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MP153

ENDOSCOPIC RESPONSE AT 1-YEAR AND ASSOCIATION WITH LONG-TERM CROHN'S DISEASE OUTCOME: A POOLED CLINICAL TRIAL ANALYSIS ADJUSTING FOR 1-YEAR CLINICAL REMISSION STATUS

S. Neff-Baro[1], A. Gauthier[1], M. Sanon[2], S. Kachroo[3], D. Wirth[4], L. Eisele[5], K. Gurjar[1], D. Naessens[6]
[1]Amaris Consulting, Paris, France, [2]Janssen Global Services, Horsham, United States of America, [3]Janssen Scientific Affairs, Horsham, United States of America, [4]Janssen Cilag GmbH, Neuss, Germany, [5]Jan-Cil Germany, Neuss, Germany, [6]Janssen-Cilag, Beerse, Belgium

Contact E-Mail Address: msanon@its.jnj.com

Introduction: Therapeutic goals and clinical guidelines in Crohn's disease (CD) have evolved to include endoscopic outcomes being a key prognostic parameter in disease management. STRIDE-II guidelines comprise of clinical and patient-reported outcome remission, along with biomarker normalization and endoscopic healing. While available publications have correlated achievement of endoscopic response with long-term outcomes, few if any have adjusted for clinical remission status. Moreover, most of the data comes from patients treated with immunomodulators and/or TNFs. The objective of this analysis was to assess the impact of endoscopic response at the end of maintenance and long-term outcomes while adjusting for clinical remission status at maintenance.

Aims & Methods: Data from two randomized clinical trials (GALAXI-1, NCT03466411 and IM-UNITI, NCT01369355) were pooled to assess the impact of endoscopic response at 1 year on long-term patient relevant outcomes including clinical response, clinical remission, quality of life as assessed by the Inflammatory Bowel Disease Questionnaire (IBDQ), and risk for hospitalizations/surgeries. This post-hoc analysis assessed endoscopic response at the end of maintenance (~48 weeks) and patient relevant outcomes in the long-term extension (LTE) duration (~96 weeks). Patients without LTE outcome data and placebo treated patients were excluded. Multivariate analyses with trial as a random effect were conducted and adjusted for treatment arm during maintenance, clinical remission status at end of maintenance (EOM), and endoscopic response at EOM.

Results: A total of 461 patients had available endoscopy and clinical remission status at EOM (IM-UNITI, N=177; GALAXI-1, N=284). The number of patients with available LTE outcomes ranged from 290 (IBDQ remission) to 383 (clinical remission/clinical response). Endoscopic response at EOM was significantly associated with higher odds of LTE clinical remission and IBDQ remission with ORs of 1.91 and 1.99 respectively, with corresponding p values below 0.05. Endoscopic response at EOM was also associated with lower odds of LTE C-reactive Protein abnormality (OR=0.46, p<0.005), a marker of inflammation and disease activity. Lastly, a greater percentage of patients without endoscopic response at EOM experienced hospitalizations/surgeries though the difference was not significant due to low event counts (16% versus 9%, p=0.1237).

Conclusion: This analysis uses clinical data from robust trials and adjusted for patients' clinical remission status at the end of maintenance to isolate the benefit of endoscopic response in predicting long-term outcomes. Endoscopic response is significantly associated with more patients reaching clinical remission and better quality of life. Further investigation in large datasets with longer follow-up is needed to better understand whether measures of endoscopic improvement are also good surrogates for reductions in hospitalizations and surgeries.

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MP154

EFFECTIVENESS OF INTRAVENOUS VEDOLIZUMAB INDUCTION AND DOSE ESCALATION IN ULCERATIVE COLITIS AND CROHN'S DISEASE; A LARGE-SCALE, CANADIAN REAL-WORLD COHORT.

E.-J. Bernard[1,2], J.-F. LeBlanc[3,2], A.H. Steinhart[4], A. Wadhwa[5], R. Ward[5], J. Weiss[6], C. Pettengell[6], B. Bressler[7]
[1]CHUM, Montreal, Canada, [2]Université de Montréal, Montréal, Canada, [3]Sacre-Coeur Hospital, Montréal, Canada, [4]University of Toronto, Toronto, Canada, [5]Takeda Canada Inc, Toronto, Canada, [6]Pentavere Research Group, Toronto, Canada, [7]University of British Columbia, Vancouver, Canada

Contact E-Mail Address: jean-frederic.leblanc@mail.mcgill.ca

Introduction: Vedolizumab (VDZ) is a gut-selective anti-lymphocyte trafficking drug indicated for the treatment of CD and UC [1] administered by intravenous (IV) infusion at Weeks 0, 2, and 6 followed by IV infusions every 8 weeks (Q8W) or subcutaneous injections every 2 weeks [2,3].

