progressor. If a disease takes an average of X years to reach the terminal stage, the rapid progressors would be all those patients who reach that point before that X average, and slow progressors, who last longer than the average for that process. I believe that the overall average age at initiation of renal replacement therapy should not be used as a reference point since other diseases present at more advanced ages (diabetic nephropathy and nephroangiosclerosis) have an impact and therefore increase that average age. According to the logic used by the authors, it could also be said that any person who starts dialysis before the average life expectancy of the general population (80.6 years in men and 86 in women before the pandemic)[3] is a rapid progressor. Therefore most of our patients could be included in that definition. In type 1 polycystic kidney disease, the average onset of end-stage kidney failure is 54 years old,[4,5] and that should be, in my opinion, the point at which a person with polycystic disease is considered a rapid or slow progressor.

In addition, it is suggested to start treatment with tolvaptan in patients until 60 years old. I have only seen one study[6] (REPRISE) including patients >55 years. In that study, in the subgroup of patients >55 years old, the difference in progression was similar with respect to the placebo group (GFR drop: 2.54 vs 2.34 ml/min [p = 0.65]). The study included a limited number of patients, but no other study affirms otherwise; therefore, no treatment should be started at these ages outside of a controlled clinical trial.

I believe that the society allows us to manage public funds, that are limited, with a commitment to maximum efficiency. That means using them in those cases in which these treatments are truly useful. If we cannot manage these funds, we will totally lose the capacity of managing them.

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Reply to Comments on the SENefro Consensus Document on Autosomal Dominant Polycystic Kidney Disease

Respuesta a Comentarios sobre el Documento de Consenso de Poliquistosis Renal Autosómica Dominante de la SENefro

Dear Editor,

We appreciate the interest in the Ċonsensus Document on Autosomal Dominant Polycystic Kidney Disease (ADPKD).[1,2] The problem of the concept of rapid progression is raised, which has not been resolved. KDIGO defines rapid progression as a loss of glomerular filtration rate (GFR) >5 ml/min/1.73 m^2/year.[3] Based on the results of the REPRISE trial, it does not appear to be an adequate definition to identify those ADPKD patients who may benefit from tolvaptan[4]; the group of patients under 55 years of age treated with placebo lost GFR at a rate of −4.60 ml/min/1.73 m^2 in one year, and yet tolvaptan slowed the loss of GFR by 33%, a result offered by few or none of the chronic kidney disease (CKD) treatments. For instance, at 12 months neither dapagliflozin nor canagliflozin

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showed a difference in GFR compared to placebo.[5,6] Therefore, an alternative definition of rapid progression must be sought and we have proposed one.

As indicated in the letter, REPRISE did not demonstrate benefit during the follow-up period (one year in the context of a disease with a natural history to renal replacement therapy of 58 years on average in Europe and Spain, with a peak between 50 and 65 years)[7] in a subgroup characterised by an age greater than 55 years, but also by a slow progression with placebo (−2.34 ml/min/1.73 m^2 in one year).[4] The author of the letter emphasises the age of the patients. Still, from the pathophysiological point of view, it is not plausible that an effective treatment at 55 years of age ceases to be effective at age 56 years. It is plausible that it is difficult to assess the efficacy after one year of treatment in patients who progress slowly or that it is ineffective in patients who progress more slowly. However, the trajectory of GFR loss in ADPKD is not linear and it is accelerated with age.[8] So a patient can become a rapid progressor after the age of 55. Therefore if the safety of tolvaptan has been demonstrated in ADPKD at least up to age of 60, we find no reason to deny the treatment to patients of 55 to 60 years of age, a treatment that has been accepted as effective by the EMA.

We share the concern for the rational use of resources. Accordingly, there is a generic version of tolvaptan. Still, dialysis continues to cost around €45,000/year/patient, and is associated with a considerable loss of quality of life and cardiovascular mortality 10–100 times higher than that of the general population.[9]

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Conflicts of interest

AO has received grants from Sanofi and consulting fees for talks or financing travel to congresses held by Advicciene, Astellas, AstraZeneca, Amicus, Amgen, Fresenius Medical Care, GSK, Bayer, Sanofi-Genzyme, Menarini, Mundipharma, Kyowa Kirin, Alexion, Freeline, Idorsia, Chiesi, Otsuka, Novo-Nordisk, Sysmex and Vifor Fresenius Medical Care Renal Pharma and is Director of the Catedra Mundipharma-UAM of diabetic kidney disease and the Catedra Astrazeneca-UAM of chronic kidney disease and electrolytes. RT has received consulting fees for talks or financing trips to congresses held by Advicciene, AstraZeneca, Amicus, Amgen, Sanofi-Genzyme, Kyowa Kirin, Alexion, Chiesi, Recordatti, Otsuka.

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