P0712 - Integrated summary of safety of obefazimod in Phase 3 ABTECT induction trials

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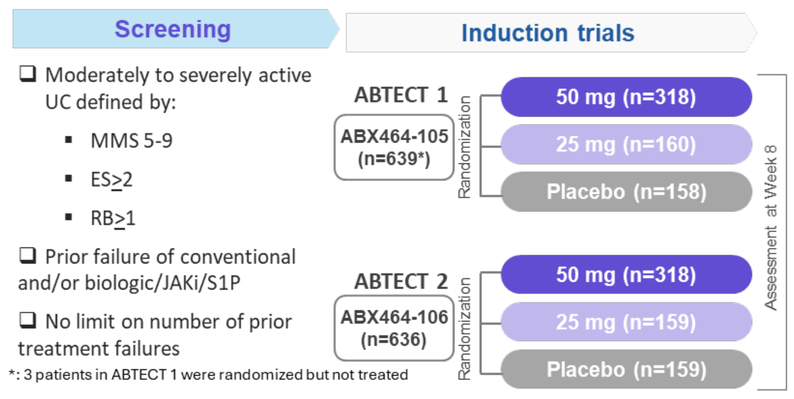
Background

- Obefazimod (Obe) is an oral, once-daily (QD), small molecule that enhances expression of microRNA-124, which restores mucosal immune balance through regulation of Th17 cells and macrophages. Obe has shown efficacy in patients (pts) with moderately to severely active ulcerative colitis (UC) [1-3].
- In the two Phase 3 ABTECT induction trials (Fig. 1), Obe achieved clinically meaningful improvements in clinical, endoscopic and histologic endpoints.
- Here, we report an integrated safety analysis of Obe in the two ABTECT trials.

Fig. 1: Design of ABTECT induction trials



Methods

- Treatment emergent adverse events (TEAEs), serious TEAEs, discontinuation rates and primary reasons were assessed in the pooled population from ABTECT-1 [NCT05507203] and ABTECT-2 [NCT05507216] among pts who received Obe 50 mg QD (Obe-50), Obe 25 mg QD (Obe-25), or placebo (PBO) for 8 weeks, randomized to 2:1:1.

Results

- 1272 pts were randomized and treated in ABTECT induction trials. Baseline demographics and disease characteristics were comparable across Obe-50, Obe-25 and PBO groups with median exposures of 60, 61, and 61 days, respectively (Table 1).
- Proportions of pts who reported at least one TEAE were 60.2%, 48.9%, and 50.8% for Obe-50, Obe-25, and PBO, respectively (Table 1).
- The most frequent TEAEs included headache, nausea, abdominal pain, and lipase increased.
- TEAEs leading to study discontinuation occurred at similar rates across treatment groups (Obe-50: 4.7%, Obe-25: 1.9%, PBO: 4.1%) (Table 1).
- No signal for serious, severe, or opportunistic infections or malignancies was observed (Table 1).
- The overall rates of serious TEAEs for pts were comparable across groups (Obe-50: 3.1%, Obe-25: 2.2%, PBO: 3.2%) (Tables 1 & 2).
- No clustering of serious TEAEs was observed; only worsening of UC and pneumonia were reported more than once in any individual treatment arm (Table 2).

Table 1: Integrated Summary of Adverse Events of Obe in Phase 3 ABTECT Induction Trials: Safety Set

	Obe-50 (n=636)	Obe-25 (n=319)	PBO (n=317)
Duration of exposure, days, mean (SD)	58.8 (12.6)	59.5 (11.1)	58.7 (11.1)
Median	60.0	61.0	61.0
[Min, Max]	[1, 106]	[4, 96]	[5, 102]
Any TEAEs, n (%)	383 (60.2)	156 (48.9)	161 (50.8)
TEAE related to study drug, n (%)	226 (35.5)	86 (27.0)	55 (17.4)
TEAE leading to study discontinuation, n (%)	30 (4.7)	6 (1.9)	13 (4.1)
Related TEAE leading to study discontinuation, n (%)	20 (3.1)	4 (1.3)	6 (1.9)
Serious TEAE, n (%)	20 (3.1)	7 (2.2)	10 (3.2)
Related serious TEAE, n (%)	3 (0.5)	2 (0.6)	2 (0.6)
TEAE leading to death, n (%)	0	0	0
Malignancies	1 (0.2)[a]	0	0
Serious/severe/opportunistic infections	4 (0.6)[§]	1 (0.3)[¥]	1 (0.3)[‡]
TEAEs occurring in patients (≥3% in Obe groups and greater than PBO), n (%)			
Headache	148 (23.3)	48 (15.0)	18 (5.7)
Nausea	46 (7.2)	16 (5.0)	4 (1.3)
Abdominal pain	24 (3.8)	2 (0.6)	2 (0.6)
Lipase increased[b]	27 (4.2)	9 (2.8)	7 (2.2)

a: Prostate cancer stage I. b: To date, no safety signals have been observed related to either elevations in lipase or more specifically to pancreatitis.
§: Pneumonia (2), anal abscess, COVID-19; ¥: Appendicitis; ‡: Bronchopulmonary aspergillosis.

