Structural damage progression in active PsA: Latest evidence with guselkumab

PsA=psoriatic arthritis.

 08/25 cp-530536v2

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Patients with PsA may develop significant structural damage before diagnosis and treatment initiation[1-3]

~50% of patients

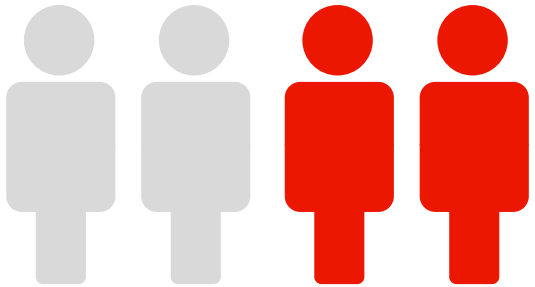
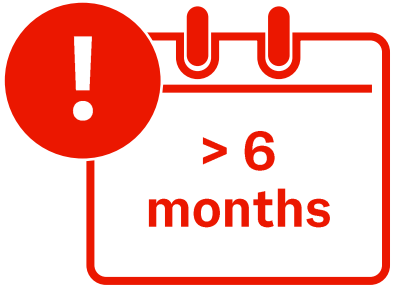


exhibit **structural damage** and **functional impairment** within 2 years of developing symptoms[2]

- Bone erosions
- Joint space narrowing
- Joint destruction

Diagnostic delay of



between symptom onset and the first rheumatologist visit may lead to **increased peripheral joint erosions** and **worse long-term physical function**[1]

1. Haroon M, et al. *Ann Rheum Dis.* 2015;74(6):1045-1050. 2. van der Heijde D, et al. *Arthritis Res Ther.* 2020;22(1):18. doi:10.1186/s13075-020-2103-8 3. Hioki T, et al. *J Clin Med.* 2022;11(7):2051. doi:10.3390/jcm11072051

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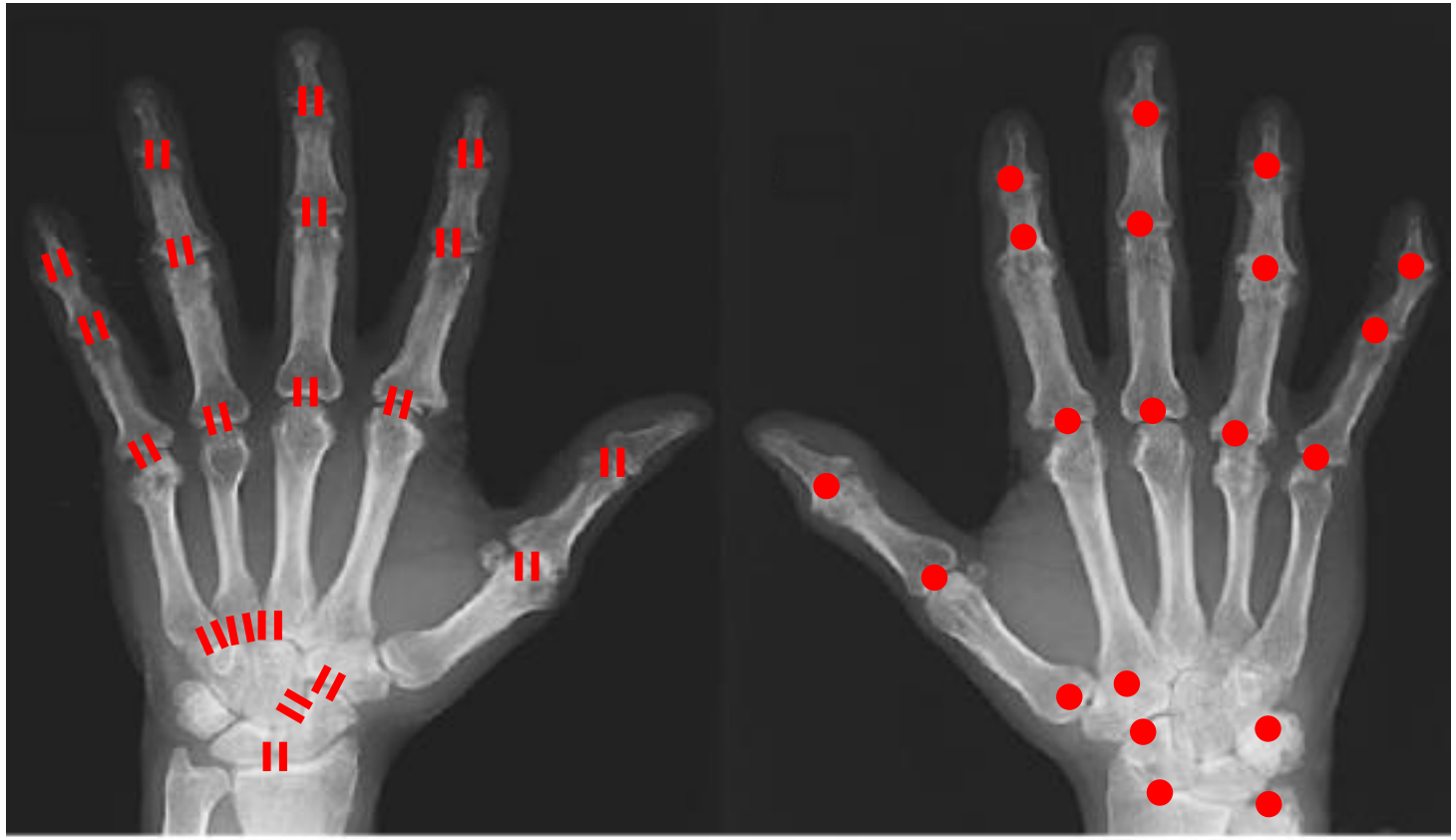
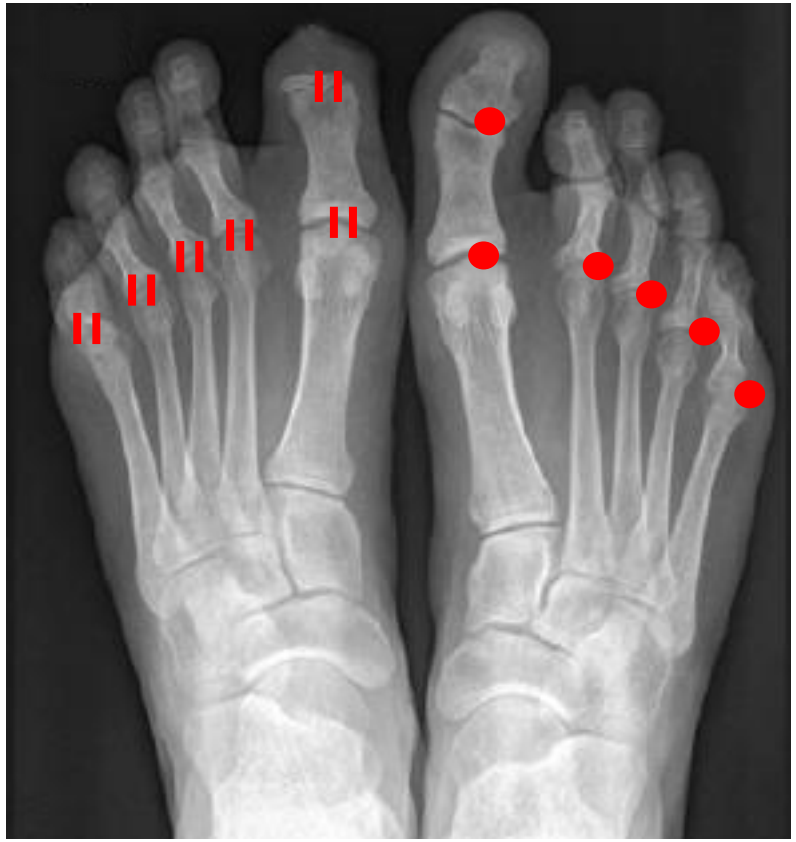
Assessing structural damage in patients with PsA: modified vdH-S score[1-3]

