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114 - EFFICACY AND SAFETY OF UPADACITINIB MAINTENANCE THERAPY IN PATIENTS WITH MODERATELY TO SEVERELY ACTIVE CROHN'S DISEASE: RESULTS FROM A RANDOMIZED PHASE 3 U- ENDURE MAINTENANCE STUDY

Julián Panés[1], Edward V. Loftus Jr[2], Ana Lacerda[3], Laurent Peyrin- Biroulet[4], Geert D'Haens[5], Remo Panaccione[6], Walter Reinisch [7], Edouard Louis[10], Minhu Chen[8], Hiroshi Nakase[9], Jakob Begun[11], Brigid S. Boland[12], Jianzhong Liu[3], Elena Dubcenco[3], Mohamed-Eslam F. Mohamed[3], Tian Feng[3] and Jean-Frederic Colombel[13]

[1]Hospital Clinic Barcelona, IDIPABS, CIBERehd, Barcelona. [2]Mayo Clinic College of Medicine and Science, Rochester, Minnesota, USA. [3]AbbVie Inc, North Chicago, IL, USA. [4]University Hospital of Nancy, Lorraine University, Vandoeuvre, France. [5]Amsterdam University Medical Centres, Amsterdam, Netherlands. [6]University of Calgary, Alberta, Canada. [7]Medical University of Vienna, Austria. [8]The First Affiliated Hospital of Sun Yat-sen University, Guangzhou, China. [9]Sapporo Medical University School of Medicine, Sapporo, Japan. [10]University Hospital CHU of Liège, Belgium. [11]Mater Hospital Brisbane, Brisbane, QLD Australia. [12] University of California, San Diego, CA, USA. [13]Icahn School of Medicine at Mount Sinai, New York, NY, USA.

Resumen

Introduction: Upadacitinib (UPA), an oral, reversible Janus kinase (JAK) inhibitor was evaluated for efficacy and safety of UPA 15 mg (UPA15) and UPA 30 mg once daily (QD) (UPA30) as maintenance therapy in patients with Crohn’s disease (CD) in U-ENDURE (NCT03345823), a phase 3, double-blind, placebo (PBO)-controlled trial.

Methods: Eligible patients who achieved clinical response per stool frequency (SF)/abdominal pain score (APS) (≥ 30% decrease in average daily very soft/liquid SF and/or average daily APS, neither greater than baseline) after 12 weeks (wk) of induction treatment with UPA45 in the U-EXCEED or U-EXCEL studies, were re-randomized (1:1:1) to UPA30, UPA15 or PBO for 52 wks of maintenance therapy. The co-primary endpoints, clinical remission per Crohn’s disease activity index (CDAI, US) or SF/APS (EU) and endoscopic response and safety were evaluated at wk 52.

Results: Baseline demographics/characteristics were similar between groups, 75% of subjects failed a prior biologic. At wk 52, a significantly greater proportion of patients receiving UPA15 (n = 169) and UPA30 (n = 168) achieved clinical remission per CDAI (UPA15 37.3% and UPA30 47.6 *vs.* PBO 15.1%) and per SF/APS (UPA15 35.5% and UPA30 46.4% vs, PBO 14.4%), p 0.0001 for all comparisons. Patients treated UPA also attained significantly greater rates of endoscopic response (UPA15 27.6% and UPA30 40.1 *vs.* PBO 7.3%, p 0.0001 for both comparisons), and both doses were superior to PBO for key secondary endpoints, including clinical response, clinical and endoscopic remission, maintenance of clinical remission and corticosteroid (CS)-free clinical remission adverse events (AE) and serious AEs were lower with UPA compared to PBO; AE leading to treatment discontinuation were similar across groups. The most common AE was CD worsening (58.0 events/100 patient-years [E/100PY] in PBO, (29.7 E/100PY) UPA15, and (12.0 E/100PY) UPA30. Serious infection rates were similar across treatment groups (6.1 -8.4 E/100PY); herpes zoster rate was higher in UPA30 (7.2 E/100PY) compared to PBO (4.7 E/100PY) and UPA15 (4.0 E/100PY). Malignancies excluding non-melanoma skin cancer (NMSC) were reported in 1 patient on UPA15, 2 patients on UPA30, all events were diagnosed within 9 months from the first UPA exposure. One gastrointestinal

perforation was reported in each treatment group. One event of hepatic vein thrombosis was reported in UPA30. No deaths, tuberculosis, NMSC, or adjudicated cardiovascular events occurred.

Conclusions: Maintenance treatment with both UPA doses was superior to PBO for all clinical and endoscopic outcomes in patients who responded to induction treatment; with CS-free clinical remission and maintenance of clinical remission at wk 52. UPA was well tolerated, with safety profiles comparable to previous studies.