



*ASF reached out to members of our Medical Advisory Committee (MAC) and Scientific Advisory Research Network (SARN) with a list of journal articles published on Alport syndrome treatment and novel research during 2025. The following is a summary of one of the Alport treatment articles that a MAC/SARN member selected and their comments about its impact on the field.*

Ioannou P, Odiatis C, Hadjisavva R, et al. Chemical chaperone 4-phenylbutyrate treatment alleviates the kidney phenotype in a mouse model of Alport syndrome with a pathogenic variant in Col4a3. *Kidney Int.* 2025 Oct;108(4):609-625. DOI: [10.1016/j.kint.2025.05.016](https://doi.org/10.1016/j.kint.2025.05.016). Open access.

*“This article provides evidence for a therapeutic approach that could be developed and tested in patients. It also directly targets the underlying pathogenesis [of Alport] versus general CKD effects.”*

### **Abstract Summary**

This study investigated a new way to treat Alport syndrome using "chemical chaperones." In Alport syndrome, genetic mutations cause the body to misfold collagen IV, which cannot be used correctly to build the kidney's filters. The researchers in this article tested two compounds, 4-PBA and TUDCA, to see if they could act like molecular assistants to help this protein fold into the right shape.

The results showed that while TUDCA had no effect, 4-PBA significantly improved kidney health in mice. Treatment with 4-PBA led to a 54% reduction in damage to the kidney's filtering membrane and reduced scarring (fibrosis) within the organ. By helping the collagen fold

properly, the drug allowed the protein to be secreted and used as a building block for the kidney filter rather than being trapped or destroyed inside the cells. This suggests that repurposing 4-PBA could be a promising new strategy for protecting kidney function in patients with Alport syndrome.