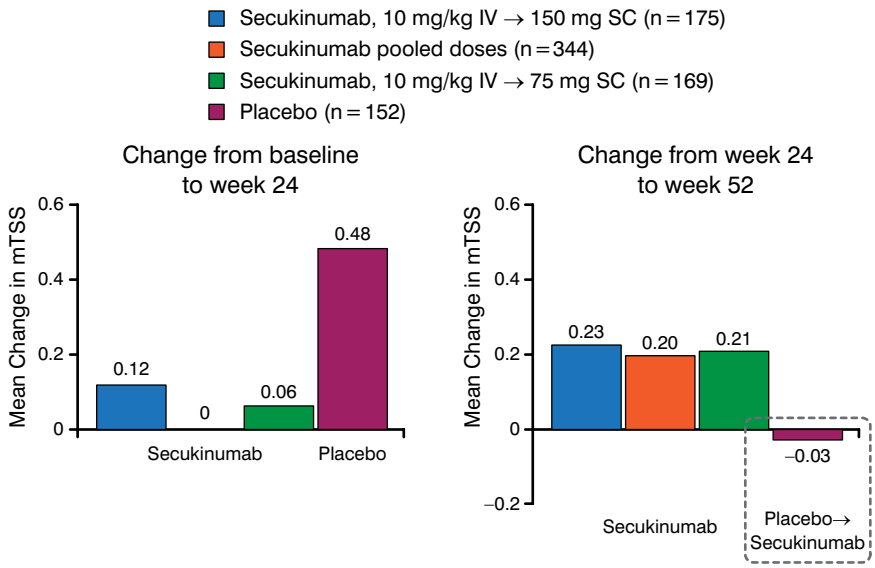
Figure 3. Inhibition of Radiographic Disease Progression Sustained Through Week 52 With Secukinumab[a]



IV, intravenous; mTSS, modified total Sharp score; SC, subcutaneous.

Radiographic disease progression was inhibited in placebo-treated subjects upon switching to secukinumab.

[a]X-ray completers (those subjects who had X-ray measures at baseline, week 16/24, and week 52).

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and that radiographic disease progression was inhibited between 24 and 52 weeks in patients initially treated with placebo who switched to secukinumab (Figure 3).

The inhibition of structural damage seen with secukinumab was seen in patients regardless of prior treatment with TNF inhibitor, or concurrent MTX use.

Negative Results End Development Program of Treating JIA With GLM

Written by Mary Beth Nierengarten

Children with juvenile idiopathic arthritis (JIA) treated with subcutaneous golimumab (GLM) showed a rapid response during the initial 16 weeks of treatment, which resulted in inactive disease in 34% of the patients. Despite this response, at week 48, there was no difference in flare rate between patients who continued on GLM and those randomized to placebo.

Hermine I. Brunner, MD, Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio, USA, presented the 48-week results of the Study of the Safety and Efficacy of CNTO 148 (Golimumab) in Children With Juvenile Idiopathic Arthritis (JIA) and Multiple Joint Involvement Who Have Poor Response to Methotrexate [GO KIDS; NCT01230827].

The multicenter, double-blind, randomized-withdrawal phase 3 trial involved 2 parts. In the first part, 173 children with JIA received GLM 30 mg/m^2 every 4 weeks with methotrexate (MTX) until week 16. In part 2, children who achieved clinical response at week 16 were randomized to placebo or continued GLM from week 16 to week 48, with GLM given to patients in the placebo group on flare.

Patients included in this analysis were children aged 2 to 17 years with JIA, active arthritis involving ≥5 joints despite >3 months of MTX at 10 to 30 mg/m^2, disease duration of ≥6 months, and prior exposure to one anti–tumor necrosis factor drug or background therapy with a stable dose of prednisone.

Patients were excluded if they had current or prior uveitis, latent or active tuberculosis or other chronic infection, a history of severe progressive or uncontrolled liver or renal insufficiency (or significant other organ involvement), or a history of or current malignancy.

The primary end point of the study was the proportion of treatment responders at week 16 who did not display flare-up to week 48. Among the secondary end points was the proportion of patients with inactive disease status in part 2.

For part 1, the study found that 151 of 173 (87.3%) children achieved a 30% improvement from baseline in 3 of 6 criteria. Overall, 34.3% of children displayed inactive disease status at the end of part 1 of the study.