Hands[2,3*]



- 20 bone erosion locations per hand (Erosion score: 0-5)[2]
- 20 JSN locations per hand (JSN score: 0-4)[2]

Feet[2,3*]



- 6 bone erosion locations per foot (Erosion score: 0-10)[2]
- 6 JSN locations per foot (JSN score: 0-4)[2]

***Note: Radiographs are not sourced from the DISCOVER trials or the APEX trial.**

JSN=joint space narrowing; mvdH-S=van der Heijde-Sharp.

1. van der Heijde D, et al. *Ann Rheum Dis.* 2005;64(Suppl 2):ii61-ii64. 2. Merola, J et al. 2023. Mendeley Data, V1, doi: 10.17632/wkzc5xmp6m 3. Salaffi F, et al. *Radiol Med.* 2019;124(11):1071–1086.

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TREMFYA® (guselkumab) Selected Important Safety Information

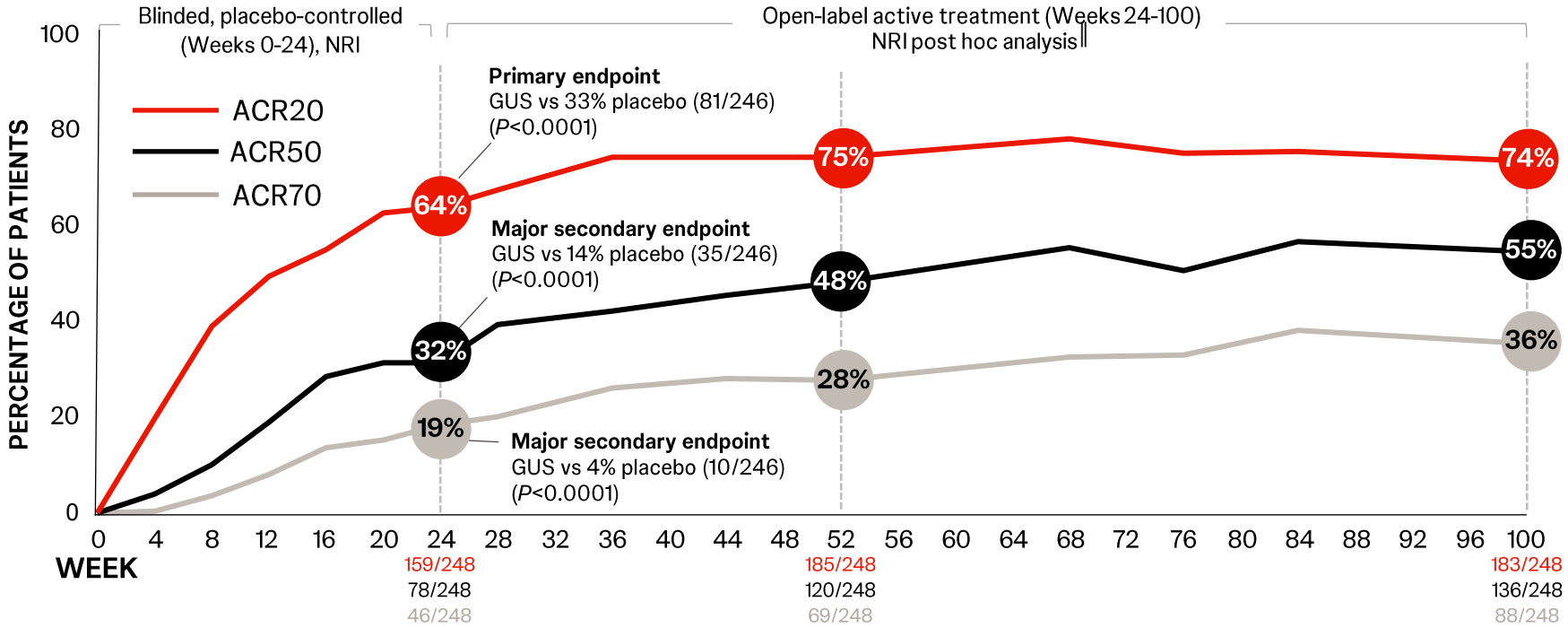
SELECTED IMPORTANT SAFETY INFORMATION

TREMFYA® is contraindicated in patients with a history of serious hypersensitivity reaction to guselkumab or to any of the excipients. Serious hypersensitivity reactions, including anaphylaxis, may occur. TREMFYA® may increase the risk of infection. Do not initiate treatment in patients with clinically important active infection until the infection resolves or is adequately treated. If such an infection develops, discontinue TREMFYA® until infection resolves. Evaluate for tuberculosis (TB) before treating with TREMFYA®. Monitor patients for signs and symptoms of active TB during and after treatment with TREMFYA®. Drug-induced liver injury has been reported. Interrupt treatment if drug-induced liver injury is suspected, until this diagnosis is excluded. Avoid use of live vaccines in patients treated with TREMFYA®. Related and other Important Safety Information can be found at the landing page and at the end of this asset.

