A turning story towards ulcerative colitis and other inflammatory diseases

"In general, less than 1/3 of patients with ulcerative colitis achieve "clinical remission" with currently available treatments during induction treatment. Among those, about 50% lose their responsiveness to treatment after 6 to 12 months, so there is a large unmet need for new safe and effective therapies."
Prof. W. Sandborn, M.D., UC San Diego School of Medicine.

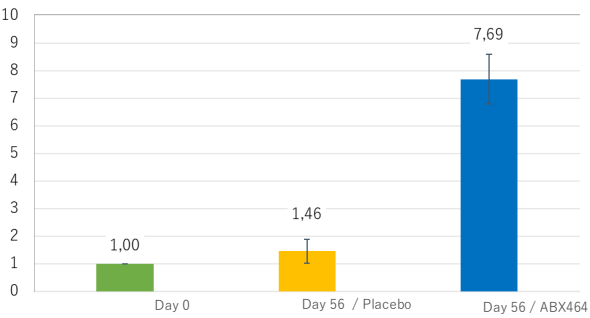
ABOUT ABIVAX

Abivax is a clinical stage biotechnology company developing therapies that modulate the immune system to treat inflammatory diseases, infectious diseases, and cancer. Having recently published the unique mechanism of action of its lead clinical drug candidate, ABX464, Abivax has discovered this oral candidate's broad therapeutic potential across multiple inflammatory diseases and is studying its effects in Ulcerative Colitis in an ongoing Phase 2b clinical trial, as well as in Rheumatoid Arthritis and Crohn's Disease in two Phase 2a trials.

More information on the company is available at www.abivax.com. Follow us on LinkedIn and Twitter @ABIVAX_

ABOUT ABX464

ABX464 is an orally administered small molecule drug candidate, which has been shown to exert its anti-inflammatory effects through a novel mechanism of action[(1)]. ABX464 binds to the cap binding complex (CBC), which essentially sits at the 5' end of every RNA molecule in the cell. By binding to the CBC, ABX464 reinforces the biological functions of this complex in cellular RNA biogenesis. Specifically, ABX464 enhances the selective splicing of a single long non-coding RNA to generate in patients the anti-inflammatory microRNA, miR-124.



miR-124 expression in rectal biopsies of patients with Ulcerative Colitis Fold induction (ratio) / Phase 2a Study

miR-124 downregulates pro-inflammatory cytokines and chemokines like TNF-α, IL-6 and MCP-1, thereby putting a brake on inflammation and suggesting broad potential as a novel anti-inflammatory therapeutic agent. A seven- to ten-fold increase in miR124 levels was observed in peripheral blood mononuclear cells (PBMCs) from healthy volunteers upon exposure to ABX464 and also in colorectal biopsies of UC patients treated with ABX464. ABX464 does not impact the splicing of cellular genes.

CLINICAL EXPERIENCE WITH ABX464 IN ULCERATIVE COLITIS

The ABX464-101 induction study showed a rapid onset of clinical improvements as well as efficacy in patients naïve or resistant to biologics

The Phase 2a induction study ABX464-101 was a randomized, double-blind, placebo-controlled Phase 2a induction study evaluating the safety and efficacy of ABX464. Patients with moderate to severe active ulcerative colitis who have failed immunomodulators, anti-TNF-α, vedolizumab and/or corticosteroids were given 50 mg of ABX464 orally, once-daily for two months. The study was conducted at 15 centers in six European countries. Of the 32 recruited patients, randomized 2:1 to receive ABX464 as a once-daily oral tablet or placebo, 29 completed the study per protocol.

The results of this study were reported in September 2018 and showed a rapid onset of efficacy within 2 weeks after initiation of treatment[(2)]. At the end the 8-week induction of treatment, clinical remission was observed in 35% of the ABX464 treated patients (placebo: 11%) and mucosal healing in 50% (placebo: 11%, p = 0.03). The efficacy of ABX464 was similar in patients naive or resistant to biologics (e.g. anti-TNF-α or Vedolizumab).

As shown in the table, the results from all the endpoints were in favor of the ABX464 arm.

	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

ABIVAX presented 9-month ABX464-102 maintenance study results that confirmed durability of safety and efficacy of ABX464

Patients who completed the ABX464-101 study had the option to roll over into a 12-month open-label extension study, ABX464-102, in which 22 out of 23 eligible patients were enrolled. Nine-month interim data from ABX464-102 presented at the DDW (Digestive Disease Week) annual conference in May 2019 in San Diego showed that 19 of 22 patients were still on study, and similar to the induction study ABX464-101, ABX464 was safe and well tolerated. The Partial Mayo Score continued to decrease, and fecal calprotectin levels went down to normal levels. Of these 19 patients, 18 demonstrated a sustained clinical response. Clinical remission, including results of endoscopy will be assessed at Month 12 according to the study protocol.

Levels of fecal calprotectin, the biological marker for inflammatory bowel disease (IBD), sharply decreased from a median of 1,044 μg/g at baseline of the induction study to 24 μg/g at nine months of the maintenance study, thus reaching normal levels in healthy individuals (< 50 μg/g), which is indicative of mucosal healing.

The initial 12-month maintenance study was approved by all concerned regulatory authorities and ethics committees to be extended for a second year.

Please join us at the breakfast symposium chaired by Prof. William Sandborn, M.D., from the University of California San Diego School of Medicine to be held on Monday 21st October from 7:00 am to 8:00 am in room E2 where the 12-Month maintenance data will be presented.

This symposium is not affiliated with UEG.

THE PHASE 2B DOSE RANGING HAS STARTED

The Phase 2b trial ABX464-103 is a randomized, double-blind, placebo-controlled, dose-ranging study in 232 UC patients that has four arms: three with escalating doses of once-daily oral ABX464 (25 mg/day, 50 mg/day and 100 mg/day) and one placebo arm.

The study is conducted at up to 150 study sites in more than 15 countries under the leadership of its steering committee (Prof. Séverine Vermeire, M.D., Ph.D., University Hospitals Leuven, Belgium, Prof. Herbert Tilg, M.D. Ph.D., Medical University Innsbruck, Austria, Prof. Xavier Hebuterne, M.D., Ph.D., University Hospital Nice, France, and Prof. William Sandborn, M.D., University of California San Diego School of Medicine, USA) and includes an induction phase followed by an open-label maintenance study with ABX464.

Patient enrollment has commenced, and the study continues to recruit additional new trial centers.

For further information, please contact either Dr. Jean-Marc Steens (Jean-Marc.Steens@abivax.com) **or Dr. Paul Gineste** (Paul.Gineste@abivax.com)

References:

1) Nature Scientific Reports volume 9, article number 792 (2019): "BOTH ANTI-INFLAMMATORY AND ANTIVIRAL PROPERTIES OF NOVEL DRUG CANDIDATE ABX464 ARE MEDIATED BY MODULATION OF RNA SPLICING"

2) San Diego abstract: DDW San Diego May 21 2019: Vermeire et al: "ABX464 IS SAFE AND EFFICACIOUS IN PROOF OF CONCEPT STUDY IN ULCERATIVE COLITIS PATIENTS" (Presentation Number: 1007)

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