Cosentyx® clinical trial program in spondyloarthritis (SpA)[1-7]

- There are five pivotal trials; three in psoriatic arthritis, two in ankylosing spondylitis
- More than 10,000 patients have been treated with Cosentyx across multiple indications in the clinical trial program
- There have been three major publications in *The New England Journal of Medicine (NEJM)* and *The Lancet*

Clinical trials in psoriatic arthritis (PsA) and ankylosing spondylitis (AS)

Pivotal studies: strength speed and sustainability

Cosentyx was assessed in more than 1,999 adult patients, in three randomized, double-blind, placebo-controlled studies (FUTURE 1, FUTURE 2 and FUTURE 5) in adult patients with active PsA, and in 590 patients in two randomized, double-blind, placebo-controlled studies (MEASURE 1 and MEASURE 2) in adult patients aged 18 years and older with active AS[2-6].

Psoriatic arthritis

FUTURE 1: A randomized, double-blind, placebo-controlled study, in 606 patients with active PsA, to demonstrate the 24 week efficacy and assess the long-term safety, tolerability and efficacy up to two years of a 10 mg/kg intravenous loading dose followed by subcutaneous doses of Cosentyx 75 mg, 150 mg[4].

In addition to the core study, a three-year extension has been designed to obtain further long term efficacy, safety and tolerability information. This study is currently ongoing[8].

FUTURE 2: A randomized, double-blind, placebo-controlled study in 397 patients with active PsA, to demonstrate the efficacy of subcutaneous Cosentyx 75 mg, 150 mg, 300 mg in prefilled syringes at 24 weeks and to assess the long-term efficacy, safety and tolerability for up to five years[5].

Both studies included patients who were anti-TNF therapy naïve or inadequate responders; randomization was stratified so that approximately 70% and 65% were required to be anti-TNF therapy naïve in FUTURE 1 and FUTURE 2, respectively. In both trials, the primary endpoint was the percentage of patients achieving an ACR20 response (American College of Rheumatology response criteria) at Week 24. Extensions of both studies are currently ongoing to investigate long-term efficacy of Cosentyx.

FUTURE 5: A randomized, double-blind, placebo-controlled study in 996 patients with active PsA, to demonstrate the efficacy and safety of subcutaneous Cosentyx 300 mg and 150 mg in prefilled syringes at 16 weeks, and the long-term effect on radiographic structural disease progression at 24 weeks[2]. FUTURE 5 is the largest randomized controlled trial of a biologic conducted to date in PsA, with nearly 1,000 patients studied[2].

This study includes patients who are randomized to 2:2:2:3 to subcutaneous secukinumab 300 mg with loading dosage (LD), 150 mg with LD, 150 mg without LD, or placebo. The primary endpoint is the percentage of patients achieving an ACR20 response at Week 16[2].

Results so far[2,4,5,9,10]

- The primary endpoint was achieved in FUTURE 1 and FUTURE 2 with 50–51% of patients on Cosentyx 150 mg achieving an ACR20 response at Week 24, compared with 15–17% on placebo
- Clinical improvements were observed within one to three weeks of treatment
- FUTURE 1 two-year data showed no progression in joint damage in 84% of patients treated with 150 mg Cosentyx
- In FUTURE 2, significantly more Cosentyx patients, 54% on 300 mg and 51% on 150 mg, achieved an ACR20 at Week 24, compared to 15% on placebo
- In FUTURE 2, improvements seen with Cosentyx 150 mg and 300 mg were sustained over one year of treatment in 64% of patients as measured using ACR 20. ACR 50 response rates were also sustained to one year; 39% in the 150 mg group and 44% in the 300 mg group
- A high number of patients (77%) achieved an ACR 20 response at three years in the open-label extension study in FUTURE 1
- The results from FUTURE 1 and its subsequent extension study represent the longest Cosentyx Phase III studies in PsA to date
- The primary endpoint was met in FUTURE 5 with 55.5–62.6% of patients on Cosentyx 150 mg and 300 mg respectively, achieving ACR20 response at Week 16, compared with 27.4% on placebo
- Radiographic progression (mTSS) was significantly inhibited at Week 24 in all secukinumab arms versus placebo
- A greater proportion of patients had no radiographic progression (change from baseline in mTSS ≤0.5) with secukinumab versus placebo: 88% (300 mg), 79% (150 mg), 83% (150 mg without LD), and 73% (placebo)

Analyses of Matching-Adjusted Indirect Comparisons (MAIC) suggested that Cosentyx may lead to a higher response rate than Humira®* in improving the signs and symptoms of people living with PsA at 48 weeks[11]. The head-to-head study EXCEED 1 was initiated in patients with PsA to directly compare Cosentyx versus Humira®*[12].

