

Re: A Randomized, Double-blind, Placebo-controlled Trial of Certolizumab Pegol in Women with Refractory Interstitial Cystitis/Bladder Pain Syndrome

Bosch, PC

Eur Urol 2018;74:623–30

Experts' summary:

Interstitial cystitis/bladder pain syndrome (IC/BPS) remains a disease with no cure, and treatment can only provide symptomatic relief. Certolizumab pegol, a new anti-TNF- α agent, was evaluated in a pilot study in a group of 42 female patients with moderate to severe IC/BPS for whom previous therapies had been unsuccessful [1]. The primary endpoint was the difference in global response assessment (GRA) between certolizumab pegol and placebo at week 2, which did not significantly differ between the study groups. However, there was a significant difference in GRA pain ($p = 0.002$), GRA urgency ($p = 0.02$), and GRA overall symptoms ($p = 0.006$) by week 18. In terms of secondary endpoints at week 18, there was a significant difference of -3.6 ($p = 0.03$) for the Interstitial Cystitis Symptom Index, -3.0 ($p = 0.042$) for the Interstitial Cystitis Problem Index, -2.0 ($p = 0.02$) for the pain scale, and -1.7 ($p = 0.03$) for the urgency scale, as well as a $>30\%$ reduction in pain ($p = 0.02$).

Experts' comments:

The etiology of IC/BPS is described as multifactorial, with genetic and environmental factors, which is the main obstacle in clinical trials. However, the presence of serum and urinary antibodies specific to the bladder epithelium in IC/BPS patients is consistent with autoimmune involvement. Thus, immunotherapy, specifically human monoclonal antibodies inhibiting NGF and TNF- α , have shown high efficacy in pain control for PBS/IC [2,3]. However, one study failed to prove the efficacy of adalimumab as a result of a significant placebo effect [4]. The present study therefore included a 1-mo washout period, which decreased the placebo effect on overall GRA from 50% in the previous study [4] to an average of 14%.

The time to obtain significant improvement in each individual autoimmune disease varies for anti-TNF- α agents. As the underlying mechanism could be similar, the primary endpoint was chosen at 2 wk because some authors observed a positive effect on rheumatoid arthritis by this time, while others reported improvement in psoriatic arthritis at 24 wk [1]. However, the time period

for a significant improvement for women with moderate to severe IC/BPS appears to be longer (ie, 10–18 wk) as IC/BPS represents a longstanding disease. There was a similar GRA treatment response rate obtained when treating IC/BPS patients with adalimumab, so a head-to-head comparison would be interesting [4], as well as combinations with other immunopathway-modulating agents. Some limitations of the study were the small sample size and the fact that neither cystoscopy nor cytology was performed, so tuberculosis or carcinoma in situ could possibly have been missed and it was not possible to rule out Hunner's ulcers.

The debate concerning PBS/IC diagnostic criteria continues, leading to high heterogeneity of patients enrolled in treatment studies. The small number of randomized clinical trials is a major limitation that must be addressed in the future.

Conflicts of interest: The authors have nothing to disclose.

References

- [1] Bosch PC. A randomized, double-blind, placebo-controlled trial of certolizumab pegol in women with refractory interstitial cystitis/bladder pain syndrome. *Eur Urol* 2018;74:623–30.
- [2] Mykoniatis I, Katafigiotis I, Sfoungaristos S, Yutkin V. Immunotherapy options for painful bladder syndrome: what's the potential? *Expert Opin Biol Ther* 2018;17:1471–80.
- [3] Duh K, Funaro MG, DeGouveia W, et al. Crosstalk between the immune system and neural pathways in interstitial cystitis/bladder pain syndrome. *Discov Med* 2018;25:243–50.
- [4] Bosch PC. A randomized, double-blind, placebo controlled trial of adalimumab for interstitial cystitis/bladder pain syndrome. *J Urol* 2014;191:77–82.

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Re: Are We Improving Erectile Function Recovery After Radical Prostatectomy? Analysis of Patients Treated over the Last Decade

Capogrosso P, Vertosick EA, Benfante NE, et al

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The devil's in the Details?

Experts' summary:

A retrospective analysis delivered recently by Capogrosso et al. [1] was intended to answer whether advances in

radical prostatectomy (RP) technique and post-RP care brought any improvement in functional outcomes. The authors identified 2364 patients treated with RP at a single academic center during 2008–2015. To remove surgical experience as a confounder, individuals treated by a surgeon who performed <100 procedures were excluded. The endpoint was established as erectile function (EF) assessed by International Index of Erectile Function (IIEF)-6, with recovery defined as IIEF-6 ≥ 24 . The analysis was conducted in patients in whom bilateral nerve-sparing (NS) surgery was performed and who obtained no adjuvant or salvage treatment.