


## Conflict of interest

The authors declare no conflicts of interest.

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# In response to optimizing osteoporosis management in CKD patients

## Respuesta a: Optimizing osteoporosis management in CKD patients

Dear Editor,

In response to Drs. Yong Wang and Wei Zhou, we would like to express our gratitude for their interest in our national ERCOS study<sup>1</sup> and for their additional contributions. We all agree that this is another critical area of patient care that warrants further exploration as highlighted in the recent KDIGO Chronic Kidney Disease-Mineral and Bone Disorder (CKD-MBD) Controversies Conference.<sup>2</sup> Notably, a new conceptual framework was proposed to move to a framework of two clinical syndromes in adults: CKD-associated osteoporosis (OP)

and CKD-associated cardiovascular disease. This approach aims to advance towards a personalized care in adults with CKD-MBD.<sup>2</sup>

The ERCOS study (Spanish acronym for CKD-OP)<sup>1</sup> was designed to intentionally include the profile of patients with CKD G3-5D diagnosed of densitometric OP and/or fragility fractures. By focusing on patients in whom these two highly prevalent conditions already coexist (as an inclusion criterion), the study does not allow conclusions to be drawn about the prevalence of OP in patients with CKD. Our results confirmed a previously suspected general therapeutic nihilism,



coupled with a notably low sensitivity/awareness of nephrologists regarding OP, despite recent important updates in our guidelines, consensus statements and calls to action.<sup>2-5</sup> We agree with the authors that including patients with CKD without prior OP diagnosis could provide a more comprehensive understanding of bone health across the entire CKD population. In fact, in our manuscript, we specifically emphasized that our results cannot be extrapolated to the entire population and must be interpreted with consideration of other potential biases, such as the small sample size (particularly on dialysis patients) and the involvement of centres and physicians with a specific interest in these conditions, among others.

The authors also suggest that including data from recently published studies on OP treatment outcomes in different CKD populations would have been interesting. Their data on treatment outcomes from recent studies is highly valuable and complements previous publications in *Nefrologia* and other journals.<sup>2,5-7</sup> However, we would like to reiterate that this was not the aim of our study though it could represent a valuable opportunity for a focused and comprehensive review.

Finally, the authors stated that incorporating emerging options such as romosozumab could provide a broader overview of available treatments. We fully agree, but unfortunately, when the ERCOS study was conducted, neither romosozumab nor abaloparatide was available in Spain. In fact, given the significant high prevalence of adynamic bone disease among CKD patients, OP treatment should not be limited to antiresorptives; anabolic or dual-action therapies (teriparatide, abaloparatide, romosozumab, etc.) should also be considered, although data on these agents remains even more limited (e.g. differences in femoral bone density benefits between abaloparatide and teriparatide, and warnings persist for romosozumab).<sup>8,9</sup> Thus, knowledge of bone turnover may also influence the choice of bone-targeted therapies.<sup>2</sup> In most cases, bone formation and resorption markers suffice for assessing bone turnover.<sup>10</sup> However, nephrologists should revive the practice of bone biopsies, at least in cases of complex bone diseases. While treatment decisions for most CKD patients can proceed without biopsies, they remain important for mineralization defects or complex bone diseases not identifiable noninvasively, particularly when bone markers are not aligned.<sup>2,10</sup>

In conclusion, we also fully agree with Drs Yong Wang and Wei Zhou in looking forward to future research that advances the care for CKD patients. This begins with the early diagnosis, classification and codification of patients with CKD, balancing renalism with therapeutic nihilism, and recognizing that bone and mineral disorders in CKD, including CKD-associated OP, may impact cardiovascular health and ageing. Personalized treatment approaches should especially be considered in CKD patients,<sup>2</sup> not only for those already diagnosed with OP and/or fragility fractures but also for those at risk. Given the challenges of conducting necessary randomized clinical trials on this issue, we propose an alternative approach: the prospective registration of key information by relevant scientific societies. This strategy could serve as an intermediate step in generating actionable knowledge and addressing current evidence gaps. Ultimately, we must remember that the best treatment

for CKD-MBD is preventing the progression of CKD using the therapies already available.

