EVIDENCE & VALUE SUMMARY: STELARA® (ustekinumab)

Moderate to severe Crohn's disease & ulcerative colitis

STELARA® is a human IL-12/IL-23 antagonist indicated for the treatment of[1]:

Adult and pediatric patients 6 years and older with:

- Moderate to severe plaque PsO who are candidates for phototherapy or systemic therapy
- Active PsA

Adult patients with:

- Moderately to severely active CD and UC

- The only FDA-approved biologic for CD and UC that **targets IL-12 and IL-23**[1]
- **1 induction dose and 6 maintenance doses** per year[1a]

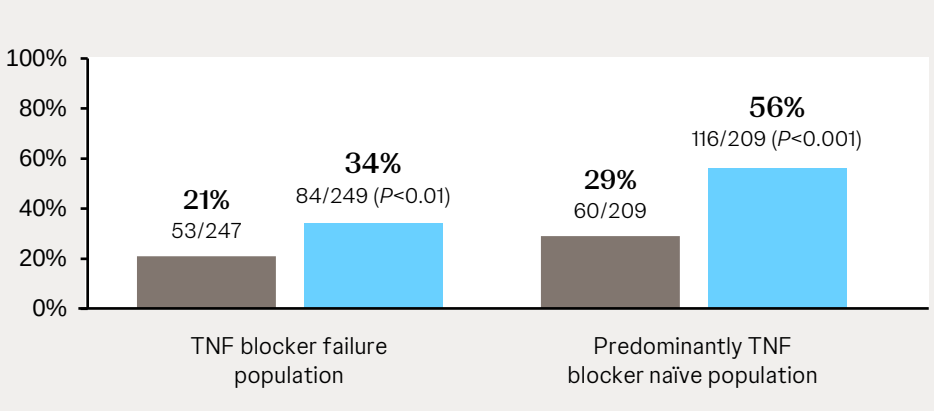
STELARA® has demonstrated clinical efficacy in CD and UC

Crohn's disease

UNITI clinical trial program consisted of three phase 3, multicenter, double-blind, placebo-controlled trials in adults with moderately to severely active CD. The program included two induction studies of STELARA® IV (6 mg/kg) (N=741, TNF-blocker failure or intolerant population and N=627, predominantly TNF-blocker naïve population who failed conventional therapy) versus placebo and one maintenance study of STELARA® subQ q8w (90 mg) versus placebo (N=388). The primary endpoint of the induction studies was clinical response at Week 6[b], and the primary endpoint of the maintenance study was clinical remission one year after induction dose.[1c]

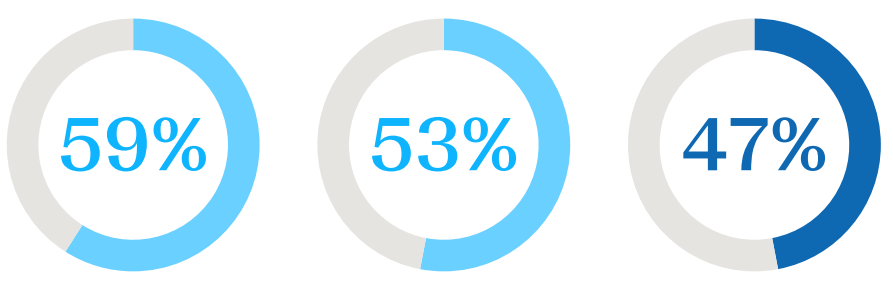
Rapid response as early as Week 6

UNITI-1 & -2, clinical responses at Week 6 for STELARA® versus placebo groups (Primary Endpoint)[1]:



Sustained responses at Year 1 and clinical remission at Year 5[1f,g]

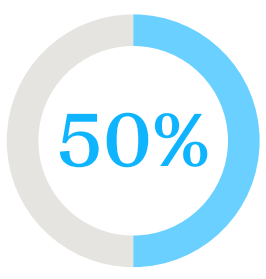
UNITI



of STELARA® patients (76/128) maintained clinical response at 1 Year
versus 44% (58/131) in placebo group (0.01 ≤ *P*≤0.05)

of STELARA® patients (68/128) were in clinical remission at 1 Year
versus 36% (47/131) in placebo group (*P*<0.01)

of STELARA® patients were in steroid-free clinical remission at 1 Year[h]
versus 30% in placebo group