cp-510980v1

Guselkumab (GUS) ACR responses in DISCOVER 1 and DISCOVER 2*

DISCOVER 2 ACR20/50/70: Open-label active treatment, NRI post hoc analysis (Weeks 24-100)[1-4†‡§‖¶]



DISCOVER 1[4-6]

Week 24 (blinded, placebo-controlled phase, NRI)

ACR20 response (primary endpoint)†‡§:

52% GUS (66/127) **vs 22% placebo** (28/126) (*P*<0.0001)

ACR50 response (major secondary endpoints)†‡§:

30% GUS (38/127) **vs 9% placebo** (11/126) (*P*<0.0001)

ACR70 response (major secondary endpoints)†‡§:

12% GUS (15/127) **vs 6% placebo** (7/126) (*P*=NS)

Week 52 (Open-label active treatment, NRI post hoc analysis)†‡§¶#

ACR20 response: 60% GUS (76/127)

ACR50 response: 39% GUS (49/127)

ACR70 response: 26% GUS (33/127)

ACR50 and ACR70 responses in DISCOVER 1 and DISCOVER 2 at Week 24 were not part of the sequential testing procedure but were prespecified to be tested upon achieving statistical significance for ACR20 at Week 24.

***DISCOVER Study Designs:** DISCOVER 1 and DISCOVER 2 were 2 phase 3, multicenter, randomized, double-blind, placebo-controlled studies evaluating the efficacy and safety of GUS administered q8w subcutaneously after starter doses at Week 0 and Week 4 (n=127 and n=248, respectively) or placebo (n=126 and n=246, respectively), with starter doses at Week 0, and then every 4 weeks in patients with active PsA (fulfilling CIASsification criteria for Psoriatic ARthritis [CASPAR]) despite standard therapies (nonbiologic DMARDs, apremilast, and nonsteroidal anti-inflammatory drugs [NSAIDs]). A stable dose of 1 selected nonbiologic DMARD, corticosteroids, and NSAIDs was permitted but not required. In DISCOVER 1, eligible patients (≥18 years of age) had active PsA (swollen/tender joints ≥3, CRP ≥0.3 mg/dL) for at least 6 months and included patients with prior biologic experience of ≤2 tumor necrosis factor alpha inhibitors. Patients with other inflammatory diseases and those who had previously received Janus kinase inhibitors or biologics other than TNFis were excluded. In DISCOVER 2, eligible patients (≥18 years of age) had active PsA (swollen/tender joints ≥5, CRP ≥0.6 mg/dL) for at least 6 months and no prior JAK inhibitor or biologic experience. At Week 16, patients in all treatment groups who had <5% improvement from baseline in both swollen and tender joint counts were considered as meeting early escape and were allowed to initiate or increase the dose of one of the permitted concomitant medications up to the maximum dose allowed. The primary endpoint in DISCOVER 1 and DISCOVER 2 was ACR20 response at Week 24. Treatment failure criteria: discontinued study agent for any reason, terminated study participation for any reason, initiated or increased the dose of DMARDs or oral corticosteroids over baseline for PsA, or initiated protocol-prohibited medications/therapies for PsA.[1,4,5,7]

†**The same patients may not have responded at each time point.** ‡Through Week 24, patients were considered to be nonresponders after meeting treatment failure criteria: discontinued study agent for any reason, terminated study participation for any reason, initiated or increased dose of DMARDs or oral corticosteroids over baseline for PsA, or initiated protocol-prohibited medications/therapies for PsA. **After Week 24, treatment failure rules were not applied.** §Patients with missing data were considered nonresponders. ‖After Week 24, patients and doctors knew that all patients were on TREMFYA® (open label with a blinded dosing interval), which may have affected the results. ¶The DISCOVER 2 prespecified as-observed analysis from Week 24 to Week 100 is not shown. #The DISCOVER 1 prespecified as-observed analysis from Week 24 to Week 52 is not shown.

ACR20=American College of Rheumatology 20% improvement criteria; ACR50=American College of Rheumatology 50% improvement criteria; ACR70=American College of Rheumatology 70% improvement criteria; CD64=cluster of differentiation 64; CRP=C-reactive protein; DMARD=disease-modifying antirheumatic drug; JAK=Janus kinase; NRI=nonresponder imputation; NS=not significant; q8w=every 8 weeks; TNFi=tumor necrosis factor inhibitor.

1. Mease PJ, et al. *Lancet*. 2020;395(10230):1126-1136. 2. McInnes IB, et al. *Arthritis Rheumatol*. 2021;73(4):604-616. 3. McInnes IB, et al. *Arthritis Rheumatol*. 2022;74(3):475-485. 4. Data on file. Janssen Biotech, Inc. 5. Deodhar A, et al. *Lancet*. 2020;395(10230):1115-1125. 6. Ritchlin CT, et al. *RMD Open*. 2021;7(1):e001457. 7. TREMFYA® (guselkumab) [Prescribing Information]. Horsham, PA: Janssen Biotech, Inc.

