



Gastroenterología y Hepatología



<https://www.elsevier.es/gastroenterologia>

49 - CLINICAL AND ENDOSCOPIC RESPONSE TO TREAT-TO-TARGET VERSUS STANDARD OF CARE IN CROHN'S DISEASE PATIENTS TREATED WITH USTEKINUMAB: WEEK 48 RESULTS OF THE STARDUST TRIAL

S. Danese¹, S. Vermeire², G. D'Haens³, J. Panés⁴, A. Dignass⁵, F. Magro⁶, M. Nazar⁷, M. Le Bars⁸, M. Lahaye⁹, L. Ni¹⁰, F. Lavie⁸, I. Bravata¹¹, S. Sloan¹², M. Daperno¹³, M. Lukas¹⁴, A. Armuzzi¹⁵, M. Löwenberg³, D. R. Gaya¹⁶ and L. Peyrin-Biroulet¹⁷

¹Department of Gastroenterology, Humanitas University, Milan (Italy). ²University Hospitals Leuven, Leuven (Belgium). ³Academic Medical Centre, University of Amsterdam (The Netherlands). ⁴Department of Gastroenterology, Hospital Clinic of Barcelona, CIBERehd, Barcelona. ⁵Department of Medicine I, Agaplesion Markus Hospital, Frankfurt/Main (Germany). ⁶Department of Pharmacology & Therapeutics, Institute for Molecular and Cell Biology, Faculty of Medicine University of Porto and Department of Gastroenterology, Hospital de Sao Joao, Porto (Portugal). ⁷Janssen-Cilag Polska Sp. zoo., Warsaw (Poland). ⁸Janssen-Cilag, Issy-les-Moulineaux (France). ⁹Janssen-Cilag BV, Breda (The Netherlands). ¹⁰Janssen-Cilag Russia, Moscow (Russian Federation). ¹¹Janssen-Cilag S.p.A., Milan (Italy). ¹²Janssen Global Services, LLC, Horsham, PA, (USA, at the time of study). ¹³Gastroenterology Unit, Mauriziano Hospital, Turin (Italy). ¹⁴Clinical and Research Center for Inflammatory Bowel Diseases, Clinical Center ISCARE, Prague (Czech Republic). ¹⁵IBD Unit, Fondazione Policlinico Universitario A. Gemelli IRCCS, Università Cattolica del Sacro Cuore, Rome (Italy). ¹⁶Department of Gastroenterology, Glasgow Royal Infirmary, Glasgow (United Kingdom). ¹⁷INSERM Unité 954 and Department of Hepato-Gastroenterology, University Hospital of Nancy, University of Lorraine, Hudemont (France).

Resumen

Introduction: STARDUST, a phase 3b randomized trial, compared treat-to-target (T2T) maintenance strategy vs standard of care (SoC) in Crohn's disease (CD) patients (pts) treated with ustekinumab (UST). Here we describe Week (W) 48 endoscopic (1° endpoint) and clinical results.

Methods: Adults with moderate-severely active CD ([CDAI] 220-450), [SES-CD] ≥ 3); received IV UST ~6 mg/kg at W0 (baseline [BL]); SC UST 90 mg at W8. At W16, CDAI 70 responders were randomized 1:1 to T2T or SoC. T2T pts received SC UST q12w/q8w based on 25% improvement in SES-CD score vs BL and intensified to q4w from W16-48 if failure to meet: CDAI 70 point improvement, and CRP ≤ 10 mg/L or faecal calprotectin (FCal) # 50% reduction in SES-CD score vs BL).

Results: Of 500 pts, 441 achieved CDAI 70 response at W16 and were randomized to T2T (n = 220, 79.1%) or SoC (n = 221, 87.3%); and completed W48. More pts in T2T (37.7%) vs SoC (29.9%) achieved the 1° endpoint at W48: (p = 0.0933; NRI, non-responder imputation). At W48, clinical response rates were T2T 68.2% and SoC 77.8% (p = 0.0212; NRI); clinical remission 61.4% vs 69.7% (NS;NRI), respectively; ≥ 50% improvement in FCal 39.4% vs 46.5% (NS;NRI)/63.1% vs 60.6% (NS; LOCF, last observation carried forward) and CRP 41.7% vs 53.3% (p = 0.032; NRI)/53.2% vs 57.2% levels (NS; LOCF), (Table). In T2T and SoC, 59.2% (122/206) and 53.2% (116/218) of pts started on

UST q12w; of those, 59.8% (73/122) and 63.8% (74/116) were still on q12w at W48. Of pts who started on q8w, T2T, 40.5% (34/84) and SoC 78.4% (80/102) remained on q8w at W48. At W48, 17% (35/206) of pts were on UST q4w in T2T. No new safety signals were reported.

Table: Endpoint data by treatment arm

Variable	T2T arm (n=220)			SoC arm (n=221)			p value ^b
	Mean (95% CI) Baseline ^a	Mean (95% CI) change from baseline at Week 16	Mean (95% CI) change from baseline at Week 48	Mean (95% CI) Baseline ^a	Mean (95% CI) change from baseline at Week 16	Mean (95% CI) change from baseline at Week 48	
SES-CD score	13.4 (12.2, 14.6) n=220	-4.6 (-5.5, -3.7) n=220	-5.0 (-5.9, -4.0) n=220	12.7 (11.7, 13.7) n=221	NA	-4.1 (-4.9, -3.3) n=221	0.4856
CDAI score	287.2 (279.9, 294.5) n=219	-178.0 (-188.0, -168.0) n=219	-187.6 (-198.4, -176.8) n=219	287.2 (278.6, 295.8) n=221	-179.3 (-189.7, -169.0) n=221	-187.1 (-199.4, -174.8) n=221	0.9270
Fcal, µg/g	1952.7 (1461.4, 2443.9) n=197	-990.4 (-1445.0, -535.8) n=197	-1191.9 (-1674.3, -709.6) n=197	1658.8 (1304.9, 2012.7) n=189	-728.2 (-1049.4, -407.0) n=189	-744.4 (-1115.9, -372.8) n=189	0.1564
CRP, mg/L	16.405 (13.233, 19.577) n=219	-7.704 (-10.631, -4.777) n=219	-7.831 (-10.844, -4.818) n=219	15.838 (12.725, 18.952) n=219	-7.345 (-9.684, -5.006) n=219	-7.909 (-10.867, -4.950) n=219	0.9133

^aBaseline values for patients with at least one post-baseline assessment.
^bp values for changes at Week 48 are based on ANCOVA, with baseline value and stratification factors SES-CD score (≤ 16 , > 16) and prior exposure to biologics (none or 1) as covariates. Patients who had missing data at the designated analysis timepoint had their last value carried forward.
 Secondary endpoints included endoscopic remission (SES-CD score ≤ 2), clinical remission (CDAI < 150 points), clinical response (CDAI < 150 points or decrease from baseline of ≥ 100 points), change from baseline in biomarkers (Fcal and CRP).
 ANCOVA, analysis of covariance; CDAI, Crohn's Disease Activity Index; CI, confidence interval; CMH, Cochran–Mantel–Haenszel; CRP, C-reactive protein; Fcal, faecal calprotectin; SES-CD, Simple Endoscopic Score in Crohn's Disease; SoC, standard of care; T2T, treat-to-target; NA, not assessed.

Conclusions: STARDUST is the first trial to use endoscopy to guide dose escalation in pts with CD. After 48W of maintenance therapy with UST, more pts achieved the endoscopic response with T2T vs SoC.