For IV treated patients who experience a suboptimal or loss of response (LOR), dose escalation to every four-week infusions (Q4W) may recapture response to treatment [4] but there is a lack of large-scale real-world data describing outcomes of dose-escalated patients [5].

Aims & Methods: Patients with moderately to severely active UC or CD were prospectively followed in a patient support program in Canada from 2015 to 2023. Harvey-Bradshaw Index (HBI, CD) and Partial Mayo Scores (PMS, UC) were assessed 2, 6, and 14 weeks after treatment initiation to understand VDZ induction effectiveness. HBI or PMS were assessed 12 weeks post dose Q4W escalation to understand the effectiveness of dose escalation in the presence of suboptimal or LOR.

Results are presented for patients who dose escalated to Q4W from Q8W maintenance (Q8W > Q4W), initiated Q4W at week 14 (w14>Q4W), or at week 10 (w10>Q4W). Remission was defined as HBI <5, or PMS <3. Response was defined as achieving remission or an HBI decrease of ≥3 points from baseline, or a PMS decrease of ≥2 points and ≥25% from baseline.

Results: 1056 CD (45% bio-naïve) patients and 1959 UC patients (71% bio-naïve) were eligible for this study. The median follow up was 18 months (range 3-61). The median age was 48 years (range: 18-92), and 44 years (range:18-89) for CD and UC patients respectively. 60% of CD patients and 51% of UC patients were female. For CD patients the median baseline HBI score was 10 (range 8-40), and for UC patients the median baseline PMS score was 6 (range 5-20).

Disease duration prior to VDZ was longer in bio-experienced patients compared to bio-naïve; CD (Medians: 14 vs 4 years) and UC (Medians: 6 vs 4 years). To further characterise the patient cohort induction effectiveness is reported. For CD patients, remission and response were 25% and 56% at 2 weeks, 34% and 66% at 6 weeks and 40% and 68% at 14 weeks.

For UC patients, remission and response were 32% and 64% at 2 weeks, 48% and 78% at 6 weeks and 55% and 81% at 14 weeks. In CD, 39% (183 of 473) of bio-naïve patients and 52% (302 of 583) of bio-experienced patients dose-escalated to Q4W within the first two years. In UC, 37% (520 of 1399) of bio-naïve patients and 49% (275 of 560) of bio-experienced patients dose-escalated to Q4W within the first two years. At Q4W dose escalation, 319 CD patients (110 bio-naïve, 209 bio-experienced) and 514 UC patients (334 bio-naïve, 180 bio-experienced) were not in HBI or PMS remission. For these patients, remission and response 12-weeks post dose escalation to Q4W are presented in table 1.

Conclusion: Conclusion: IBD patients experienced clinically meaningful remission and response rates following induction with IV VDZ. For those that have a suboptimal or LOR this study demonstrates the real-world effectiveness of dose escalating VDZ to Q4W in Canadian patients with IBD to complement previous clinical trials, and real-world studies.

	CD Bio- Naïve (N =110)			CD Bio- Experienced (N =209)			UC Bio-Naïve (N =334)			UC Bio-Experienced (N =180)		
	Q8W> Q4W (N=58)	W14> Q4W (N=36)	W10> Q4W (N=16)	Q8W> Q4W (N=119)	W14> Q4W (N=45)	W10> Q4W (N=45)	Q8W> Q4W (N=163)	W14> Q4W (N=100)	W10> Q4W (N=71)	Q8W> Q4W (N=79)	W14> Q4W (N=56)	W10> Q4W (N =45)
In Remission N (%)	25 (47%)	4 (13%)	2 (15%)	27 (24%)	9 (23%)	9 (22%)	65 (42%)	31 (42%)	15 (29%)	27 (37%)	19 (40%)	8 (22%)
In Response N (%)	33 (62%)	13 (43%)	4 (31%)	52 (47%)	23 (59%)	21 (52%)	86 (56%)	44 (59%)	26 (50%)	42 (58%)	26 (55%)	14 (38%)
Missing	5	6	3	8	6	5	9	26	19	6	9	8

