

Wyeth Presents New Analyses of Data from Three Studies of ENBREL® at the European League Against Rheumatism (EULAR) Annual Meeting

- *Two-year data from COMET study in early active moderate-to-severe rheumatoid arthritis indicated sustained halt of progressive joint damage*
 - *New analyses from ASCEND study in ankylosing spondylitis indicated improvement in patients with and without peripheral joint involvement*
- *Results from PRESTA study in psoriatic arthritis indicated improvement in joint and skin symptoms*

Wyeth Europa, Maidenhead, UK: Analyses of data from three studies provide insight into the use of ENBREL® (etanercept) in the treatment of three conditions for which ENBREL is indicated: moderate-to-severe rheumatoid arthritis (RA), psoriatic arthritis (PsA) and ankylosing spondylitis (AS). These analyses, presented this week during the European League Against Rheumatism (EULAR) Annual Meeting in Copenhagen, add to the body of evidence that supports treatment with ENBREL for patients with these conditions.

Analyses from three separate trials of ENBREL -- COMET*, ASCEND** and PRESTA*** -- showed that:

- The group of patients with early-active moderate-to-severe RA treated with ENBREL and methotrexate, who achieved and sustained a halt of progressive joint damage, maintained this level at two years, according to the **COMET** study
- In patients with AS (including those with and without peripheral joint involvement), ENBREL therapy significantly improved signs, symptoms, function, and mobility when compared to treatment with the DMARD sulfasalazine, according to the **ASCEND** study
- At step-down and usual doses, ENBREL provided significant improvement in joint symptoms compared to baseline in patients with active PsA in addition to achieving clearer skin, according to the **PRESTA** study

"Inflammatory diseases such as rheumatoid arthritis, ankylosing spondylitis and psoriatic arthritis significantly impact the daily lives of the patients who live with these conditions. These analyses support the role of etanercept therapy in the management of these diseases. The EULAR congress provides an important platform to present new information regarding ENBREL as a treatment option for patients with rheumatoid arthritis, ankylosing spondylitis and psoriatic arthritis," said Maxime Dougados, Professor of Rheumatology, René Descartes University Paris, France.

***The COMET Study**

The COMET (**CO**mbination of **M**ethotrexate and **E**Tanercept in early rheumatoid arthritis) study was designed to compare the clinical efficacy and safety of ENBREL and methotrexate combination therapy (EM) with methotrexate alone (M) on clinical disease activity and progressive joint damage in patients with early active rheumatoid arthritis. COMET was the first published study to use clinical remission as a primary endpoint.

Subjects were randomised at baseline. Those who completed 1 year of treatment entered year 2 (n=411). The original combination group either continued combination (EM/EM; n=111) or received ENBREL monotherapy (EM/E; n=111) in year 2; the original methotrexate monotherapy group either received combination (M/EM; n=90) or continued monotherapy (M/M; n=99). Efficacy endpoints included clinical remission (DAS28<2.6) and radiographic non-progression (change in mTSS \leq 0.5) at year 2.

Following are the year 2 COMET study results:

- From the end of year 1 to the end of year 2, fifty percent of patients receiving ENBREL monotherapy achieved clinical remission compared to 35 percent of methotrexate monotherapy patients
- The percentage of subjects achieving clinical remission was significantly greater in the groups containing ENBREL (continued combination therapy EM/EM, E/ME and delayed combination M/EM) than in the continued methotrexate monotherapy (M/M) group (using both LOCF and NRI measurements)
- Non-progression of joint damage was achieved by a significantly greater percentage in the continued combination group compared with all other groups ($P<0.01$; LOCF)
- No new safety signals or clinically important between-group differences in serious adverse events were seen
- Patients who achieved clinical remission had an almost two-fold greater improvement in patient reported outcomes than patients who did not achieve clinical remission, measured using the Health Assessment Questionnaire (HAQ), pain visual analogue scale, fatigue VAS, EuroQoL-5D, EQ-5D utility and the Short Form-36

Professor Paul Emery, lead COMET trial investigator and Professor of Rheumatology, University of Leeds, UK, said: “These study results indicated that when treating moderate-to-severe RA with etanercept, clinical remission is achievable and, as such, should be a primary treatment goal. These data highlight the importance of treating early with etanercept which can help stop progressive joint damage and provide the opportunity to maintain quality of life.”