Guselkumab safety outcomes in DISCOVER 1 and DISCOVER 2

Adverse events reported in the placebo-controlled phase through Week 24 combined across DISCOVER 1 and DISCOVER 2[1]

% (n) [events per 100 PYs of follow-up]	Adverse events	Serious adverse events	Infections	Serious infections
GUS (n=375)	**48.5%** (182) [257.3]	**1.9%** (7) [4.0]	**19.5%** (73) [58.3]	**0.3%** (1) [0.6]
Placebo (n=372)	**47.3%** (176) [220.0]	**3.2%** (12) [9.3]	**20.7%** (77) [58.5]	**0.8%** (3) [4.1]

In the 24-week, placebo-controlled period of the combined DISCOVER 1 and DISCOVER 2 clinical trials[2]:

The overall safety profile observed in patients with active PsA treated with GUS is generally consistent with the profile in patients with plaque PsO, with the addition of bronchitis (occurred in 1.6% and 1.1% of patients in the GUS q8w group and placebo group, respectively) and neutrophil count decreased (occurred in 0.3% and 0% of patients in the GUS q8w group and placebo group, respectively).

- The majority of events of neutrophil count decreased were mild, transient and not associated with infection, and did not lead to discontinuation

Adverse events reported through Year 1 combined across DISCOVER 1 and DISCOVER 2[1*]

% (n) [events per 100 PYs of follow-up]	Adverse events	Serious adverse events	Infections	Serious infections
GUS (n=375)	**64.5%** (242) [217.7]	**4.8%** (18) [5.7]	**33.3%** (125) [56.5]	**1.3%** (5) [1.6]

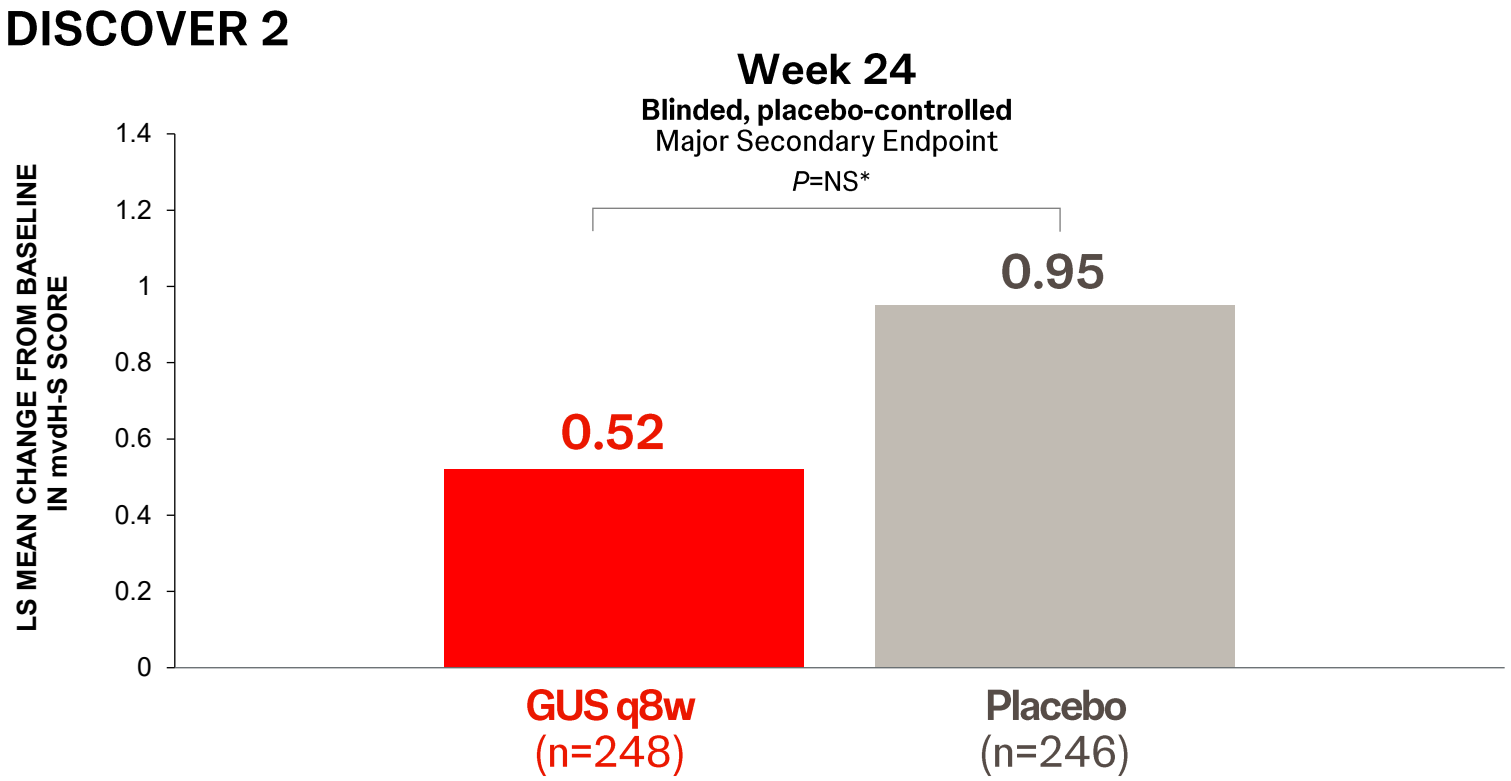
Adverse events reported through end of study (Week 112) in DISCOVER 2[1]

% (n) [events per 100 PYs of follow-up]	Adverse events	Serious adverse events	Infections	Serious infections
GUS (n=248)	**71.8%** (178) [158.0]	**8.9%** (22) [6.1]	**37.9%** (94) [40.5]	**3.2%** (8) [2.2]

*1 year is defined as 60 weeks (through the end of the study) in DISCOVER 1 and 52 weeks in DISCOVER 2.
PsO=psoriasis; PY=patient-year.

1. Data on file. Janssen Biotech, Inc. 2. TREMFYA® (guselkumab) [Prescribing Information]. Horsham, PA: Janssen Biotech, Inc.

Change in mvdH-S score from baseline to Week 24 in DISCOVER 2[1]



The APEX study design builds upon the DISCOVER program by further evaluating the effect of GUS on adult patients with active PsA who are at a higher risk for structural damage progression (≥2 joints with erosions on baseline radiographs of the hands and feet). The APEX study population also has a CRP of ≥0.3 mg/dL[2-4]

The results are not statistically significant; therefore, treatment effect for inhibition of structural damage has not been established.

Patients received GUS 100 mg SC at Week 0, Week 4, and every 8 weeks thereafter.

