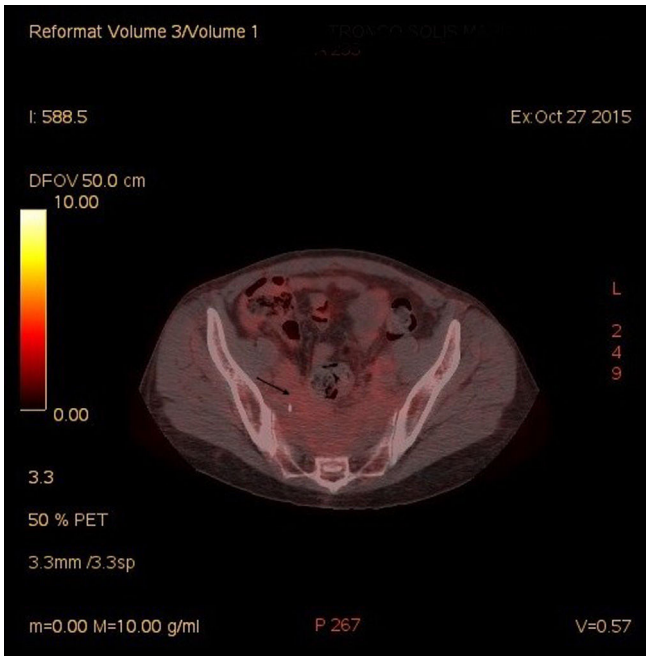

Fig. 1. PET-CT scan image with 18F-FDG showing presacral capture with little glucidic avidity.

Our patient, with limited SD, developed valvulopathy and RPF due to ergotamines. Although both toxicities are well-known, they are exceptional in the same patient. On the other hand, the association of SD and RPF, profibrotic diseases that may have similar physiopathological mechanisms, is exceptional.[8,9] In spite of sophisticated current diagnostic procedures, our diagnosis is still based on directed anamnesis, which is often overlooked. In SD, as is the case for other systemic diseases,[10] other processes and drugs which may simulate their clinical manifestations must always be taken into account.

Financing

This research received no specific grant from any agency in the public or private sector or those which are not-for-profit.

References

1. Denton CP, Khanna D. Systemic sclerosis. Lancet. 2017;390:1685–99.
2. Bissell LA, Anderson M, Burgess M, Chakravarty K, Coghlan G, Dumitru RB, et al. Consensus best practice pathway of the UK Systemic Sclerosis Study group: management of cardiac disease in systemic sclerosis. Rheumatology (Oxford). 2017;56:912–21.
3. Plasín M, Lluch E, Piulats R, Trullàs JC, Espinosa G. Acute cardiomyopathy as a clinical manifestation of systemic sclerosis [Article in Spanish]. Rev Clin Esp. 2011;211:e51–53.
4. Vaglio A, Maritati F. Idiopathic retroperitoneal fibrosis. J Am Soc Nephrol. 2016;27:1880–9.
5. Andrejak M, Tribouilloy C. Drug-induced valvular heart disease: an update. Arch Cardiovasc Dis. 2013;106:333–9.
6. Bhattacharyya S, Schapira AH, Mikhailidis DP, Davar J. Drug-induced fibrotic valvular heart disease. Lancet. 2009;374:577–85.
7. Martínez Quintana E, Llorens León R, Redondo Martínez E, Nieto Lago V, Jiménez Cabrera F, Gross Kastanovitz E. Valvular heart disease associated with ergotamine. Rev Esp Cardiol. 2005;58:97–9.
8. Cochat P, Colon S, Laville M, Maillet P, Lefrançois N, Moskovtchenko JF, et al. Retroperitoneal fibrosis and generalized scleroderma [Article in French]. Nephrologie. 1985;6:27–30.
9. Gerth HU, Willeke P, Sunderkötter C, Spieker T, Köhler M, Pavenstädt H, et al. Systemic sclerosis and collagenous colitis in a patient with retroperitoneal fibrosis. Scand J Rheumatol. 2011;40:322–3.
10. López-Mato P, Zamora-Martínez C, Carbajal S, Estevez M, Rodriguez-Pinto I, Cervera R, et al. All that glitters is not lupus. Lupus. 2017:961203317742713, http://dx.doi.org/10.1177/0961203317742713.

Lucía Suárez Pérez[a,⁎], Luis Caminal Montero[a], Luis Trapiella Martínez[b], Jessica Rugeles Niño[a]

[a] *Unidad de Enfermedades Autoinmunes Sistémicas, Unidad de Gestión Clínica de Medicina Interna, Hospital Universitario Central de Asturias, Oviedo, Asturias, Spain*
[b] *Servicio de Medicina Interna, Hospital Universitario San Agustín, Avilés, Asturias, Spain*

* Corresponding author.
E-mail address: luciasuarezp27@gmail.com (L. Suárez Pérez).