****The ASCEND Study**

Ankylosing spondylitis (AS) is a debilitating condition that affects three times as many men as women. It typically causes inflammation and pain in the spine (known as axial disease), but can also affect the peripheral joints. As a result of this pain, patients with AS are three times more likely to stop working than the general population.

The ASCEND study compared the efficacy of ENBREL with the DMARD sulfasalazine in subjects with AS, including those with peripheral joint involvement. It was the first published study to use an active comparator.

A post-hoc analysis compared the efficacy of ENBREL 50 mg once weekly with sulfasalazine up to 3 g daily in subjects with and without swollen peripheral joint involvement from a 10-week randomized, double-blind study in subjects with AS.

Regardless of swollen peripheral joint involvement, subjects receiving ENBREL showed significantly greater improvement than subjects receiving sulfasalazine in all efficacy assessments, including physical function and spinal mobility. In particular, 76 percent of patients taking ENBREL versus 53 percent of patients taking sulfasalazine, achieved an ASAS 20 ($p < 0.001$)

Patient-reported outcomes presented at EULAR showed a significantly greater improvement in the ENBREL group than in the sulfasalazine group at week 16 of treatment in all of the domains that the Short-Form-36 (SF-36, range 0-100) measures.

“These new analyses suggest the potential benefit of etanercept in the treatment of peripheral joint disease associated with AS,” said Maxime Dougados, Professor of Rheumatology, René Descartes University Paris, France. “That the clinical improvements seen in patients treated with etanercept bore a direct correlation in improvement in patient quality of life, highlights the importance of including etanercept in the treatment of AS.”

*****The PRESTA Study**

Psoriatic arthritis (PsA) is a disabling form of arthritis that occurs in up to 30 per cent of patients with plaque psoriasis.

The PRESTA study was designed to determine the efficacy of two ENBREL dosing regimens in treating PsA, as measured by PsA response criteria (PsARC), arthritic symptoms, skin manifestations and physical function of subjects with psoriasis and PsA over 24 weeks.

In this study, a randomised double-blind phase was followed by an open-label period. Patients received either ENBREL 50 mg once weekly (QW) or 50 mg twice weekly (BIW) for 12 weeks (double blind), followed by 50 mg QW for all patients for 12 weeks (open label).

Data from the trial showed that at usual doses as well as at step-down doses (i.e., 50 mg once a week or 50 mg twice a week for first 12 weeks, then 50 mg once a week), ENBREL provided significant improvement compared to baseline in joint symptoms in patients with active psoriatic arthritis in addition to achieving clearer skin.

Furthermore, the new data showed that ENBREL significantly relieved two painful and difficult-to-treat features of psoriatic arthritis, in which inflammation occurs in the fingers (dactylitis) and/or at any point where a tendon or ligament is inserted into bone, particularly the heel of the foot (enthesitis).

Efficacy results presented at EULAR showed – for joints:

- For physician global assessment of arthritis, HAQ and subject global assessment of joint pain, arthritis activity and stiffness, within-group improvements from baseline for the 2 regimens were significant ($p < 0.001$) at 12 and 24 weeks; between-group differences were not
- In the ENBREL 50 mg BIW group, 77 percent were PsARC responders at week 12 versus 76 percent in the ENBREL 50 mg QW group ($p = 0.264$). At week 24, PsARC responders were 82 percent and 80 percent respectively ($p = 0.722$).

