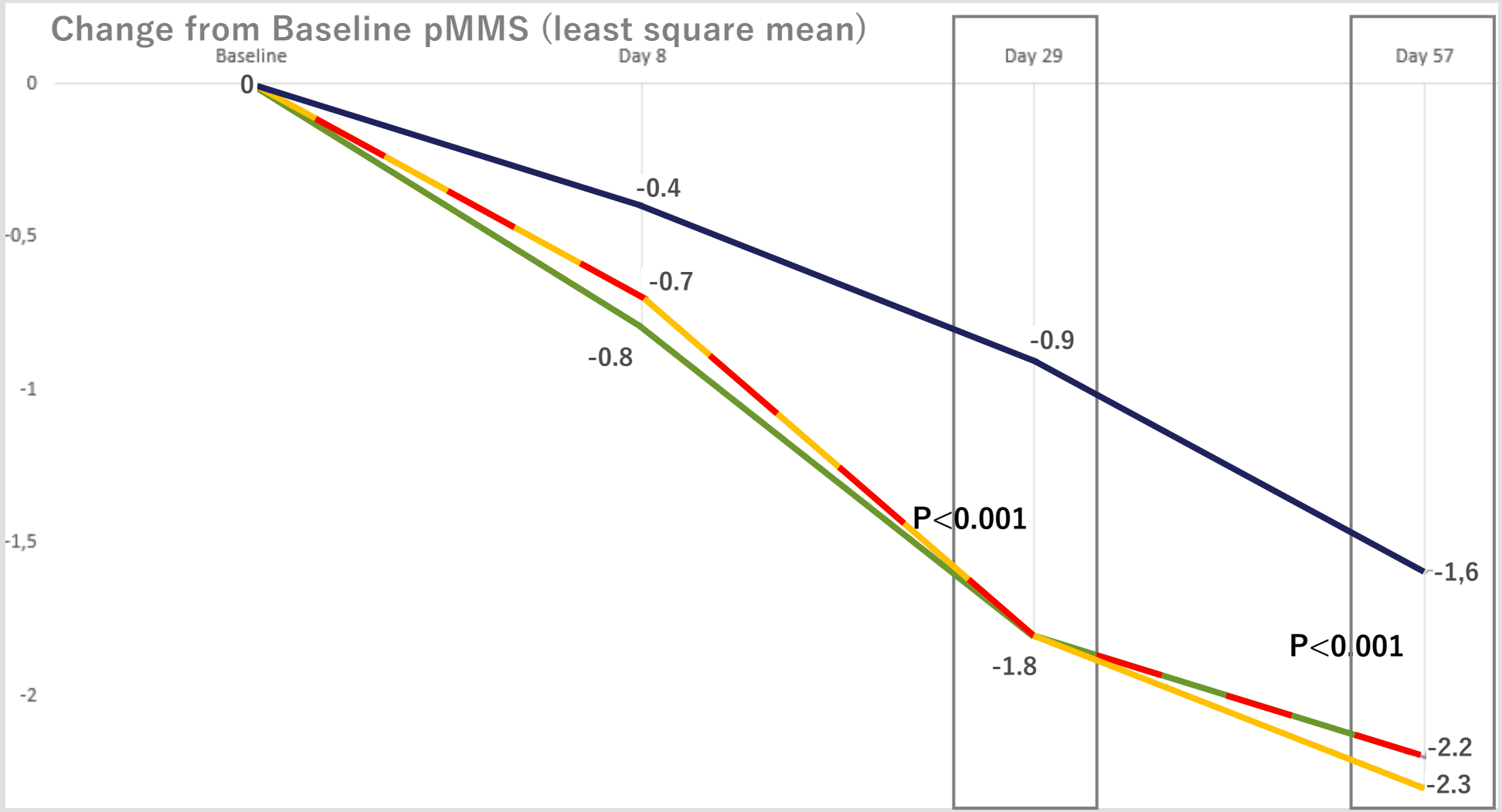
*p-values of <0.01 versus placebo (MMRM)

Change from baseline in Robarts Histopathology Index



*p-values of <0.05 versus placebo (MMRM)

