

CORRECTION

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# Correction: Effect of guselkumab on serum biomarkers in patients with active psoriatic arthritis and inadequate response to tumor necrosis factor inhibitors: results from the COSMOS phase 3b study

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Following publication of the original article [1], the authors reported that the corrections were not carried out during the revisions.

The corrections are provided below and the changes have been set in **bold typeface**.

The original article can be found online at <https://doi.org/10.1186/s13075-023-03125-4>.

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## Abstract

### Methods

Adults with active PsA ( $\geq 3$  swollen joints,  $\geq 3$  tender joints) and IR to one or two TNFi (TNFi-IR) were randomized 2:1 to guselkumab at Weeks 0, 4, then every 8 weeks (Q8W) or placebo → guselkumab Q8W at Week 24 with possible early escape at Week 16. Levels of serum cytokines, including interferon  $\gamma$  (IFN $\gamma$ ), IL-10, and tumor necrosis factor  $\alpha$  (TNF $\alpha$ ); T helper 17 (Th17) effector cytokines IL-17A, IL-17E, and IL-22; and acute phase proteins C-reactive protein (CRP), IL-6, and serum amyloid A (SAA), were assessed and compared with **demographically** matched healthy controls; guselkumab pharmacodynamics through Week 24 were also assessed.

## Results

Baseline serum levels of IL-6, IL-10, IL-17A, IL-17E, IL-22, TNF $\alpha$ , and IFN $\gamma$  were significantly higher in COSMOS TNFi-IR participants than in healthy controls...



...Guselkumab-treated participants achieving ACR20 response at Week 24 exhibited higher baseline IL-22 and IFN $\gamma$  levels versus nonresponders...

### **Keywords**

Serum biomarkers, IL-23/IL-17 pathway, Guselkumab, Psoriatic arthritis

### **Background**

... Treatment recommendations from the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis have highlighted interleukin (IL)-23 inhibitors (IL-23i), along with TNFi, IL-17i, and IL-12/IL-23i, as appropriate for use in both biologic-naive and biologic-experienced patients with **peripheral joint symptoms**...

...The objectives of this analysis were to evaluate baseline serum levels of proinflammatory biomarkers in participants with TNFi-IR PsA in the COSMOS trial in comparison **with** healthy controls and **the relationship of these biomarker levels with**...

### **Clinical assessments**

...ACR20 response was used to assess efficacy in **the** joints at Week 24. Skin responses were assessed among participants with  $\geq 3\%$  BSA and Investigator's Global Assessment (IGA) **score**  $\geq 2$  [22] at...To assess consistency of response in the biomarker cohort versus **the** overall COSMOS population, additional efficacy outcomes **at Week 24** determined in the biomarker cohort **were**  $\geq 50\%$  improvement by ACR criteria (ACR50) response,  $\geq 75\%$  improvement in PASI (**PASI75**), change...

### **Biomarker sample collection**

In COSMOS, blood samples for biomarker **analyses** were collected from all participants at Weeks 0, 4, 16, 24, and 48 into standard serum separation tubes...

Serum samples from 24 healthy control **volunteers** (defined as those with no signs of active inflammation,...

### **Biomarker analyses**

Serum samples for biomarker **analyses** were analyzed using qualified antibody-based assays.... Acute phase proteins and markers of inflammation, CRP, serum amyloid A (SAA), IL-6, IL-10, interferon  $\gamma$  (IFN $\gamma$ ), tumor necrosis factor  $\alpha$  (TNF $\alpha$ ), soluble...

### **Statistical analyses**

This analysis included **participants with available baseline values and follow-up** biomarker and clinical

data over time. All analyses were post hoc; thus, reported *p* values are nominal....

### **Analysis of baseline serum biomarker levels and correlation with disease activity**

...Differences in baseline **serum cytokine** levels between participants with PsA and healthy controls were assessed **using** log<sub>2</sub>-transformed data **with** a general linear model...

...Correlations between baseline **serum biomarker** levels and baseline disease activity (i.e., DAPSA **scores**, PASDAS, and PASI scores) were assessed using Spearman linear regression, with a Spearman correlation (*rho*)  $> 0.25$  and *p*  $< 0.05$  considered significant...

### **Analysis of association between biomarker levels and clinical response**

...Differences in baseline biomarker levels by clinical response at Week 24 (i.e., **response versus nonresponse for ACR20/50, IGA 0/1, and PASI75**)....

### **Baseline serum levels and correlation with baseline disease activity**

...Baseline CRP, SAA, and IL-6 levels were positively associated with baseline joint disease severity as measured by the DAS28-CRP (*p*  $\leq 0.0001$  for each **biomarker**)....

...IL-17A levels showed a trend towards a correlation with PASDAS. No statistically significant correlations were observed between baseline levels of other biomarkers evaluated **and** measures of baseline disease activity assessed (Table 1)...

### **Effect of treatment on biomarker levels**

In participants **randomized to** guselkumab, reductions from baseline in the **levels of**... Th17 effector cytokines IL-17A, IL-17E,....

...biomarkers at Week 48 were similar to those observed in participants receiving guselkumab Q8W from **baseline** (Fig. 2)....

### **Discussion**

...These findings were generally consistent with results from an exploratory biomarker analysis [16] in **patients with active PsA** from the DISCOVER-1 and -2 trials [13, 14]....

...The present study extends these findings by demonstrating that the pharmacodynamic effect of **guselkumab** is sustained through Week 48 in the COSMOS TNFi-IR population, with levels of IL-17E, IL-22,

CRP, and SAA approximating the levels seen in healthy controls at Week 48....

...The current limited data on predictors of response across biomarker studies make it difficult to incorporate precision medicine in **the management of PsA** at this stage....

...While analysis of serum levels allows for collection of serial samples in the clinic, evaluation of tissue would further our knowledge of disease pathogenesis and could potentially help further elucidate the mechanism(s) of action of guselkumab in joints, as pre-clinical evidence suggests that IL-17 is a key mediator of PsA joint pathogenesis [40]....

### Figure captions

Fig. 1 Baseline levels of serum cytokines (IL-10, TNF $\alpha$ , and IFN $\gamma$ ), Th17 effector cytokines (IL-17A, IL-17F, and IL-22)...

Fig. 2 **Serum** levels of IL-17A, IL-17F, IL-22, CRP, SAA, and IL-6 in participants with TNFi-IR PsA from COSMOS compared with healthy controls over time....

Fig. 3 Baseline serum cytokine levels and clinical response at Week 24 in participants with TNFi-IR PsA from COSMOS by ACR20 response or IGA 0/1 response and change from baseline in serum IL-6 level by ACR20 or IGA 0/1 response over time. (A) Baseline serum levels of IL-22 and IFN $\gamma$  levels by ACR20 response at Week 24; (B) Baseline serum levels of SAA, IFN $\gamma$ , IL-17A, and IL-6 by IGA 0/1 response at Week 24; (C) Change from baseline in IL-6 levels by ACR20 and IGA 0/1 responses through Week 24. \* $p < 0.05$  between responders and nonresponders. ACR20,  $\geq 20\%$  improvement in American College of Rheumatology **response** criteria;...

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The original article [1] has been updated.

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### Reference

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