Efficacy results presented at EULAR showed – for enthesitis and dactylitis:

- At weeks 12 and 24, patients with dactylitis at baseline from both study groups showed comparable improvement, with the mean number of digits affected substantially lower than at baseline: ENBREL 50 mg BIW/QW 1.5 and 1.6 for ENBREL 50 mg QW/QW at week 12, and ENBREL 50 mg BIW/QW 1.2 and 1.3 for ENBREL 50 mg QW/QW at week 24
- In those patients with enthesitis at baseline, both step-down and usual dose ENBREL regimens provided comparable improvements in ≥ 1 tendon or ligament insertion at weeks 12 and 24: 74 percent for ENBREL 50 mg BIW/QW versus 70 percent 50mg QW/QW at week 12 and 81 percent for both groups at week 24. These improvements were accompanied by improved quality of life

Efficacy results presented at EULAR showed – for skin:

- At week 24, PASI 75 improvement was achieved by 70 percent in the BIW/QW group and 62 percent in the QW/QW group
- Similarly at week 24, the percentage of psoriasis responders, clear or almost clear on the physician global assessment, was 56 percent for the ENBREL 50 mg BIW group and 50 percent for the 50 mg QW group

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To participate in a virtual on-demand press briefing where you can hear expert commentary relating to the above data, please log on to the media centre at www.wyeth.eu. Further media information relating to this press release, additional information on ENBREL and future media announcements can also be found on the site.

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Notes to editors

About ENBREL

ENBREL is a fully human soluble tumour necrosis factor (TNF) receptor antagonist. ENBREL was first approved in 1998 for moderate to rheumatoid arthritis and has since been used in 505,000 patients worldwide across indications.

ENBREL is approved for the following indications:

Rheumatoid arthritis

ENBREL in combination with methotrexate is indicated for the treatment of moderate to severe active rheumatoid arthritis in adults when the response to disease-modifying antirheumatic drugs, including methotrexate (unless contraindicated), has been inadequate. ENBREL can be given as monotherapy in case of intolerance to methotrexate or when continued treatment with methotrexate is inappropriate. ENBREL is also indicated in the treatment of severe, active and progressive rheumatoid arthritis in adults not previously treated with methotrexate. ENBREL, alone or in combination with methotrexate, has been shown to reduce the rate of progression of joint damage as measured by X-ray and to improve physical function.

Polyarticular juvenile idiopathic arthritis

Treatment of active polyarticular juvenile idiopathic arthritis in children and adolescents aged 4 to 17 years who have had an inadequate response to, or who have proved intolerant of, methotrexate. ENBREL has not been studied in children aged less than 4 years.

Psoriatic arthritis

Treatment of active and progressive psoriatic arthritis in adults when the response to previous disease-modifying antirheumatic drug therapy has been inadequate. ENBREL has been shown to improve physical function in patients with psoriatic arthritis, and to reduce the rate of progression of peripheral joint damage as measured by X-ray in patients with polyarticular symmetrical subtypes of the disease.

Ankylosing spondylitis

Treatment of adults with severe active ankylosing spondylitis who have had an inadequate response to conventional therapy.

Plaque psoriasis

Treatment of adults with moderate to severe plaque psoriasis who failed to respond to, or who have a contraindication to, or are intolerant to other systemic therapy including cyclosporine, methotrexate or PUVA. ENBREL is also licensed in the European Union for treatment of chronic severe plaque psoriasis in children and adolescents from the age of 8 years who are inadequately controlled by, or are intolerant to, other systemic therapies or phototherapies.

ABOUT WYETH:

Wyeth Pharmaceuticals, a division of Wyeth, has leading products in the areas of women's health care, infectious disease, gastrointestinal health, central nervous system, inflammation, transplantation, hemophilia, oncology, vaccines and nutritional products.

Wyeth is one of the world's largest research-driven pharmaceutical and health care products companies. It is a leader in the discovery, development, manufacturing and marketing of pharmaceuticals, vaccines, biotechnology products, nutritionals and non-prescription medicines that improve the quality of life for people worldwide. The Company's major divisions include Wyeth Pharmaceuticals, Wyeth Consumer Healthcare and Fort Dodge Animal Health.