Phase 2b efficacy results (ITT): Onset of action



------ Placebo

------ 100mg

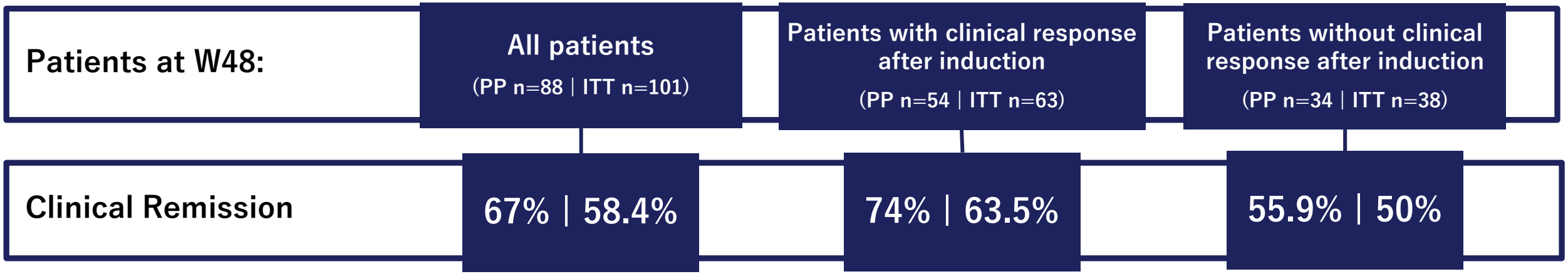
------- 50mg

------- 25mg

ABX464 phase 2b maintenance study

217/222 eligible patients enrolled into maintenance

The first 101 patients* of the 217 were to complete 1st year of maintenance by 15/09/21:
(12 patients were drop-outs, and no data available for 1 patient at W48,
these 13 patients were considered treatment failures in ITT)



*Irrespective of patient outcome at the end of the induction phase

Safety data from 16-week induction study
Most common (> 5%) Adverse Events (AE): Drug-related or non-drug-related

System Organ Class	Adverse effect	Placebo (N=64)	ABX464 25mg (N=63)	ABX464 50mg (N=63)	ABX464 100mg (N=64)
		n (%) of pts with AE (Incidence)	n (%) of pts with AE (Incidence)	n (%) of pts with AE (Incidence)	n (%) of pts with AE (Incidence)
Nervous System Disorders	Headache	5 (7.8)	13 (20.6)	19 (30.2)	27 (42.2)
Gastrointestinal Disorders	Nausea	4 (6.3)	5 (7.9)	4 (6.3)	9 (14.1)
	Vomiting	1 (1.6)	1 (1.6)	2 (3.2)	5 (7.8)
	Upper abdominal pain	0 (0)	3 (4.8)	3 (4.8)	4 (6.3)
Musculo-skeletal Disorders	Arthralgia	3 (4.7)	1 (1.6)	1 (1.6)	5 (7.8)
	Myalgia	0 (0)	0 (0)	0 (0)	5 (7.8)

Most frequently reported adverse events are transient (few days) and mild (headache, nausea, gastrointestinal pain) and manageable with or without OTC medications

No death and no malignancy

25mg shows a similar safety profile as observed in the placebo group (except transient headaches)

Summary

- In this Phase 2b induction study with ABX464, the primary endpoint (reduction of Modified Mayo Score) was met with once-daily ABX464 (25mg, 50mg, 100mg) at week 8
- Key secondary endpoints, including endoscopic improvement, clinical response and remission, and reduction in fecal calprotectin showed significant difference in patients on ABX464 compared to placebo
- ABX464 showed a fast onset of action, including in patients who were refractory to biologics and/or JAK inhibitors treatment
- ABX464 was safe and well tolerated
- Data from the first 101 patients treated with ABX464 50mg in the open-label maintenance study showed durable clinical remission after 48 weeks
- Based on these results, a phase 3 program in moderate to severe UC will soon be initiated

Abivax Industry Symposium at UEG Week Virtual 2021

Program

Prof. William Sandborn, M.D.

San Diego, CA, USA

The continued need to develop novel drugs for ulcerative colitis

Didier Scherrer, Ph.D.

Montpellier, France

ABX464 novel mechanism of action: Upregulation of the anti-inflammatory microRNA miR-124

Prof. Bruce Sands, M.D., M.S.

New York City, NY, USA

Safety and efficacy of ABX464 in a phase 2b study in ulcerative colitis