Treatment failure rules were not applied, and missing data were assumed to be missing at random and were imputed using multiple imputation.

**P* value is not significant.

SC=subcutaneous.

1. Mease PJ, et al. *Lancet*. 2020;395(10230):1126-1136. 2. Ritchlin CT, et al. *Trials*. 2023;24:22. https://doi.org/10.1186/s13063-022-06945-y 3. Mease PJ, et al. Abstract presented at EULAR 2025; June 11-14, 2025; Barcelona, Spain. 4. Mease PJ, et al. Oral presentation at EULAR 2025; June 11-14, 2025; Barcelona, Spain.

APEX*: Phase 3b trial to evaluate the effect of GUS on structural damage progression[1-3]

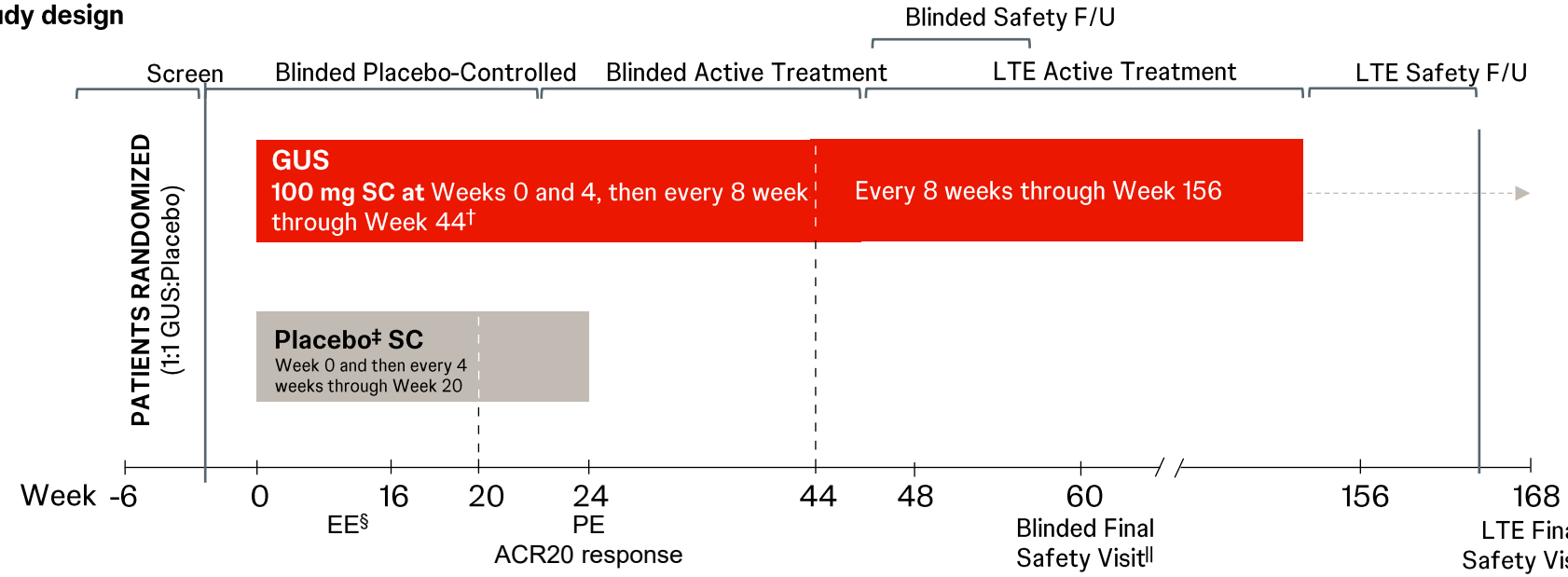
Purpose

- To further evaluate the impact of GUS in patients with active PsA and known risk factors for radiographic progression

Primary Endpoint:
ACR20 response at Week 24

Major Secondary Endpoint:
PsA-modified vdH-S score mean change from baseline at Week 24

Study design



Selected Inclusion and Exclusion Criteria

- ✓ Age ≥18 years
- ✓ Diagnosis of PsA for ≥6 months and met the CASPAR criteria at screening
- ✓ Active PsA (despite previous csDMARD, apremilast, and/or NSAID therapy): ≥3 swollen/tender joints
- ✓ **CRP ≥0.3 mg/dL**
- ✓ **≥2 joints with erosions on baseline radiographs of the hands and feet**
- ✓ Active plaque PsO, with ≥1 psoriatic plaque of ≥2 cm diameter and/or nail changes consistent with PsO
- × No previous biologic or Janus kinase inhibitor therapy
- × Currently receiving ≥3 csDMARDs precluded participation

*In APEX, patients were originally randomized to a q4w dosing regimen. GUS 100 mg q4w is not an approved dosing regimen. †Placebo SC was administered at Week 8, then q8w through Week 48 to maintain blinding. ‡At Week 24, patients taking placebo crossed over to receive GUS 100 mg every 4 weeks thereafter. GUS 100 mg dosed q4w is not an approved dosing regimen. §At Week 16, subjects in all treatment groups who had <20% improvement from baseline in both tender and swollen joint counts were considered as meeting early escape criteria and were allowed to initiate or increase the dose of one of the permitted concomitant medications up to the maximum dose allowed. ‖Final safety visit for patients who do not enter LTE. ¶Final safety visit for patients who enter LTE.
csDMARD=conventional disease-modifying antirheumatic drug; EE=early escape; F/U=follow-up; LTE=long-term extension; PE=primary endpoint; q4w=every 4 weeks; vdH-S=van der Heijde-Sharp.

1. Ritchlin CT, et al. *Trials*. 2023;24(1):22. doi:10.1186/s13063-022-06945-y 2. A study of guselkumab in participants with active psoriatic arthritis (APEX). ClinicalTrials.gov. Accessed June 22, 2025. Last Updated June 22, 2025. https://clinicaltrials.gov/study/NCT04882098 3. Mease PJ, et al. Oral presentation at EULAR 2025; June 11-14, 2025; Barcelona, Spain.

