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# 118 - EFFICACY OF UPADACITINIB DOSE ESCALATION IN A PHASE 3 LONG-TERM EXTENSION ULCERATIVE COLITIS STUDY

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## Resumen

**Introduction:** We evaluated the efficacy of dose escalation to UPA 30 mg QD (UPA30) among patients who demonstrated an inadequate response to UPA 15 mg QD (UPA15) during the long-term extension (LTE) study U-ACTIVATE.

**Methods:** In the UPA UC program, patients who did not achieve a clinical response per Adapted Mayo score at week (wk) 8 in the phase 2 induction study and patients who had inadequate or loss of response in the phase 3 maintenance study could enroll into the 288-wk U-ACTIVATE study and receive open-label UPA15 regardless of their treatment and dose in the precedent studies. Dosing could then be escalated to UPA30 if the patients demonstrated inadequate response to UPA15 and met the criteria for dose escalation. In those with dose escalation prior to wk 48, efficacy endpoints were assessed at wk 48 (the first visit with endoscopy evaluation in U-ACTIVATE). All patients who received at least one dose of the study drug (ITT analysis) were included in this study. Results were based on non-responder imputation with 95% confidence intervals (CI) calculated by normal approximation to binomial distribution.

**Results:** The analysis was performed among 190 patients who have completed the wk 48 visit or had entered the study at least prior to wk 48 and the data cut-off. At wk 48, 30.0% achieved clinical remission, 27.9% achieved CS-clinical remission, 15.8% achieved clinical remission at wk 48 and CS-free clinical remission ≥ 90 days prior to the wk 48 visit, 41.1% achieved endoscopic improvement, and 19.5% achieved endoscopic remission.

**Table 1. Efficacy of Upadacitinib Dose Escalation in Patients that Entered U-ACTIVATE Long-Term Extension Study**

| Endpoint | Patients with Dose Escalation, n (%) [95% CI][a] |
|---|---|
| Clinical remission per Adapted Mayo score[b] | 57 (30.0) [63.5, 76.5] |
| Clinical remission per Adapted Mayo score and corticosteroid-free remission at wk 48[c] | 53 (27.9) [65.7, 78.5] |
| Clinical remission per Adapted Mayo score at wk 48 and corticosteroid-free clinical remission ≥ 90 days prior to the wk 48 visit[c] | 30 (15.8) [79.0, 89.4] |
| Endoscopic improvement[d] | 78 (41.1) [52.0, 65.9] |
| Endoscopic remission[e] | 37 (19.5) [74.9, 86.2] |

The criteria for a loss of response or an inadequate response depended on the patient's response at wk 0. For patients who were responders upon completion of U-ACHIEVE Maintenance wk 44, an inadequate response was defined as: a stool frequency subscore (SFS) and rectal bleeding subscore (RBS) at least 1 point greater than the wk 0 value on two consecutive visits at least 7 days apart; or

- For patients with SFS or RBS ≥ 2.1 at wk 0, loss of response is defined as an increase in either the SFS or RBS of at least 1 point greater than the wk 0 value on two consecutive visits at least 7 days apart and associated with the presence of signs/symptoms of UC progression of UC disease.
- For patients enrolled from U-ACHIEVE Maintenance due to loss of response, inadequate response was defined as: SFS + RBS value that remains unchanged or has increased from wk 0 on two consecutive visits at least 7 days apart.

a. Non-responder imputation with no special data handling for missing due to COVID-19 was applied. 95% CI calculated by normal approximation to binomial distribution.
b. Clinical remission per Adapted Mayo score: SFS≤1 and not greater than baseline (of induction), RBS=0, and endoscopic subscore (ES) ≤ 1.
c. Clinical remission per Adapted Mayo score and CS-free clinical remission (clinical remission at wk 48 and CS-free for ≥90 days prior to wk 48 among patients with clinical remission at the end of the induction therapy).
c. Endoscopic improvement: ES ≤ 1
d. Endoscopic remission: ES= 0

**Conclusions:** In patients with an inadequate or loss of response to UPA15, dose escalation to UPA30 was associated with improved efficacy outcomes including clinical remission, CS-free clinical remission, endoscopic improvement, and endoscopic remission.