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113 - IMPACT OF INFLAMMATORY BURDEN ON EFFICACY OF UPADACITINIB MAINTENANCE THERAPY IN ULCERATIVE COLITIS: RESULTS FROM THE PHASE 3 U-ACHIEVE STUDY

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Resumen

Introduction: Upadacitinib (UPA) is an oral selective and reversible Janus kinase inhibitor. Data are limited on the impact of inflammatory burden on the efficacy of the two maintenance doses of UPA (30 mg and 15 mg once daily [QD]).

Methods: The primary efficacy analysis of U-ACHIEVE Maintenance included the first 451 patients who achieved a clinical response after 8 weeks of UPA 45 mg QD treatment. The primary endpoint was clinical remission per Adapted Mayo score at week (wk) 52 and a key secondary endpoint was endoscopic improvement at wk 52. This post hoc analysis evaluated the efficacy, based on these endpoints, of UPA 30 mg *vs.* UPA 15 mg maintenance therapy in patients in U-ACHIEVE Maintenance stratified by three measures of inflammatory burden: baseline Full Mayo score > 9 *vs.* ≤ 9, presence of pancolitis (yes *vs.* no), and presence of ≥ 1 extraintestinal manifestation (yes *vs.* no).

Results: Both UPA 30 mg and UPA 15 mg demonstrated favorable efficacy compared with PBO, regardless of the inflammatory burden. However, the differences in proportions of responders who achieved clinical remission at wk 52 with UPA 30 mg *vs.* UPA 15 mg were greater in patients with a high inflammatory burden (difference: 12.0 -22.0%) than those without high inflammatory burden (difference: 1.4-6.2%). Similar results were seen for endoscopic improvement at wk 52 (high inflammatory burden [difference: 12.0-26.1%] relative to those without high inflammatory burden [difference: 0.2-14.1%]).

	PBO, n/N (%) (N=149)	UPA 15 mg QD, n/N (%) (N=148)	UPA 30 mg QD, n/N (%) (N=154)	Difference between UPA 30 mg vs UPA 15 mg[a], %
Primary endpoint: Clinical remission[b] at Week 52 per Adapted Mayo Score				
BL Full Mayo score ≤9	7/74 (9.5)	40/75 (53.1)	40/73 (54.5)	1.4
BL Full Mayo score >9	11/75 (14.8)	23/73 (31.2)	40/79 (50.4)	19.2
Pancolitis at BL, no	13/79 (16.5)	31/66 (46.6)	36/68 (52.8)	6.2
Pancolitis at BL, yes	5/70 (7.1)	32/82 (38.8)	44/86 (50.8)	12.0
EIM at BL, no	13/112 (11.6)	50/112 (44.3)	56/113 (49.4)	5.1
EIM at BL, yes	5/37 (13.7)	13/36 (36.1)	24/41 (58.1)	22.0
Key secondary endpoint: Endoscopic improvement[c] at Week 52				
BL Full Mayo score ≤9	8/74 (10.8)	45/75 (60.4)	44/73 (60.6)	0.2
BL Full Mayo score >9	14/75 (18.1)	27/73 (36.7)	50/79 (62.8)	26.1
Pancolitis at BL, no	16/79 (20.3)	33/66 (49.6)	43/68 (63.7)	14.1
Pancolitis at BL, yes	6/70 (8.0)	39/82 (47.9)	52/86 (59.9)	12.0
EIM at BL, no	15/112 (13.7)	57/112 (50.9)	68/113 (60.2)	9.3
EIM at BL, yes	6/37 (16.9)	15/36 (41.7)	27/41 (65.4)	23.7

Data are from the ITT population, defined as the first 450 randomized and treated patients with 8-week UPA 45 mg QD induction treatment who were enrolled in Cohort 1 under the protocol for the 52-week maintenance treatment period. The actual number of patients in the analysis was 451 due to the same enrollment date of the 450th and 451st patients. Non-responder imputation incorporating multiple imputations was performed to handle missing data due to COVID-19 incidence.
[a]Not part of the predefined statistical analyses.
[b]Adapted Mayo score ≤2, with stool frequency subscore ≤1 (and not greater than induction baseline), rectal bleeding subscore of 0, and endoscopic subscore ≤1.
[c]Endoscopic subscore ≤1.
BL, baseline; EIM, extraintestinal manifestation; ITT, intent-to-treat; PBO, placebo; QD, once daily; UPA, upadacitinib.

Conclusions: Both UPA maintenance doses were efficacious compared with PBO, regardless of inflammatory burden, in the achievement of clinical remission and endoscopic improvement. Although results should be interpreted with respect to the small sample size in some subgroups and the post hoc nature of the analysis, these data suggest that patients with a high inflammatory burden of UC may have a relatively greater benefit from UPA 30 mg than UPA 15 mg, compared with those without high inflammatory burden.