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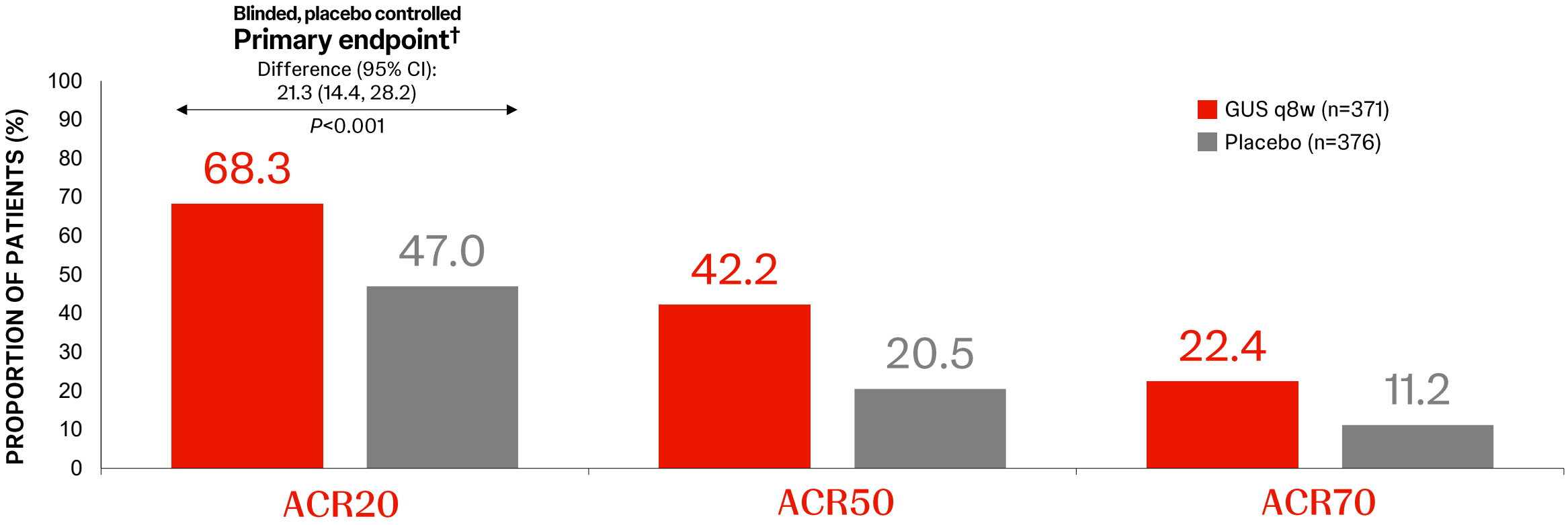
ACR20/50/70 response in APEX[1,2]

APEX ACR20/50/70 response at Week 24[1,2*]



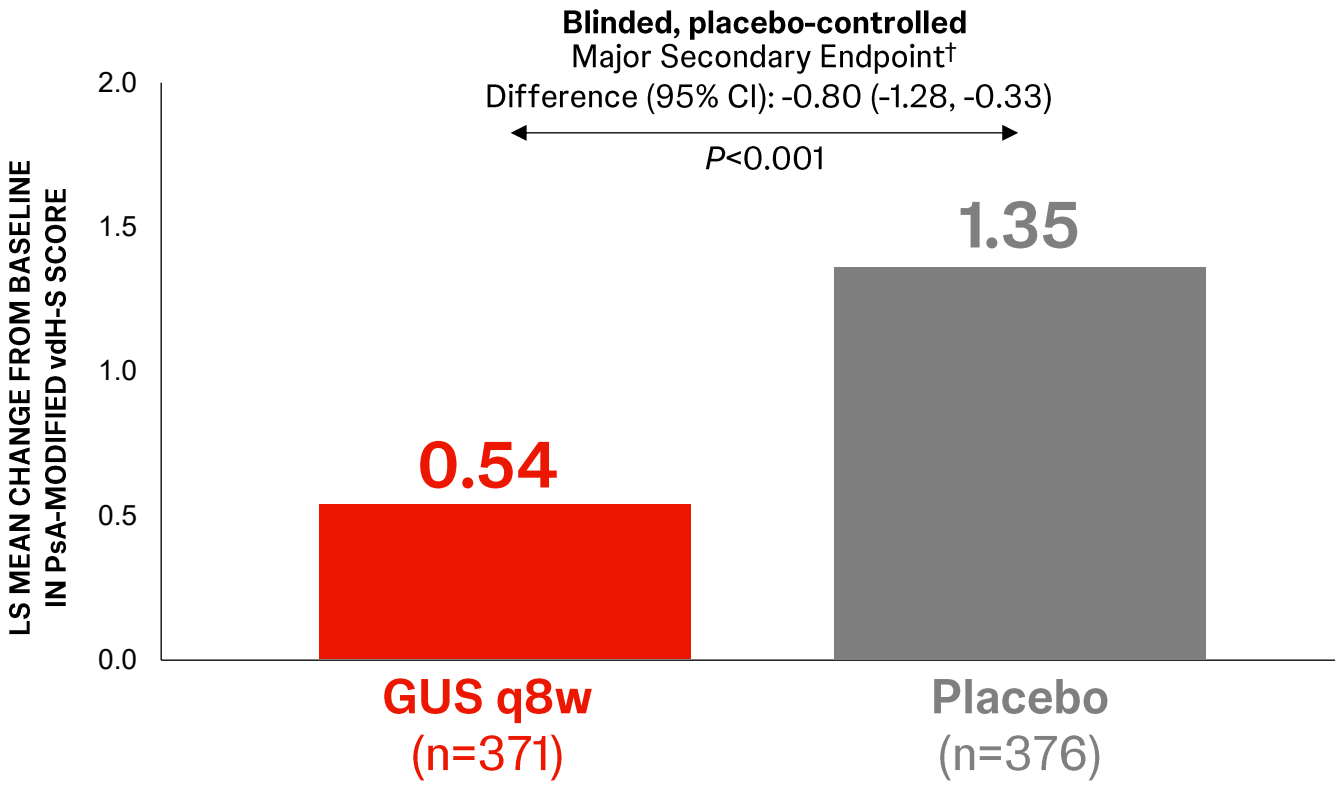
ACR50 and ACR70 responses at Week 24 were not adjusted for multiplicity; therefore, statistical significance has not been established.

