Phase III, multi-center, randomized, double-blind, placebo controlled study for treatment of juvenile ankylosing spondylitis with Adalimumab.

G.Horneff, K. Minden, G.Ganser, R. Küster, I. Foeldvari, A. Thon, M. Borte, R. Trauzeddel, N. Tzaribachev, H.I. Huppertz

Source

Paediatric rheumatology centre Sankt Augustin, Department of general Paediatrics, Asklepios Clinic Sankt Augustin, Arnold Janssen Str. 29, 53757 Sankt Augustin, Germany, g.horneff@asklepios.com

Abstract

Background

Ankylosing spondylitis (AS) is a chronic inflammatory rheumatic disease of the spine that affects 0.2 – 0.8% of the population. Although AS typically presents in the late teens or early twenties, it can present in childhood. In Juvenile AS (JAS) symptoms' onset occurs in individuals < 16 years of age and individuals go on to develop radiographic sacroiliitis and spine involvement later on.

OBJECTIVE:

The tumor necrosis factor-alpha (TNF-alpha) inhibitor adalimumab has been proven effective for the treatment of adult AS. The primary objective of this double-blind, placebo-controlled study was to assess the safety and efficacy of adalimumab therapy in JAS.

The primary objectives are to demonstrate the superiority of adalimumab with respect to the Assessments in Ankylosing Spondylitis criteria (ASAS40) as compared to placebo and to contrast the safety profile of adalimumab with placebo in subjects with juvenile ankylosing spondylitis

METHODS:

Multi-center, randomized, double-blind, placebo-controlled parallel group study of 12 weeks, followed by open-label treatment phase of further 12 weeks.In the 12-week double-blind phase of the study, patients (N = 34) were randomized to receive 40 mg adalimumab every other week of placebo. The primary endpoint was 40% improvement in Assessments in Ankylosing Spondylitis criteria (ASAS40) at 12 weeks. In the open-label extension phase, all patients received scheduled adalimumab every other week for further 12 weeks.
Male and female patients 12 – <18 years of age (weight of the patient is > 30 kg) with active juvenile AS refractory to at least two different non-steroidal antiphlogistic drugs given at appropriate dosage and for an appropriate period of time.
Patient had to have active disease, i.e. 1. spinal inflammation score of at least 3 *AND* at least 2 of the following domains: 2. back pain score of at least 3; 3. patient global assessment of disease activity of at least 3; 4. physical function score of at least 3.

RESULTS:

At 12 weeks, 78% of ADA-treated patients achieved ASAS40, compared with 19% of placebo-treated patients (p = 0.001). ADA -treated patients showed significant improvement in various measures of disease activity (Table): Spinal inflammation (BASDAI) , functional measures (BASFI), CHAQ disability score, number of affected joints and patient's and physician's assessment of global disease activity.

At the end of the open label the extension phase, 70% of patients showed an ASAS40 response.. In general, ADA was safe and well tolerated. Two patients withdrew from the study before week 12 for inefficacy (1 on ADA, one on PLC). There were 86 adverse events in 29 patients throughout the 24 week study, mostly injection site reactions and upper airway infections, 7 were graded serious (appendicitis, pyelonephritis, colitis, disease flare, trauma, vertigo, secondary pain amplification syndrome).

CONCLUSION:

This double blind placebo controlled study demonstrates efficacy of adalimumab in reducing the signs and symptoms of active JAS. Improvement was already evident after 12 weeks of treatment. Adalimumab was generally safe and well tolerated.

	PLC Baseline	PLC Wk 12	improvement	ADA Baseline	ADA Wk 12	Improvement
spinal inflammation	4.6*7-2.4	3.7+/-2.9	20%	5.0+/-2.0	1.3+/-1.7	74%*
Back pain	5.8+/-1,8	4.8+/-2.2	18%	5.8+/-1.4	1.96+/-2.6	66%
Active joints	1.6+/-2.1	1.75+/-2.2	-7%	3.8+/-5.1	0.9+/-1.8	76%
Limited joints	3.1+/-3.8	2.4+/-2.0	20%	4.1+/-5,5	1.5+/-2.7	63%
Pat Global	6.1+/-1.7	5.2+/-2.6	14%	9.5+/-13	2.1+/-2.2	78%
Phys Global	5.9+/-2.2	4.3+/-3.1	27%	5.6+/-2.0	2.1+/-2.7	62%
BASFI	3.9+/-2.1	3.8+/-2.4	2%	4.4+/-1.9	1.3+/-2.0	71%
CHAQ	0.88+/-0.39	0.73+/-0.65	18%	1.34+/-0.83	0.33+/-0,53	75%

* $p<0.001$ (t-test)