However, the study failed to reach its primary end point because no difference was found in flares at week 48 between patients randomized to placebo and those given GLM (52.6% vs 59.0%; $P = .414$). The study also found no difference in patients with inactive disease from weeks 16 through 48 between GLM and placebo.

On secondary analysis, the study found that only patients with elevated baseline C-reactive protein level had a higher chance of flaring at week 48. However, baseline CRP levels did not influence the response rates to GLM.

In conclusion, the study failed to meet the primary end point as a result of differences in flare rate between the GLM and placebo arms in part 2 of the study. Because of these negative findings, Dr Brunner said that the development program for GLM in JIA has been discontinued.

MEASURE 1: Secukinumab an Effective Treatment for Active AS

Written by Maria Vinall

Secukinumab, a high-affinity fully human monoclonal immunoglobulin G 1K antibody that selectively binds to and inhibits interleukin-17A, improves the signs and symptoms of active ankylosing spondylitis (AS). Dominique Baeten, MD, PhD, Academic Medical Center, University of Amsterdam, Amsterdam, The Netherlands, presented the results of the 16-Week Efficacy and 2-Year Long-term Safety and Efficacy of Secukinumab in Patients With Active Ankylosing Spondylitis trial [MEASURE 1; NCT01358175], which evaluated intravenous loading and maintenance dosing of secukinumab.

The study comprised patients with radiologically confirmed AS with an inadequate response to or intolerance of nonsteroidal anti-inflammatory drugs and/or those who were tumor necrosis factor (TNF) naïve or had an inadequate response or intolerance to ≤1 TNF inhibitor. Additional requirements included a Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) score ≥4 (0 to 10 scale) and back pain visual analog scale score >40 (0 to 100 mm). Patients with total spinal ankylosis, active infections, or ongoing inflammatory conditions other than AS were excluded.

Patients were randomized to placebo or 1 of 2 secukinumab arms; at week 16, patients receiving placebo were separated into responder and nonresponder arms. Randomization was stratified according to whether patients had previous intolerance or inadequate response to anti-TNF therapy or were anti-TNF naïve.

The primary end point was Assessment of Spondyloarthritis International Society (ASAS) 20 response at week 16. Secondary end points at week 16 were ASAS 40, high-sensitivity C-reactive protein results, ASAS 5/6, BASDAI, Short Form 36 physical component summary, AS quality of life, ASAS partial remission, and safety.

The study enrolled 371 patients, 122 to 125 in each arm. Baseline demographics and clinical characteristics were well balanced across treatment groups.

ASAS 20 response at week 16 was 60.8% for the 150-mg secukinumab dose group and 59.7% for the 75-mg group vs 28.7% for the placebo group. A significant difference between each treatment group and placebo was seen at week 1 and sustained out to week 16, indicating a rapid onset of action for this drug ($P < .01$).

Similar values were noted for ASAS 40 (150 mg, 41.6%; 75 mg, 33.1%; vs 13.1% for placebo; $P < .01$), again starting at week 1. All secondary end points were significantly improved for both treatment arms compared with placebo.

Data at week 52 were also presented. ASAS 20 response was sustained out to week 52 (150 mg, 76.7%; 75 mg, 71.3%). ASAS 40 responses were similar (150 mg, 62.1%; 75 mg, 49.1%). BASDAI data indicated a rapid improvement at week 1 that was sustained out to week 52 (150 mg, –3.19; 75 mg, –2.86; vs –0.59 for placebo; $P < .001$, at week 16).

Secukinumab (75 and 150 mg) significantly reduced inflammation of the sacroiliac joint (Berlin Sacroiliac Joint Total Edema Score) as assessed by magnetic resonance imaging at week 16 ($P < .01$ vs placebo). ASAS 20 responses at week 16 were improved regardless of prior use of anti-TNF therapy.

Secukinumab was well tolerated with no unexpected safety findings. Common adverse events included nasopharyngitis, headache, diarrhea, and upper respiratory tract infections, all of which occurred somewhat less in the treatment groups compared with placebo. There were few discontinuations due to treatment. There were 3 cases of candida infection and 1 case of grade 4 neutropenia. Two patients experienced low levels of treatment-emergent antisecukinumab antibodies.

This is the first non-anti-TNF biologic therapy to demonstrate efficacy in a phase 3 clinical AS trial. Regardless of prior anti-TNF exposure, clinical benefit was observed.

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