Extension of the RENACER Study: 12-Month Efficacy, Safety and Certolizumab PEGol Survival in 501 Rheumatoid Arthritis Patients

Ampliación del estudio RENACER: eficacia, seguridad y supervivencia a 12 meses de 501 pacientes de artritis reumatoide tratados con Certolizumab PEGol

Dear Editor:

Regarding with our previous RENACER (RE*gistro* NA*cional* CER*tolizumab*) Study,[1] we would like to present data in a larger population of Rheumatoid Arthritis (RA) patients on the use of Certolizumab-PEGol (CZP). CZP is a biological agent approved for RA which inhibits Tumor Necrosis Factor-alpha (TNFi). Its unique molecular structure allows its use in particular situations.[2,3] Our study collected data in clinical practice from 2011 to present in 37 different sites in Spain, collecting socio-demographics, smoking status, clinical and safety data at baseline, 3-, 6- and 12-month visits. Clinical outcomes were defined by completion of EULAR Good/Moderate and DAS28 Remission. Drug survival was also assessed (Kaplan–Meier curve). A total of 501 RA patients were included: 78.6% women, mean age 53.6 yr (±13.2 SD), 23% were aged >65 yr; mean disease duration 7.5 yr (±7.3 SD), 27.7% having early RA (<2 yr); prior csDMARD number 1.5 (±1.1 SD); mean prior bDMARD number was 0.8 (±1.2 SD); mean exposure time to CZP was 9.8 months (±3.4 SD); concomitant steroids intake 12.6%, csDMARD 24.2% and csDMARD plus steroids 54.9%; 69.8% never smoked, 12.9% former smoker and 17.3% current smoker. A total of 135 discontinued CZP (27%). Clinical and treatment outcomes are shown in Table 1, statistically significant improvement in all parameters at 12-month visit compared to baseline was observed. 12-month EULAR Response was reached in 69.8% of patients, 64.4% when using CZP as 2nd-line treatment after 1st-bDMARD clinical failure ($N = 90$, data not shown). 12-month DAS28 Remission was achieved in 40.5% of patients (34.4% in 2nd-line). Overall CZP 12-month survival was 73.1%. We found CZP survival rate in bio-naïve patients was higher than in those who used previous bDMARD, 77.2% vs. 68.5% ($p = 0.029$), respectively (Fig. 1).

Table 1
Baseline and follow-up activity, serological and treatment data.

	Baseline	3-month	6-month	12-month	*p* value
TJC	9.3 ± 6.2	5.0 ± 5.5	3.9 ± 4.7	3.6 ± 4.9	<0.001
SJC	6.7 ± 5.1	3.4 ± 4.2	2.4 ± 3.5	2.1 ± 3.3	<0.001
RF (positive/negative)	53.8%/46.2%	53.2%/46.8%	52.3%/47.7%	49.8%/50.2%	0.165
CCP antibodies (positive/negative)	68.8%/31.2%	63.6%/36.4%	67.2%/32.8%	62.6%/37.4%	0.300
ESR	29.2 ± 23.1	23.4 ± 20.6	22.8 ± 21.3	21.3 ± 20.0	<0.001
CRP (mg/L)	6.9 ± 15.8	4.9 ± 11.1	4.3 ± 10.7	4.3 ± 10.5	<0.001
Mean Steroids Dose (mg)	7.9 ± 6.2	6.0 ± 5.5	5.1 ± 5.2	4.4 ± 4.8	<0.001
DAS28	4.7 ± 1.1	3.7 ± 1.3	3.4 ± 1.3	3.2 ± 1.3	<0.001
DAS28 Remission (%)	–	22.9	31.3	40.5	–
EULAR Good/Moderate Response (%)	–	54.8	64.8	69.7	–

Abbreviations: tender joint count (TJC); swollen joint count (SJC); rheumatoid factor (RF); anti-cyclic citrullinated peptide antibodies (CCP); erythrocyte sedimentation rate (ESR); C-reactive protein (CRP); Disease Activity Score 28-joints (DAS28); European League Against Rheumatology (EULAR); milligrams (mg); percentage (%).

Moreover, the use of CZP in combination to csDMARD showed better DAS28 Remission criteria rate than in monotherapy ($p = 0.030$). Adverse events were reported in 13% of cases, mostly mild or non-life threatening ($N = 65$; 2.4% cutaneous rash, 1% upper respiratory infection, as the most frequents). During the study we observed the following discontinuation reasons: 68 patients (50%) showed secondary inefficacy, 36 (26%) intolerance, 15 (11%) primary inefficacy and 16 (12%) others.

Since our first publication, two other studies assessing patients treated with CZP have been developed in Italy and Sweden. The Italian study in 278 RA patients found similar EULAR Response rates at one year from CZP onset (66%). The authors also found that clinical response at 3-month visit predicted low disease activity at 12-month assessment (68% as 1st-line treatment).[4] The Swedish registry collected data from 945 RA patients that received CZP (57% as 1st-line treatment, 23% as 2nd-line). The authors found a 71% EULAR Response achievement at 6-month visit and better 30-month survival drug on those TNFi-naïve.[5] In another clinical trial, a total of 38.1% ACR-50 completion at 12-month assessment was shown, with positive predictive value for those patients who showed a >1.2 points reduction in DAS28 from baseline.[6] We conclude that CZP use in severe RA patients should be specially recommended in bio-naïve patients and in those who failed to one TNFi over those who failed to two or more TNFi, with reasonable safety profile. Further studies are recommended in order to establish CZP long-term survival.