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## Conflicts of interest

Dr. Jordi Bover Sanjuán declares that he has received honoraria for conferences, consultancies and/or travel grants from Abbvie, Amgen, AstraZeneca, Bayer, CSL-Vifor, GSK, Rubió and Sanofi. Dr. Carlos Gómez declares having received fees for conferences and consultancies from Amgen, Italfarmaco, FAES, Gedeon-Richter, Rubió, UCB and Sanofi. Dr. Enrique Casado declares having received fees for conferences and consultancies from Eli Lilly, Amgen, UCB, Theramex, Italfarmaco, Gedeon-Richter, STADA, Bayer, GPPharma and Rubió. Dr. Juan Navarro states that he has received lecture and consulting fees from Abbvie, Amgen, Vifor Pharma, Rubió and Sanofi.

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## Obinutuzumab in focal segmental glomerulonephritis resistant to treatment

### Obinutuzumab en glomerulonefritis focal y segmentaria resistente al tratamiento



Dear Editor,

Obinutuzumab is a type II humanized anti-CD20 monoclonal antibody of the IgG 1 isotype, initially used in B-cell neoplasms resistant to rituximab (RTX). Randomized studies are currently underway with good results compared to other anti-CD20 monoclonal antibodies in membranous glomerulonephritis (MGN) and lupus nephropathy (LN).<sup>1,2</sup>

We present the case of a 63-year-old male with a history of arterial hypertension, under follow-up at the nephrology outpatient clinic since 2015 for clinical nephrotic syndrome and the following lab results: proteinuria of 10 g/24 h, albumin 2.4 g/dl, cholesterol 308 mg/dl, urine systematics with protein +++ and dysmorphic red blood cells in addition to the presence of edema in the lower limbs.

We extended the glomerular study (autoimmunity, serology, complement, immunoglobulins) obtaining h negative results and normal renal function. We performed a renal biopsy in July 2015 with results compatible with minimal change glomerulonephritis (MCD).

We first treated the patient with corticosteroid using prednisone at a dose of 1 mg/kg/day/for 16 weeks presenting with a partial response with proteinuria of 2.2 g/24 h. In December 2016, when trying to lower the prednisone dose to 5 mg/day, we detected a new flare of clinical nephrotic syndrome with worsening edema and proteinuria of 8.7 g/24 h and albumin 2.7 mg/dl and categorized the patient as corticoid-dependent.

Then we restarted prednisone at a dose of 1 mg/kg/day and he presented partial improvement: decrease in proteinuria to 2.4–3.5 g/24 h in June 2017. In view of the patient's relapses and corticoid dependence and following KDIGO therapeutic guidelines, we decided to associate tacrolimus to the treatment from June 2017 to July 2018; the patient had minimum proteinuria of 2 g/24 h in the February 2018 control.<sup>2,3</sup>

Subsequently, the patient presented a new biochemical flare of the disease with proteinuria of 5.8 g/24 h and hypoalbuminemia, so we discontinued tacrolimus. We treated the patient again with corticosteroids and added cyclophosphamide at 100 mg/24 h/orally for 8 weeks.

In November 2019 the patient presented a new flare of nephrotic syndrome, which we treated with mycophenolate mofetil (MMF), as a fourth line of treatment, and proteinuria decreased to 0.5 g by May 2022. We suspended MMF in May 2022 due to macroscopic hematuria and left renal tumor. We performed a partial nephrectomy and found that the histological specimen was compatible with organized hematoma. The histological specimen justified referral again to anatomic pathology and to electron microscopy, given the poor evolution of the patient with MCD. Optical microscopy showed minimal change disease with extensive acute tubulointerstitial nephritis. Electron microscopy revealed focal segmental glomerulonephritis. We performed a genetic study and observed no associated mutations. With this result and after a new biochemical flare in October 2022 (proteinuria 8 g/day, active urine and albumin 2.2 mg/dl), we restarted MMF,