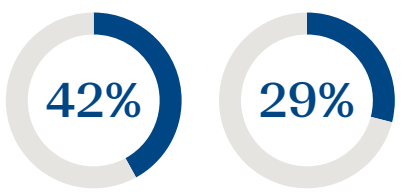


of STELARA® patients (76/153) who entered the UNITI LTE were in remission at Year 5

Among those patients, 88% (67/76) were steroid-free[2]

Endoscopic results[3]

SEAVUE

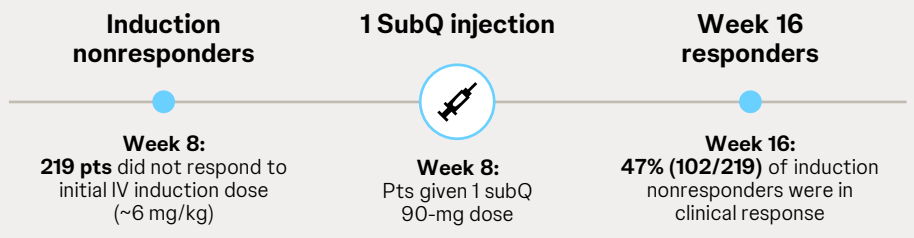


42% (75/179) of STELARA® patients achieved endoscopic response and 29% (51/179) of patients achieved endoscopic remission from baseline SES-CD at 1 Year
(Nominal *P* values of 0.35 and 0.63, respectively)

SEAVUE, a phase 3b, randomized, blinded, active-controlled trial of bio-naïve adult patients with moderate-to-severe Crohn's disease[i,j]

Clinical response among induction non-responders at Week 16

Nearly half of CD patients who did not respond to STELARA® induction achieved response after a single subQ maintenance dose[1]

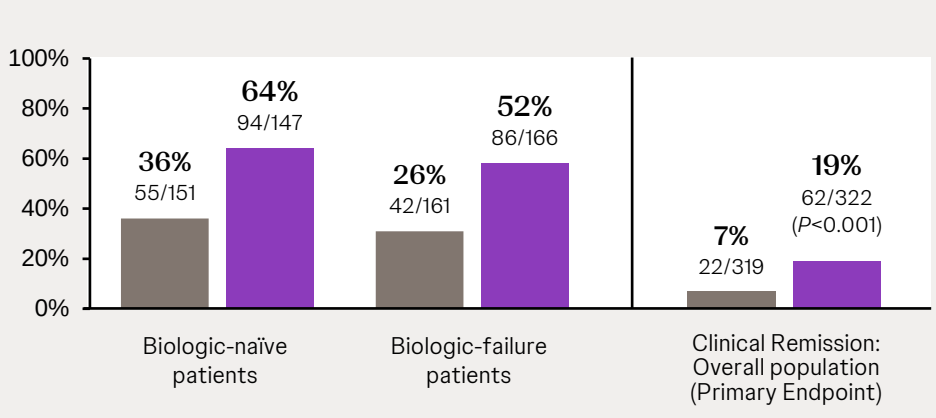


Ulcerative colitis

UNIFI clinical trial program consisted of two phase 3, multicenter, double-blind, placebo-controlled trials in adults with moderately to severely active UC who had an inadequate response to or failed to tolerate a biologic (i.e., TNF blocker and/or vedolizumab), corticosteroids, and/or 6-MP or AZA therapy. The program included one induction study of STELARA® IV (6 mg/kg) versus placebo (N=961) and one maintenance study of STELARA® subQ q8w (90 mg) versus placebo (N=523). The primary endpoint of the induction study was clinical remission at Week 8, and the primary endpoint of the maintenance study was clinical remission one year after induction dose.[1d]

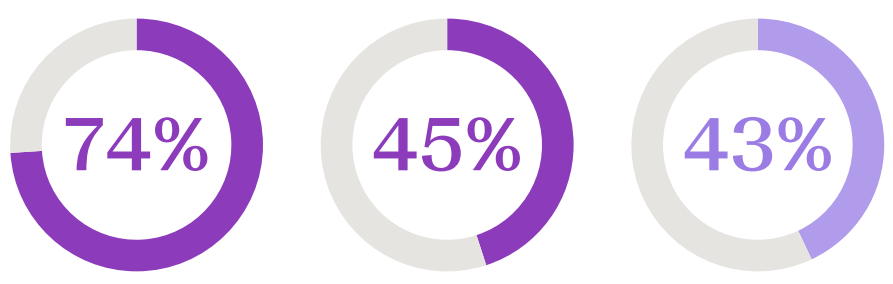
Rapid response as early as Week 8

UNIFI Induction, clinical responses at Week 8 for STELARA® versus placebo groups[1e]:



Response rate for overall population, STELARA® vs placebo: 58% (186/322) vs 31% (99/319)[1]

Sustained responses at ~Year 1 and symptomatic remission at Year 4[1f]

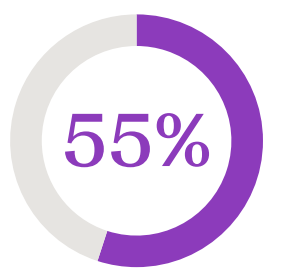


of STELARA® patients (130/176) maintained clinical response at 1 Year
versus 48% (84/175) in placebo group (*P*≤0.001)

of STELARA® patients (79/176) were in clinical remission at 1 Year
versus 26% (46/175) in placebo group (*P*≤0.001)

of STELARA® patients (76/176) were in steroid-free clinical remission at 1 Year[h]
versus 26% (45/175) in placebo group (*P*≤0.001)

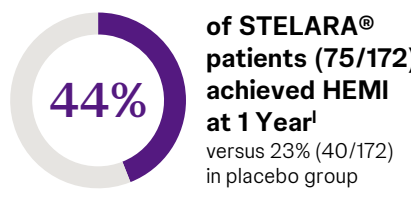
STELARA® demonstrated high clinical response and remission rates at 1 Year regardless of prior biologic exposure (*see footnote for clinical data*)[1k]



of STELARA® patients (96/176) who entered the UNIFI LTE were in symptomatic remission at Year 4

Among those patients, 95% (91/96) were steroid-free[4]

Endoscopic results[1]

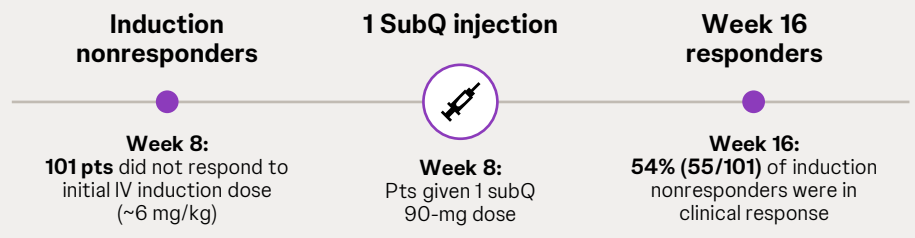


of STELARA® patients (75/172) achieved HEMI at 1 Year[l]
versus 23% (40/172) in placebo group

of STELARA® patients (83/176) achieved endoscopic improvement at 1 Year[m]
versus 27% (47/175) in placebo group (*P*<0.001)

Clinical response among induction non-responders at Week 16

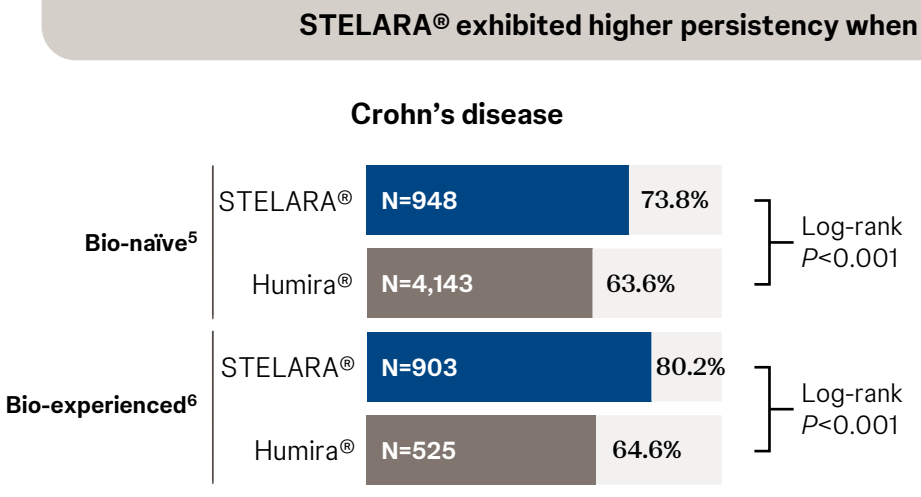
More than half of UC patients who did not respond to STELARA® induction achieved response with a single subQ maintenance dose[1]



