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Post Hoc Analysis of the **DISCOVER 1&2** Studies

Post hoc analysis of DISCOVER 1&2 data shows that patients with imaging-confirmed sacroilitis receiving TREMFYA® (guselkumab) had greater improvements in assessments for axial symptoms of active psoriatic arthritis (PsA). The data are being presented in The Lancet Rheumatology.

DISCOVER 1 & 2 are Phase III, randomized, double-blind, placebo-controlled studies evaluating the efficacy and safety of TREMFYA® (guselkumab) in patients with active psoriatic arthritis (PsA). Results showed that patients treated with TREMFYA, a human monoclonal antibody targeting the p19 subunit of interleukin (IL)-23, had greater improvements in the signs and symptoms of active PsA compared with placebo.

Post Hoc Analysis of Effect on Axial Symptoms published in *The Lancet Rheumatology*

The pooled, post hoc analysis of these two studies identified 28% of patients who had imaging-confirmed sacroiliitis (312 of the 1120 patients enrolled). These patients' scores on the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and the Ankylosing Spondylitis Disease Activity Score (ASDAS) through Week 24 were compared between patients receiving TREMFYA [n=194, of which 103 received TREMFYA every 4 weeks (q4w; not FDA approved), and 91 received TREMFYA every 8 weeks (q8w)] vs placebo (n=118).

The results suggest that by inhibiting the IL-23 p19 subunit, TREMFYA may be effective in addressing axial symptoms in patients with PsA.[4]

About Psoriatic Arthritis

A chronic, immune-mediated disease characterized by psoriatic skin lesions and peripheral arthritis.

- Axial symptoms like sacroiliitis occur in 5-28% of patients with early PsA, and in over 40% of patients with established disease.[1,2]

About Sacroiliitis

Inflammation of the sacroiliac joints (where the lower spine and pelvis connect). Sacroiliitis presents as low back pain that can extend into the buttocks and legs.

- Sacroilitis occurs in the PsA subtype of spondylitis, where inflammation reaches the spine and causes stiffness as well as pain and difficulty moving the neck, lower back, sacroiliac joints, and pelvis. This type of PsA can also affect joints in the arms, legs, hands, and feet.[3]

Efficacy Assessments

Efficacy was analyzed using:

- The **Bath Ankylosing Spondylitis Disease Activity Index (BASDAI)** score and modified BASDAI (mBASDAI) score excluding peripheral joint pain. Major clinical response = BASDAI50 (≥50% improvement).[4]
- **Ankylosing Spondylitis Disease Activity Score (ASDAS-CRP),** a composite score assessing symptoms and C-reactive protein levels, as well as ASDAS responses of inactive disease (<1·3), major improvement (change (≥2·0), and clinically important improvement (≥1·1).[5,6]

Results at Week 24 and Week 52

At Week 24, **38%** of patients receiving TREMFYA q4w and q8w achieved BASDAI50 (major clinical response), compared with **19%** of placebo patients (see right).

Least square (LS) mean changes from baseline at Week 24 in:

- **BASDAI**: -2·7 in both TREMFYA groups; -1·3 in the placebo group
- **mBASDAI**: -2·6 in q4w and -2·7 in q8w TREMFYA groups; -1·4 in placebo group
- **Spinal Pain**: -2·5 in q4w and -2·7 in q8w TREMFYA groups; -1·2 in placebo group
- **ASDAS**: -1·4 in both TREMFYA groups; -0·7 in placebo group

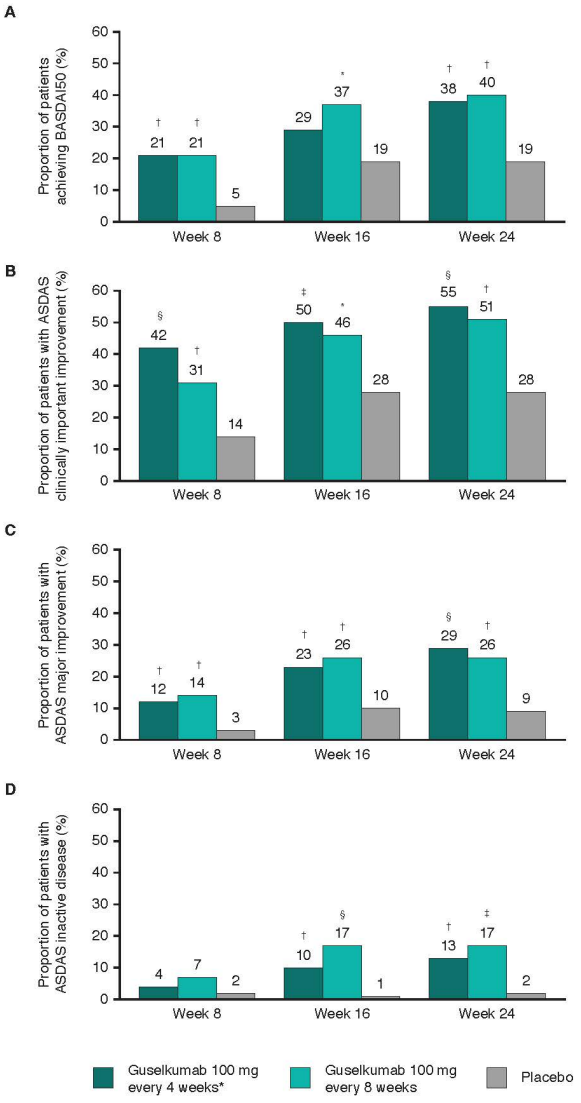
These improvements were maintained through Week 52 in the TREMFYA groups (below right).