*Efficacy analyses are from the mFAS, which included all randomized patients excluding those from Ukraine sites rendered unable to support key study operations due to major disruptions. †Primary endpoint *P* values are multiplicity-controlled using a fixed sequence testing procedure and can be used to determine statistical significance. Statistics are based on CMH across multiply imputed datasets.
CI=confidence interval; CMH=Cochran-Mantel-Haenszel; mFAS=modified full analysis set.

1. Mease PJ, et al. Abstract presented at EULAR 2025; June 11-14, 2025; Barcelona, Spain. 2. Mease PJ, et al. Oral presentation at EULAR 2025; June 11-14, 2025; Barcelona, Spain.

Structural damage endpoint in APEX[1,2]

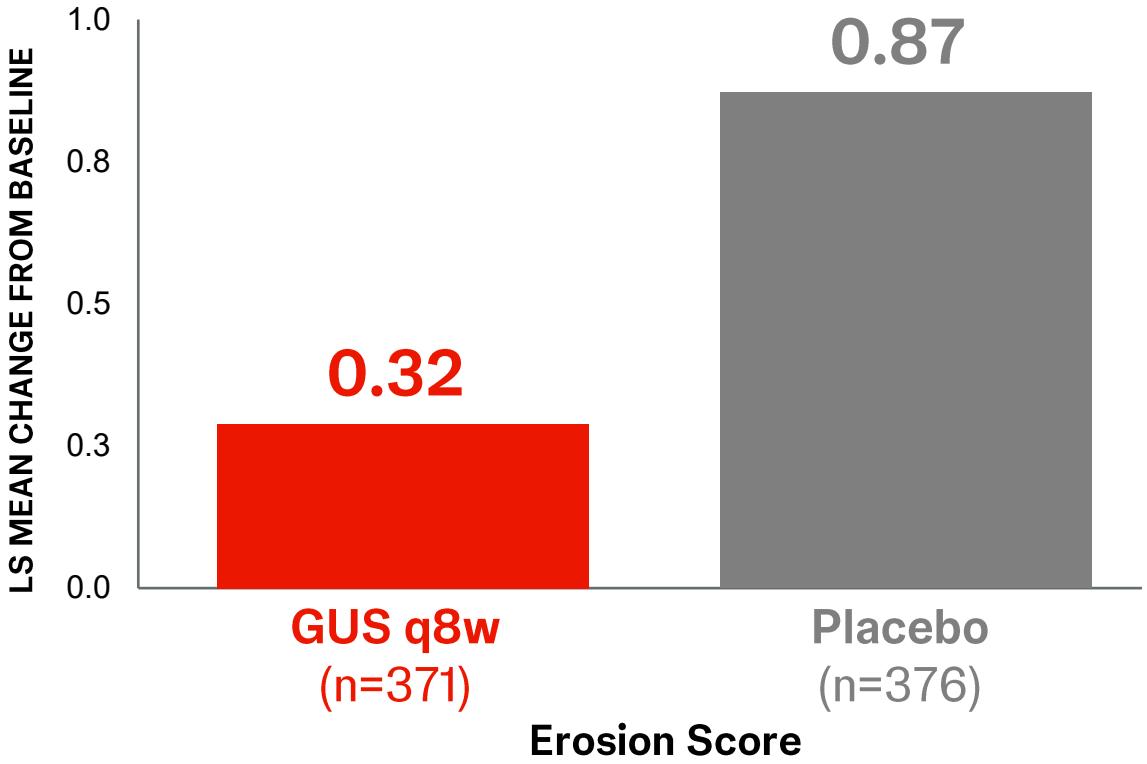
PsA-modified vdH-S score with GUS at Week 24[1,2*]



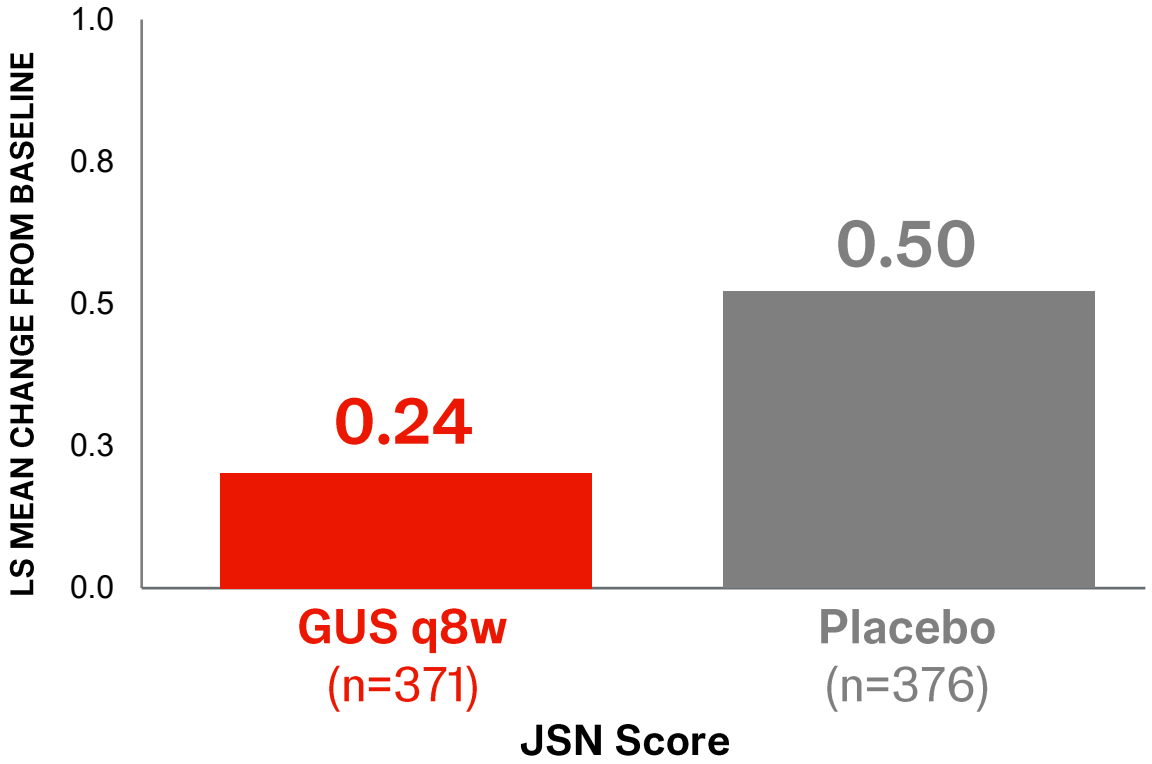
*Efficacy analyses are from the mFAS, which included all randomized patients excluding those from Ukraine sites rendered unable to support key study operations due to major disruptions.
†Major secondary endpoint *P* values are multiplicity-controlled using a fixed sequence testing procedure and can be used to determine statistical significance. Statistics are based on ANCOVA across multiply imputed datasets.
ANCOVA=analysis of covariance.
1. Mease PJ, et al. Abstract presented at EULAR 2025; June 11-14, 2025; Barcelona, Spain. 2. Mease PJ, et al. Oral presentation at EULAR 2025; June 11-14, 2025; Barcelona, Spain.