EXCEED 1: A randomized, double-blind, active control study to evaluate the efficacy of Cosentyx compared with Humira®* in patients with active PsA after 52 weeks. Patients will either receive subcutaneous administration of 300 mg Cosentyx or 40 mg Humira®*[12].

The study, which has an estimated completion date in November 2019, commenced in January 2017 and completed the First Patient First Visit (FPFV). The primary outcome of the EXCEED 1 trial is an ACR 20 response at Week 52[12]. This will be the first ever adequately powered long-term head-to-head study with biologic medicines to differentiate the effectiveness of treatment in PsA.

*Humira is a registered trademark of AbbVie Inc.

Ankylosing spondylitis

MEASURE 1: A randomized, double-blind, placebo-controlled study, in 371 patients with active AS, to demonstrate the 16-week efficacy and assess the long-term safety, tolerability and efficacy up to two years of a 10 mg/kg intravenous loading dose followed by subcutaneous doses of Cosentyx 75 mg or 150 mg[3,6].

In addition to the core study, a three-year extension study is underway, and is aimed at generating additional data on the sustainability of clinical benefits, safety and tolerability during long-term administration of Cosentyx[13].

MEASURE 2: A randomized, double-blind, placebo-controlled study, in 219 patients with active AS, to demonstrate the efficacy of subcutaneous Cosentyx 75 mg or 150 mg in prefilled syringes, and to assess long-term efficacy, safety and tolerability up to five years[6].

The primary endpoint in both studies was the proportion of patients with at least 20% improvement in Assessment of Spondyloarthritis International Society (ASAS20) response criteria at Week 16†.

†ASAS 20 is improvement of ≥20% and ≥1 unit on a 10-unit scale in at least three of the four core ASAS domains, with no worsening of ≥20% and ≥1 unit in the fourth at 104 weeks

Results so far[3,6,14-17]

- Cosentyx is the first IL-17A inhibitor to demonstrate efficacy in Phase III studies in AS patients
- Cosentyx demonstrated rapid and statistically significant improvements versus placebo in the signs and symptoms of AS at Week 16 in both studies
- The primary endpoint was met in both studies. In MEASURE 1 the ASAS20 response rates at Week 16 were 60%, 61%, and 29% for Cosentyx 75 mg and 150 mg, and for placebo, respectively. In MEASURE 2, the rates were 41%, 61%, and 28% for 75 mg and 150 mg Cosentyx, and for placebo, respectively
- In MEASURE 2 the onset of action of 150 mg Cosentyx occurred as early as Week 1 for ASAS20 and Week 2 for ASAS40 (superior to placebo)
- In MEASURE 2, Cosentyx provided sustained improvement in the signs and symptoms, physical function and quality of life. 74% of patients achieved ASAS20 response at both 52 weeks and 104 weeks
- Through MEASURE 1 and the subsequent extension study, Cosentyx has demonstrated a sustained response in improvements of signs and symptoms as well as physical function in AS patients over the three years[11]
- The MEASURE 1 study also showed nearly 80% of patients with AS treated with Cosentyx had no radiographic progression at four years (no change in the modified Stoke Ankylosing Spondylitis Spinal Score from baseline to Week 208) in the spine on X-ray assessments*

Matching-Adjusted Indirect Comparisons (MAIC) analyses suggested that Cosentyx may lead to a higher response rate in improving the signs and symptoms of people living with AS at 52 weeks than Humira®**[18]. A head-to-head study to further evaluate these findings in patients with AS is planned.

Safety

• Cosentyx has been shown to have a favorable safety profile in clinical trials across multiple indications in which more than 10,000 patients have been treated with Cosentyx[7]. Over 100,000 patients have been treated with Cosentyx in the post-marketing setting[19].
• The risk-benefit assessment for Cosentyx has not changed in the post-market setting
• The most common side effects in PsA studies were the common cold, headache and upper respiratory tract infections[1,2,4,5]
• The most common side effects in AS studies were upper respiratory tract infection and headache[1,3,6]

The Cosentyx clinical trial program includes long-term extension studies that will continue to collect safety information and data over an extended period of time. In addition, an eight-year psoriasis registry study consisting of more than 3,000 patients exposed to Cosentyx will also provide long-term safety data[7].

*Based on score of <2, indicated by the modified Stoke Ankylosing Spondylitis Spinal Score (mSASSS) X-ray assessment measure[3]
**Humira is a registered trademark of AbbVie Inc.

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