In adult patients with active PsA and imaging-confirmed sacroiliitis, TREMFYA treatment provided sustained improvements in BASDAI, mBASDAI, Spinal Pain, and ASDAS scores.

Instruments to Assess Symptoms of Axial Involvement

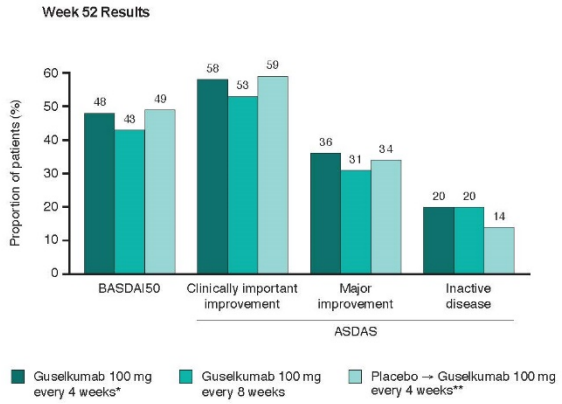
The Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) is a six-item questionnaire using a 0-10 rating scale to assess the severity of the symptoms of ankylosing spondylitis, including fatigue, spinal pain, peripheral joint pain, pain at entheseal sites, severity of morning stiffness, and duration of morning stiffness. A total BASDAI score (range: 0-10) ≥4 suggests suboptimal control of the disease. A major clinical response (BASDAI50) is defined as a ≥50% improvement in symptoms. BASDAI has demonstrated statistically significant reliability. The modified BASDAI (mBASDAI) excludes peripheral joint pain as a criterion.[4]

The Ankylosing Spondylitis Disease Activity Score (ASDAS) is a composite index to measure disease activity in ankylosing spondylitis based on patient assessment of symptoms (0-10 rating scale for back pain, duration of morning stiffness, patient global assessment, peripheral pain and swelling,) and laboratory data from blood tests. The ASDAS-CRP (preferred clinical standard) incorporates levels of C-reactive protein, which increase when inflammation is present in the body, in the ultimate composite score.[5,6]



nominal *p<0·05, †p<0·01, ‡p<0·001, and §p<0·0001

*Guselkumab q4w is not FDA approved



*Guselkumab q4w is not FDA approved
**Crossover from placebo to guselkumab was available at Week 24

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Important Safety Information

What is the most important information I should know about TREMFYA®?
TREMFYA® is a prescription medicine that may cause serious side effects, including:

- **Serious Allergic Reactions.** Stop using TREMFYA® and get emergency medical help right away if you develop any of the following symptoms of a serious allergic reaction:
  - fainting, dizziness, feeling lightheaded (low blood pressure)
  - swelling of your face, eyelids, lips, mouth, tongue or throat
  - trouble breathing or throat tightness
  - chest tightness
  - skin rash, hives
  - itching

- **Infections.** TREMFYA® may lower the ability of your immune system to fight infections and may increase your risk of infections. Your healthcare provider should check you for infections and tuberculosis (TB) before starting treatment with TREMFYA® and may treat you for TB before you begin treatment with TREMFYA® if you have a history of TB or have active TB. Your healthcare provider should watch you closely for signs and symptoms of TB during and after treatment with TREMFYA®.

  Tell your healthcare provider right away if you have an infection or have symptoms of an infection, including:
  - fever, sweats, or chills
  - muscle aches
  - weight loss
  - cough
  - warm, red, or painful skin or sores on your body different from your psoriasis
  - diarrhea or stomach pain
  - shortness of breath
  - blood in your phlegm (mucus)
  - burning when you urinate or urinating more often than normal

Do not take TREMFYA® if you have had a serious allergic reaction to guselkumab or any of the ingredients in TREMFYA®.

Before using TREMFYA®, tell your healthcare provider about all of your medical conditions, including if you:

- have any of the conditions or symptoms listed in the section **"What is the most important information I should know about TREMFYA®?"**
- have an infection that does not go away or that keeps coming back.
- have TB or have been in close contact with someone with TB.
- have recently received or are scheduled to receive an immunization (vaccine). You should avoid receiving live vaccines during treatment with TREMFYA®.
- are pregnant or plan to become pregnant. It is not known if TREMFYA® can harm your unborn baby.

- are breastfeeding or plan to breastfeed. It is not known if TREMFYA® passes into your breast milk.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

What are the possible side effects of TREMFYA®?
TREMFYA® may cause serious side effects. See "What is the most important information I should know about TREMFYA®?"

The most common side effects of TREMFYA® include: upper respiratory infections, headache, injection site reactions, joint pain (arthralgia), diarrhea, stomach flu (gastroenteritis), fungal skin infections, herpes simplex infections, and bronchitis.

These are not all the possible side effects of TREMFYA®. Call your doctor for medical advice about side effects.

Use TREMFYA® exactly as your healthcare provider tells you to use it.

Please read the full Prescribing Information, including Medication Guide for TREMFYA®, and discuss any questions that you have with your doctor.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

References

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