Erosion and joint space narrowing scores in APEX[1,2*†‡]

Other endpoints:
Change in erosion scores at Week 24[1,2*†‡]



Other endpoints:
Change in JSN scores at Week 24[1,2*†‡]



***P* values for erosion score and JSN score are not multiplicity-controlled; they are considered nominal and may not be used to claim statistical significance.**

†Efficacy analyses are from the mFAS, which included all randomized patients excluding those from Ukraine sites rendered unable to support key study operations due to major disruptions.
‡Based on ANCOVA on multiply imputation data.

1. Mease PJ, et al. Abstract presented at EULAR 2025; June 11-14, 2025; Barcelona, Spain. 2. Mease PJ, et al. Presented at: EULAR 2025; June 11-14, 2025; Barcelona, Spain.

Guselkumab safety outcomes in APEX

Safety Through Week 24	GUS q8w n=388	PBO n=386
Mean weeks of follow-up	23.9	23.8
Patients with ≥1:		
Adverse event	**165 (42.5%)**	**144 (37.3%)**
Serious adverse event	**12 (3.1%)**	**10 (2.6%)**
Adverse event leading to study agent discontinuation	6 (1.5%)	1 (0.3%)
Infections	**91 (23.5%)**	**81 (21.0%)**
Serious infection	**5 (1.3%)**	**1 (0.3%)**
Active tuberculosis	0	0
Opportunistic infection	0	0
Venous thromboembolism event	1 (0.3%)	1 (0.3%)
Anaphylactic or serum sickness reaction	0	0
Clinically important hepatic disorder	0	0

- **Study remains blinded through Week 48**
- **2 patients with malignancy (prostate, renal); 1 MACE (myocardial infarction); 1 COVID-19 death in an unvaccinated elderly patient**
- **No new-onset IBD**

COVID-19=coronavirus disease 2019; IBD=inflammatory bowel disease; MACE=major adverse cardiovascular event.

Mease PJ, et al. Oral presentation at EULAR 2025; June 11-14, 2025; Barcelona, Spain.

Important Safety Information

INDICATIONS

TREMFYA® (guselkumab) is indicated for the treatment of adult patients with moderate to severe plaque psoriasis who are candidates for systemic therapy or phototherapy.

TREMFYA® is indicated for the treatment of adult patients with active psoriatic arthritis.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

TREMFYA® is contraindicated in patients with a history of serious hypersensitivity reaction to guselkumab or to any of the excipients.

WARNINGS AND PRECAUTIONS

Hypersensitivity Reactions

Serious hypersensitivity reactions, including anaphylaxis, have been reported with postmarket use of TREMFYA®. Some cases required hospitalization. If a serious hypersensitivity reaction occurs, discontinue TREMFYA® and initiate appropriate therapy.

Infections

TREMFYA® may increase the risk of infection. Treatment with TREMFYA® should not be initiated in patients with any clinically important active infection until the infection resolves or is adequately treated.

Consider the risks and benefits of treatment prior to prescribing TREMFYA® in patients with a chronic infection or a history of recurrent infection. Instruct patients receiving TREMFYA® to seek medical help if signs or symptoms of clinically important chronic or acute infection occur. If a patient develops a clinically important or serious infection, or is not responding to standard therapy, closely monitor and discontinue TREMFYA® until the infection resolves.

Tuberculosis (TB)

Evaluate patients for TB infection prior to initiating TREMFYA® treatment. Do not administer TREMFYA® to patients with active TB infection. Initiate treatment of latent TB prior to administering TREMFYA®. Consider anti-TB therapy prior to initiating TREMFYA® in patients with a past history of latent or active TB in whom an adequate course of treatment cannot be confirmed. Monitor all patients for signs and symptoms of active TB during and after TREMFYA® treatment.

Hepatotoxicity

A serious adverse reaction of drug-induced liver injury was reported in a clinical trial subject with Crohn's disease following three doses of a higher than recommended induction regimen.

Consider other treatment options in patients with evidence of acute liver disease or cirrhosis. Prompt investigation of the cause of liver enzyme elevation is recommended to identify potential cases of drug-induced liver injury. Interrupt treatment if drug-induced liver injury is suspected, until this diagnosis is excluded. Instruct patients to seek immediate medical attention if they experience symptoms suggestive of hepatic dysfunction.

Immunizations

Prior to initiating TREMFYA®, complete all age-appropriate vaccinations according to current immunization guidelines. Avoid use of live vaccines in patients treated with TREMFYA®.

ADVERSE REACTIONS

Most common adverse reactions associated with TREMFYA® include: plaque psoriasis and psoriatic arthritis adverse reactions (≥1%): upper respiratory infections, headache, injection site reactions, arthralgia, bronchitis, diarrhea, gastroenteritis, tinea infections, and herpes simplex infections.

The overall safety profile observed in patients with psoriatic arthritis is generally consistent with the safety profile in patients with plaque psoriasis, with the addition of bronchitis and neutrophil count decreased.

Please read the full Prescribing Information and Medication Guide for TREMFYA®. Provide the Medication Guide to your patients and encourage discussion.

TREMFYA® is available as a 100 mg/mL subcutaneous injection.

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