STELARA® demonstrated higher persistency versus comparator in real-world studies across CD and UC

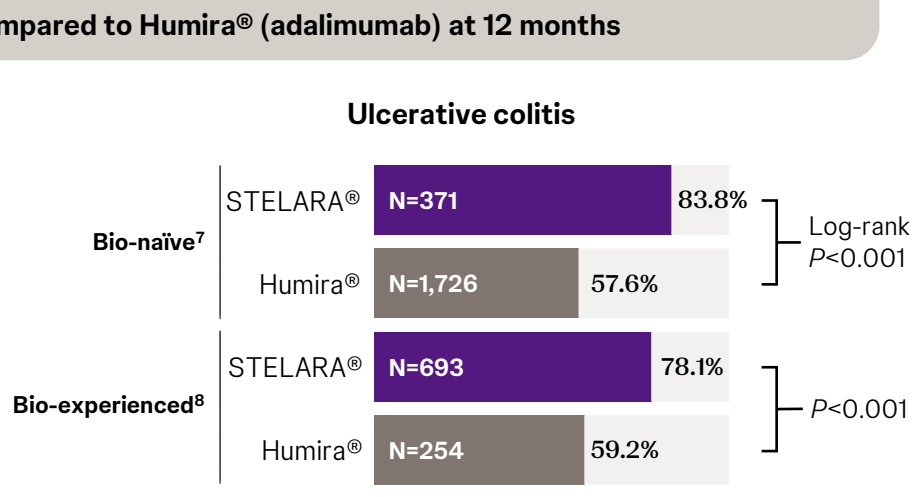
STELARA® exhibited higher persistency when compared to Humira® (adalimumab) at 12 months

Crohn's disease



Based on de-identified health claims data from IQVIA (bio-naïve) and MarketScan (bio-experienced). Not a head-to-head comparison. Results may not be generalizable to patients without health insurance or without commercial health insurance. There may be residual confounding due to unmeasured confounders.

Ulcerative colitis



Based on de-identified health claims data from IQVIA Pharmetrics® Plus database. Not a head-to-head comparison. Results may not be generalizable to patients without health insurance or without commercial health insurance. There may be residual confounding due to unmeasured confounders.

STELARA® has a consistent safety profile through 5 years for CD and 4 years for UC

Selected safety profile

Consistent safety profile across all indications through 1 year, with and low immunogenicity rates (<5%) in CD and UC[1]

Please refer to the full Prescribing Information for a complete listing of all adverse events for all indications, including other serious adverse events.

		AEs in UNITI trials, STELARA® vs PBO[1,9]		AEs in UNIFI trials, STELARA® vs PBO[1,10]	
Week 8	**Any AE**	66% vs 65%, UNITI-1 56% vs 54%, UNITI-2		51% vs 48%	
	Common ARs[n]	Vomiting	4 % vs 3%	Nasopharyngitis	7% vs 4%
Week 44	**Any AE**	82% vs 84%		77% vs 79%	
	Common ARs[n]	Nasopharyngitis	11% vs 8%	Nasopharyngitis	24% vs 20%
		Injection site erythema	5% vs 0%	Headache	10% vs 4%
		Vulvovaginal candidiasis/ mycotic infection	5% vs 1%	Abdominal pain	7% vs 3%
		Bronchitis	5% vs 3%	Influenza	6% vs 5%
		Pruritus	4% vs 2%	Fever	5% vs 4%
		Urinary tract infection	4% vs 2%	Diarrhea	4% vs 1%
		Sinusitis	3% vs 2%	Sinusitis	4% vs 1%
				Fatigue	4% vs 2%
				Nausea	3% vs 2%

Year 5 in CD and Year 4 in UC

In a pooled analysis of 2,575 patients with CD or UC across 6 phase 2/3 trials, overall rates of adverse events, serious adverse events, infections, and serious infections were not higher in the STELARA® group compared to placebo[11]

- Rates in patient years, placebo versus STELARA® group across IBD:
  - AEs: 482.41 versus 347.47
  - SAEs: 29.39 versus 18.85
  - Infections: 108.64 versus 88.87
  - Serious Infections: 5.52 versus 3.71

For additional information, please see the full Prescribing Information for STELARA® here.