- Headache TEAEs were mild, transient, short in duration (median: 2-3 days) and rarely led to discontinuation (0-1.1%) (Tables 3 & 4).

Table 3: Headaches in ABTECT Induction Trials

	Obe-50 (n=636)	Obe-25 (n=319)	PBO (n=317)
Time to onset of first TE headache per patient, days, median	1.0	1.0	7.0
Duration of headache for all TE headaches, days, median	2.0	3.0	2.0

- Rates of pts who discontinued the study occurred at similar rates across treatment groups (Table 4).

Table 4: Discontinuations in ABTECT Induction Trials

	Obe-50 (n=636)	Obe-25 (n=319)	PBO (n=317)
Patients who discontinued the study, n (%)[a]	54 (8.5)	23 (7.2)	31 (9.7)
Reason for study discontinuation, n (%)[b]			
Adverse event	31 (57.4)	8 (34.8)	14 (45.2)
Withdrawal by subject	13 (24.1)	10 (43.5)	10 (32.3)
Lack of efficacy	2 (3.7)	2 (8.7)	1 (3.2)
Lost to follow-up	4 (7.4)	1 (4.3)	1 (3.2)
Noncompliance with study drug	2 (3.7)	0	0
Protocol deviation	1 (1.9)	1 (4.3)	3 (9.7)
Physician decision	1 (1.9)	0	1 (3.2)
Never dosed	0	1 (4.3)	1 (3.2)
TEAEs (>1 in Obe groups) leading to study drug discontinuation			
Ulcerative colitis	7 (1.1)	2 (0.6)	7 (2.2)
Headache	7 (1.1)	1 (0.3)	0
Vomiting	4 (0.6)	1 (0.3)	0
Abdominal pain upper	3 (0.5)	0	0
Nausea	3 (0.5)	1 (0.3)	0
Pancreatitis acute	2 (0.3)	1 (0.3)	1 (0.3)

a: Percentages are calculated relative to the number of randomized patients (ie, n=636, 320, 319 for Obe-50, Obe-25, PBO, respectively).
b: Percentages are calculated relative to the number of patients who discontinued the study.

Table 2: Serious TEAEs in ABTECT Induction Trials

	Obe-50 (n=636)	Obe-25 (n=319)	PBO (n=317)
Serious TEAE, n (%)	**20 (3.1)**	**7 (2.2)**	**10 (3.2)**
Colitis ulcerative	5 (0.8)	2 (0.6)	5 (1.6)
Gastritis	1 (0.2)	0	0
Pancreatitis	1 (0.2)	0	0
Pancreatitis acute	1 (0.2)	1 (0.3)	1 (0.3)
Vomiting	1 (0.2)	0	0
Anal inflammation	0	0	1 (0.3)
Pneumonia	2 (0.3)	0	0
Anal abscess	1 (0.2)	0	0
Appendicitis	0	1 (0.3)	0
Clavicle fracture	1 (0.2)	0	0
Procedural dizziness	1 (0.2)	0	0
Anaemia	1 (0.2)	0	0
Blood loss anaemia	0	0	1 (0.3)
Myocardial infarction	1 (0.2)	0	0
Acute coronary syndrome	0	0	1 (0.3)
Type 2 diabetes mellitus	1 (0.2)	0	0
Prostate cancer stage I	1 (0.2)	0	0
Migraine	1 (0.2)	0	0
Calculus bladder	1 (0.2)	0	0
Pyrexia	0	0	1 (0.3)
Lipase increased	0	1 (0.3)	0
Pleurisy	0	1 (0.3)	0
Vasculitis	0	0	1 (0.3)

Conclusions

This integrated safety analysis of the two completed Phase 3 ABTECT induction trials in moderately to severely active UC showed a favorable safety and tolerability profile of obefazimod as observed in Phase 2 trials.

References 1: Vermeire S et al. *J Crohns Colitis*. 17: 1689-97, 2023 - 2: Vermeire S et al. *Gastroenterology*. 160: 2595-98, 2021 - 3: Vermeire S et al. *The Lancet Gastroenterology & Hepatology*. 7: 1024-35, 2022

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