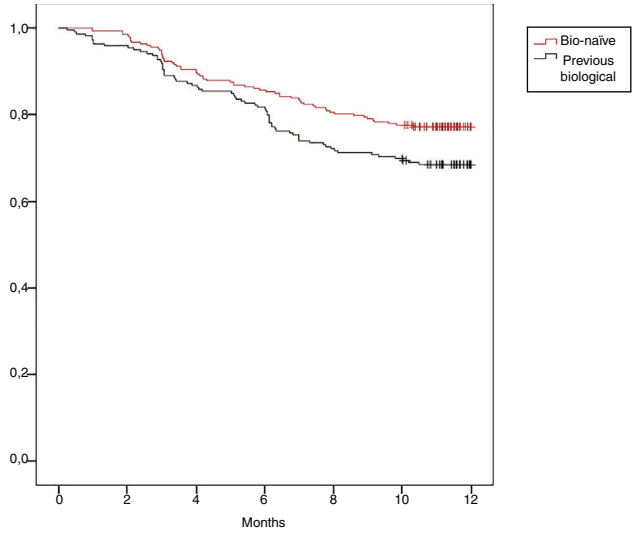

Fig. 1. Comparative cumulative survival between bio-naïve patients and patients that received previous biological therapy.

References

1. Torrente-Segarra V, Urruticoechea Arana A, Sánchez-Andrade Fernández A, Tovar Beltrán JV, Muñoz Jiménez A, Martínez-Cristóbal A, et al., RENACER Study Group. RENACER study: assessment of 12-month efficacy and safety of 168 certolizumab PEGol rheumatoid arthritis-treated patients from a Spanish multicenter national database. Mod Rheumatol. 2015;7:1–6.
2. Flint J, Panchal S, Hurrell A, van de Venne M, Gayed M, Schreiber K, et al., BSR and BHPR Standards, Guidelines and Audit Working Group. BSR and BHPR guideline on prescribing drugs in pregnancy and breastfeeding—Part I: Standard and biologic disease modifying anti-rheumatic drugs and corticosteroids. Rheumatology (Oxford). 2016;55:1693–7.
3. Götestam Skorpen C, Hoeltzenbein M, Tincani A, Fischer-Betz R, Elefant E, Chambers C, et al. The EULAR points to consider for use of antirheumatic drugs before pregnancy, and during pregnancy and lactation. Ann Rheum Dis. 2016;75:795–810.
4. Iannone F, Carlino G, Marchesoni A, Sarzi-Puttini P, Gorla R, Lapadula G, GISEA (Gruppo Italiano di Studio sulle Early Arthritides). Early clinical response predicts low disease activity at one year in rheumatoid arthritis patients on treatment with certolizumab in real-life settings. An appraisal of the Italian registry GISEA. Joint Bone Spine. 2016;83:721–5.
5. Chatzidionysiou K, Kristensen LE, Eriksson J, Askling J, van Vollenhoven R, ARTIS Group. Effectiveness and survival-on-drug of certolizumab pegol in rheumatoid arthritis in clinical practice: results from the national Swedish register. Scand J Rheumatol. 2015;44:431–7.
6. Berenbaum F, Pham T, Claudepierre P, de Chalus T, Joubert JM, Saadoun C, et al. Early non-response to Certolizumab PEGol in rheumatoid arthritis predicts treatment failure at one year Data from a randomised phase III clinical trial. Joint Bone Spine. 2018;85:59–64.

Vicenç Torrente-Segarra [a,*], Manuel Fernández Prada [b], Rosa Expósito [c], Noemí Patricia Garrido Puñal [d], Amalia Sánchez-Andrade [e], José Ramón Lamúa-Riazuelo [f], Alejandro Olivé [g], Juan Víctor Tovar [h], on behalf of RENACER Study Group

[a] *Hospital Comarcal Alt Penedès, Spain*
[b] *Hospital Universitario de Guadalajara, Spain*
[c] *Hospital Comarcal de Laredo, Spain*
[d] *Hospital Universitario Virgen del Rocío, Spain*
[e] *Complejo Hospital Universitario Lucus Augusti, Spain*
[f] *Hospital Universitario del Henares, Spain*
[g] *Hospital Germans Tries i Pujol, Spain*
[h] *Hospital General Universitario de Elche, Spain*

* Corresponding author.
E-mail addresses: vtorrente@hsjdbcn.org, vicente.torrentesegarra@sanitatintegral.org (V. Torrente-Segarra).

https://doi.org/10.1016/j.reuma.2018.12.004