

## **Abatacept in the treatment of patients with psoriatic arthritis: results of a six-month, multicenter, randomized, double-blind, placebo-controlled, phase II trial**

### **Background:**

- 30% of psoriasis patients develop psoriatic arthritis, and current treatment options are limited to disease modifying anti-rheumatic drugs(DMARDs) that have shown disappointing efficacy in clinical trials.
- Abatacept, approved for treatment of chronic inflammatory conditions including rheumatoid arthritis and juvenile idiopathic arthritis, showed clinical improvement in patients with psoriasis vulgaris in a phase I clinical trial through its action reducing intralesional T cells.
- When combined, these observations suggest that abatacept could be effective for the treatment of psoriatic arthritis.

### **Objective:**

- To assess the safety and efficacy of abatacept, a selective T cell costimulation modulator, in patients with psoriatic arthritis.

### **Methods:**

- **Design:** Six-month, multicenter, randomized, double-blind, placebo controlled phase II trial
- **Inclusion criteria:** Patients who: met the criteria of the Classification of Psoriatic Arthritis Study Group, had active arthritis with  $\geq 3$  swollen and  $\geq 3$  tender joints, active plaque psoriasis with at least one target lesion  $\geq 2$  cm in diameter, disease duration of  $\geq 3$  months, and having had an inadequate response to DMARDs were included in the study. Patients with intolerance of, or an inadequate response to, infliximab, adalimumab, or etanercept had to discontinue these therapies and go through a washout period  $\geq 28$  days prior to randomization.
- **Exclusion criteria:** Patients who: used any investigational drugs within 28 days of randomization, had any prior treatment with abatacept, had evidence of latent or active tuberculosis, had evidence of chronic or clinically significant infection or malignancy were excluded; pregnant and/or lactating women were also excluded.
- **Primary outcome measure:** American College of Rheumatology 20 (ACR20) response
- **Secondary outcome measures:** Investigators global assessment of psoriasis, scores for target lesions(TL), the disability index of the Health Assessment Questionnaire(HAQ), the Short Form 36 health survey(SF-36), ACR50, ACR70, Psoriasis Area and Severity Index(PASI), and assessment of joint damage based on MRI.
- **Enrollment:** 170 patients were enrolled into four treatment arms:
  - 43 patients in the 30/10 mg/kg abatacept arm (Initial two doses of 30 mg/kg followed by 10 mg/kg doses) [92% power]
  - 40 patients in the 10 mg/kg abatacept arm [84% power]
  - 45 patients in the 3 mg/kg abatacept arm
  - 42 patients in the placebo abatacept arm
    - All doses were given as 30 minute IV infusions, given on days 1, 15, 29 and every 28 days that followed for the 169 day duration.
- **Data handling method:** Data were handled with the intent to treat principle.

**Results:**

- 147 patients completed the study.
  - 37 in the 30/10 mg/kg arm
  - 34 in the 10 mg/kg arm
  - 43 in the 3 mg/kg arm
  - 33 in the placebo arm
- **Primary outcome measure:** ACR20 achievement results for the 30/10 mg/kg arm and the 10 mg/kg arm were statistically significant and were as follows, respectively: 42% (p-value: 0.022) and 48% (p-value: 0.006)
- **Secondary outcome measures:** Power was not significant to give meaningful results in any of the secondary measures. The authors findings were as follows: all abatacept regimens resulted in improved MRI, HAQ, and SF-36 scores, with the 10 mg/kg arm showing the greatest improvements. TL and PASI scores were improved in all abatacept arms; a response with regard to investigator global assessment was seen with only the 3 mg/kg study arm of abatacept.
- **Author's conclusion:** The results of this study suggest that 10 mg/kg of abatacept, the approved dosage for rheumatoid arthritis and juvenile idiopathic arthritis may be an effective treatment option for psoriatic arthritis.

**Strengths:**

- The study rationale and objective set
- The type of study performed is the gold standard for a phase II clinical study.

**Limitations:**

- Small sample size and associated affects (decreasing both power and likelihood of statistical significance)
- Allowing those who failed anti-TNF-alpha agents into the study
- Allowing patients to continue other medications throughout the study
- Blinding, investigator training, site standardization and enrollment were not addressed
- Gross association of authors with the drug manufacturer of abatacept providing for potential bias
- Reporting practices of results: posting SEM's instead of SD's, means instead of medians, and reporting results that were neither powered appropriately, nor had statistical significance

**Conclusion:**

- Abatacept was moderately effective with regard to the ACR20 response, and could potentially fill a void in treatment for psoriatic arthritis. However, the current study is flawed in numerous ways, and few significant facts can be taken away from this study. Future research should contain a larger study population, more specific secondary outcomes, and better result reporting practices.

**Reference:** Mease P, et al. Abatacept in the treatment of patients with psoriatic arthritis: results of a six-month, multicenter, randomized, double-blinded, placebo-controlled, phase II trial. *Arthritis Rheum.* 2011;63(4):939-48.

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