Efficacy of Dapagliflozin in Adult Autosomal Recessive Alport Syndrome

To the Editor: Alport syndrome is a hereditary kidney disease characterized by progressive renal failure especially for patients with autosomal recessive and X-linked inheritance. At present, no preventive or curative therapies are available. Current treatment includes the use of renin-angiotensin-aldosterone system inhibitors which slow progression of kidney disease and prolong life expectancy. Though the Dapagliflozin and Prevention of Adverse Outcomes in Chronic Kidney Disease (DAPA-CKD) trial suggests a beneficial effect of SGLT2 inhibitors (SGLT2i) in chronic kidney disease of nonmetabolic origin, whether a conclusion can be extrapolated for the treatment of rapidly progressive genetic kidney disease is unknown. Therefore, we explored the efficacy and safety of SGLT2i in adult autosomal recessive Alport syndrome.

This was a real-world study based on our dynamic cohort of Alport syndrome (Supplementary Methods and Supplementary Table S1). With a follow-up of 4 to 6 months, proteinuria showed a decreasing trend in all the 3 cases of autosomal recessive Alport syndrome, with 24-hour proteinuria decreasing by 0.17 g/24h (8.9%), 0.61 g/24h (39.9%), and 0.69 g/24h (52.3%) respectively (Figure 1). Urinary albumin-creatinine ratio decreased by 374.92 mg/g (26.9%), 561.03 mg/g (44.0%), and 234.33 mg/g (68.7%), respectively. Correspondingly, the serum albumin showed an increment on the whole. Importantly, the serum creatinine and estimated glomerular filtration rate remained stable. No patient discontinued dapagliflozin due to safety concerns and no clinically adverse effect was observed.

In this report, the good efficacy of dapagliflozin is reported for the first time in patients with autosomal recessive Alport syndrome who presented with decreased renal function. Proteinuria decreased steadily after administration of dapagliflozin. No patient discontinued SGLT2i therapy due to safety concerns during the follow-up period of 6 months. Limitations should be acknowledged. First, the study included patients with mild or moderate proteinuria, rather than nephrotic proteinuria. Second, this is a pilot study, and more high quality studies with control samples are needed to verify our results.

In conclusion, the pilot study showed good efficacy and tolerance of half-dose dapagliflozin in patients with Alport syndrome. Application of SGLT2i as an add-on
therapy may be considered. A high quality study with a larger number of patients given full dose dapagliflozin is needed in the future.

**DISCLOSURE**
All the authors declared no conflict of interest.

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**Data Statement**
The data will be available on request.

**ETHICAL STATEMENT**
The patients have given consent for their clinical information to be published in the journal.

**SUPPLEMENTARY MATERIAL**
Supplementary File (PDF)
Supplementary Methods.
Table S1. Main effects of SGLT2 inhibitors (dapagliflozin 5 mg) in 3 adults with autosomal recessive Alport syndrome.

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