Table 1: 12-week remission and response rates for pts dose escalated to Q4W from maintenance (Q8W>Q4W), at week 14 (W14>Q4W) or at week 10 (W10>Q4W)

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Dr. Ryan Ward - Employee of Takeda
Abhinav Wadhwa - Employee of Takeda

MP155

THE CHOICE OF FIRST-LINE BIOLOGICAL THERAPIES IS HIGHLY IMPACTING THE EVOLUTION OF ULCERATIVE COLITIS AND CANNOT BE RESCUED BY LATER TREATMENTS: RESULTS FROM THE APPETISER STUDY

D. M'Baye[1], B. Pereira[1], A. Buisson[1]
[1]*CHU Estaing Clermont-Ferrand, IBD Unit, Clermont-ferrand, France*

Contact E-Mail Address: a_buisson@hotmail.fr

Introduction: Therapeutic sequencing is a burning question in patients with ulcerative colitis (UC) requiring an advanced therapy. Whether starting with a less effective but safer and more convenient drug is a loss of chance for UC patients or can be rescued by later treatments is key point.
Aims & Methods: In the APPETISER study, we compared the effectiveness of two strategies based on the choice of the first biologic owing to either the drug efficacy in network meta-analyses and randomized controlled trials (vedolizumab or infliximab) or better acceptability (full subcutaneous therapy: adalimumab and golimumab) to induce and maintain steroid-free clinical remission during the first 24 months.
We collected real-world data from an IBD referral center including all consecutive UC patients ≥ 18 years-old who started a first line of biologic for active UC with follow-up > 6 months. Prior colectomy or severe acute colitis were excluded. Patients were included in either effectiveness-based sequencing (EBS) if they started with infliximab or vedolizumab, or in acceptability-based sequencing (ABS) if they received adalimumab or golimumab as first-line biologic.
The primary endpoint was remission defined according to PRO2 (PRO2-remission) as the absence of bleeding, normalization of transit (Mayo stool frequency subscore = 0) and no steroid. PRO2-remission was defined as a binary criterion each month (the statistical unit being the month and not the patient).
The secondary endpoints concerned the analysis by patient and were CFREM (partial Mayo score ≤ 2 without steroid) at week 12 and 52, endoscopic remission (CFREM + score Endoscopic Mayo ≤ 1) at week 12, time to drug discontinuation and time to colectomy.
All comparisons were adjusted using propensity scores on potential confounders. Analysis by month was performed using mixed models to account for repeated data.
Results: Overall, 130 patients were included including 60 patients in the EBS group (IFX= 50 and VDZ= 10) and 70 in the ABS group (ADA= 48 and GLM= 22).
The populations had similar characteristics at baseline apart from concomitant immunosuppressant more frequent in EBS group (55.9% vs 21.7%). 2nd line treatment was started in 26.7% of patients in EBS group (ADA in 48.8%, VDZ 25.5% and ustekinumab 18.8%) and 87.1% of patients in ABS group (IFX in 54.1%, VDZ 31.1%).
After adjustment, the rate of CFREM was significantly higher in EBS arm than in ABS arm at week 12 (70.8% vs 33.0%, p < 0.001) and week 52 (72.8% vs 42.1%, p = 0.017). The rate of endoscopic remission at W12 was 22.1% and 10.0% in EBS and ABS arms, respectively (p =0.086).
For the primary endpoint, 3350 months were analyzed (1180 in EBS arm and 1175 in ABS arm). The percentage of months spent in PRO2-CFREM in the first 24 months (primary endpoint) was greater in EBS arm than in ABS arm (74.2% vs 46.6%; p<0.001). The percentage of months spent in CFREM was higher in the IV arm in the first 6 months (60.4% vs 18.9%), and was not rescued later: between M7 and M12 (73.1% vs 38.6%), M13 and M18 (79.9% vs 57.0%) or M19 and M24 (83.3% vs 64.6%) (p < 0.001 for all comparisons).
Regarding long-term data, EBS group had a lower risk to first-line biologic discontinuation (aHR=6.5 [2.8-15.3], p <0.001) and a clear trend for lower risk of colectomy (aHR=4.5 [0.9-22.3], p =0.068).