[a]Weight-based (6 mg/kg) induction IV dose per Prescribing Information; SC 90mg dose 8 weeks following induction dose and every 8 weeks thereafter. [b]Defined as reduction in CDAI score of ≥100 points or CDAI score of 150. [c]Defined as CDAI score of <150. [d]Defined as Mayo stool frequency subscore of 0 or 1, Mayo rectal bleeding subscore of 0, and Mayo endoscopy subscore of 0 or 1 (modified so that 1 does not include friability). [e]Defined as a decrease from baseline in the modified Mayo score by ≥30% and ≥2 points, with either a decrease from baseline in the rectal bleeding subscore ≥1 or a rectal bleeding subscore of 0 or 1. [f]The placebo group consisted of patients who were in response to STELARA® and were randomized to receive placebo at the start of maintenance therapy. [g]The STELARA® group was composed of patients who achieved clinical response to STELARA at the end of the induction study. [h]Steroid-free remission was defined as patients in clinical remission and not receiving corticosteroids. [i]Endoscopic response defined as ≥50% reduction in SES-CD score from baseline or SES-CD score ≤3 or 0 in patients with a baseline SES-CD score of 3.12. [j]Endoscopic remission defined as SES-CD ≤3, or SES-CD =0 for patients with baseline SES-CD 3. [k]Maintenance of clinical response at 1 year, STELARA® versus placebo, prior biologic failure patients: 70% (64/91) versus 40% (35/88); biologic-naïve patients: 78% (62/79) versus 58% (49/84). Clinical remission at 1 year, STELARA® versus placebo, prior biologic failure patients: 41% (37/91) versus 18% (16/88); biologic-naïve patients: 49% (39/79) versus 36% (30/84). [l]Defined as neutrophil infiltration in <5% of crypts, no crypt destruction, and no erosions, ulcerations, or granulation tissue. [m]Defined as Mayo endoscopy subscore of 0 or 1. [n]Occurring in ≥3% of STELARA®-treated subjects and higher than placebo.

6-MP, 6-mercaptopurine; AE, adverse event; AZA, azathioprine; CD, Crohn's Disease; CDAI, Crohn's Disease Activity Index; HEMI, histo-endoscopic mucosal improvement; IBD, inflammatory bowel disease; IL-12, interleukin-12; IL-23, interleukin-23; IV, intravenous; LTE, long-term extension; PBO, placebo; PPPY, per-patient-per-year; PsA, psoriatic arthritis; PsO, psoriasis; pts, patients; q8w, every 8 weeks; SES-CD, Simple Endoscopic Score for Crohn's Disease; subQ, subcutaneous; TNF, tumor necrosis factor; UC, ulcerative colitis; Wk, week.

1. STELARA® [Prescribing Information]. Horsham, PA: Janssen Biotech, Inc. 2. Sandborn WJ, et al. *Clin Gastroenterol Hepatol*. 2022;20:578–590. 3. Sands B, et al. *Lancet*. 2022;399:2200-2211.4. Afif W, et al. *Am Jour Gastroenterol*. 2023; ePub. 5. Pilon D, et al. Poster presented at ACG 2021; October 22-27, 2021; Las Vegas, NV. 6. Zhdanava M, et al. Poster presented at Digestive Disease Week 2022; May 21-24, 2022; San Diego, CA. 7. Zhdanava M, et al. Poster presented at ACG 2023; October 23-25, 2023; Vancouver, CAN. 8. Zhdanava M, et al. Poster presented at Crohn's & Colitis Congress 2024; January 25-27, 2022; Las Vegas, NV . 9. Feagan B, et al. *NEJM*. 2016; 375:1946-1960. 10. Sands B, et al. *NEJM*. 2019; 381(13):1201-1214. 11. Ghosh S, et al. *Journal of Crohn's and Colitis*. 2024; ePub.12. Sands B, et al. *Lancet*. 2022; 399: Supplement.

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