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Efficacy and Safety of Telitacicept as an Add-On Therapy for Refractory Immunoglobulin A Nephropathy or Immunoglobulin A Vasculitis Nephropathy in Children

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Received 30 September 2024; revised 16 November 2024; accepted 26 November 2024; published online 2 December 2024

Kidney Int Rep (2025) **10,** 940–943; https://doi.org/10.1016/j.ekir.2024.11.1363
KEYWORDS: IgAN/IgAVN; pediatric; refractory

INTRODUCTION

IgA nephropathy (IgAN) and IgA vasculitis nephritis (IgAVN) represent prevalent forms of glomerulonephritis in the pediatric population, with significant risk of progression to renal failure. The pathogenesis of both conditions is explained by the 4-hit hypothesis: (i) elevated galactose-deficient IgA1 (Gd-IgA1), (ii) anti-Gd-IgA1 IgG autoantibody formation, (iii) Gd-IgA1–containing immune complexes development, and (iv) glomerular deposition of these complexes leading to renal injury. Gd-IgA1–containing immune complexes are central to disease pathogenesis,[1,2] with B cell lymphocyte stimulator and a proliferation-inducing ligand playing crucial roles in Gd-IgA1 generation. Telitacicept, a novel recombinant fusion protein that targets both B cell lymphocyte stimulator and a proliferation-inducing ligand, presents an alternative therapeutic strategy for IgAN.[3] Clinical studies demonstrate its efficacy in reducing proteinuria among adult patients with IgAN, accompanied by decreased circulating Gd-IgA1– and IgA-containing immune complexes during treatment.[4,5]

Given the pathogenic similarities between IgAN and IgAVN, telitacicept emerges as a promising therapeutic agent for pediatric patients with IgAN or IgAVN.[6] Therefore, we used telitacicept in pediatric patients with refractory IgAN and IgAVN in clinical practice. This study evaluates the efficacy and safety of telitacicept in children with refractory IgAN and IgAVN in a real-world setting.

RESULTS

Study Population

This study was performed on pediatric patients with refractory IgAN or IgAVN treated with telitacicept between October 2022 and March 2024 at 4 tertiary medical centers. The detailed methods are described in the Supplementary Material. A total of 16 patients (11 with IgAN and 5 with IgAVN) with a mean age of 11 years were enrolled. The baseline characteristics of the patients are shown in Table 1 and Supplementary Table S1. Before telitacicept initiation, the median disease duration was 21 months. At baseline, the median 24-hour urinary protein (UP) excretion was 1.83 g/1.73 m^2, the median urine protein-to-creatinine ration (UPCR) was 1.13 mg/mg, the mean estimated glomerular filtration rate eGFR was 97.0 ml/min per 1.73 m^2, and the mean serum albumin was 35.9 g/l. While

Table 1. Participants demographics and baseline characteristics of participants

Characteristics	Patients ($N = 16$)
Age, mean ± SD, yrs	11.0 ± 3.5
Male, *n* (%)	7 (43.8%)
Time since diagnosis before telitacicept treatment, median (IQR), mo	21 (6–30)
Previous use of systemic immunosuppressive therapy, *n* (%)	
Oral glucocorticoids	16 (100%)
Methylprednisolone pulses	13 (81.3%)
Mycophenolate mofetil	14 (87.5%)
Cyclophosphamide pulses	11 (68.8%)
Tacrolimus	5 (31.3%)
Cyclosporine A	1 (6.3%)
Concomitant medications with telitacicept, *n* (%)	
ACEI/ARBs	16 (100%)
Oral glucocorticoids	15 (93.8%)
Mycophenolate mofetil	13 (81.3%)
SGLT2 inhibitor	2 (12.5%)
Baseline 24-h UP, median (IQR), g/1.73 m^2	1.83 (0.87–4.91)
Baseline UPCR, median (IQR), mg/mg	1.13 (0.74–3.96)
Baseline serum albumin, mean ± SD, g/l	35.90 ± 6.08
Baseline eGFR, mean ± SD, ml/min per 1.73 m^2	97.0 ± 36.58

ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin 2 receptor blocker; eGFR, estimated glomerular filtration rate; IQR, interquartile range; SGLT2, sodium-glucose cotransporter 2; UP, urinary protein; UPCR, urinary protein-to-creatinine ratio.

concomitant medications remained stable throughout the treatment, glucocorticoid dosages were gradually reduced. The median follow-up duration post-telitacicept initiation was 24 weeks.

Efficacy

Effects on Proteinuria

Significant proteinuria reduction was observed 4 weeks after initiating telitacicept, with mean reduction in 24-hour UP of −47.62% (95% confidence interval: −25.43 to −69.82, $P < 0.01$) and UPCR of −46.83% (95% confidence interval: −30.43 to −63.23, $P < 0.0001$). By week 48, reduction reached −79.12% for 24-hour UP (95% confidence interval: −68.0 to −90.24, $P < 0.0001$) and −78.14% for UPCR (95% confidence interval: −57.31 to −98.97), $P < 0.001$). Median 24-hour UP decreased from 1.83 (0.87–4.91) g/1.73 m^2 at baseline to 0.28 (0.12–3.23) g/1.73 m^2 at 24 weeks ($P < 0.05$), whereas median UPCR decreased from 1.13 (0.74–3.96) mg/mg to 0.27 (0.15–0.64) mg/mg at 36 weeks ($P < 0.05$). At final follow-up, 10 patients (62.5%) achieved complete remission (Figure 1).

Similar to the trend observed in the full cohort, subgroup analysis revealed that proteinuria gradually decreased during treatment in both the IgAN and IgAVN groups (Supplementary Figure S1).

Effects on Hematuria

For the 3 patients with recurrent macroscopic hematuria, no further episodes were observed during follow-up after telitacicept administration.

Effects on Serum Albumin and Estimated Glomerular Filtration Rate

Serum albumin level significantly improved from 35.9 ± 6.08 g/dl to 39.11 ± 4.76 g/dl at week 12 ($P < 0.001$), and further increased to 41.43 ± 7.17 g/dl at week 48 ($P < 0.05$). Estimated glomerular filtration rate remained stable throughout the 48 weeks of follow-up, ranging from 91.73 ± 32.46 to 103.6 ± 23.49 ml/min per 1.73 m^2, with no significant difference from baseline (97.0 ± 36.58 ml/min per 1.73 m^2, $P = 0.95$) (Figure 1).

Influence on Immunoglobulins and Lymphocyte Subset Cells

Telitacicept treatment led to a significant reduction in serum levels of immunoglobulins. There were no significant differences in CD4+ T cells during the treatment; however, the number of CD19+ B cells significantly decreased from week 12 to week 48 (Supplementary Figure S2).

Steroid-Sparing Effect

Telitacicept demonstrated a notable steroid-sparing effect. In our study, the median glucocorticoid dose decreased from 25 mg/d at baseline to 2.5 mg/d at the end of follow-up, representing 85.7% reduction in steroid dosage. In addition, 8 patients achieved complete steroid discontinuation.

Safety

Adverse events occurring during the telitacicept treatment are summarized in Supplementary Table S2. Decreased IgG levels were the most common adverse events, with 6 patients (37.5%) reporting hypogammaglobulinemia and 3 of them experienced upper respiratory tract infections that did not require hospitalization. No patients discontinued telitacicept because of adverse events, and no serious adverse events were recorded during the study.

DISCUSSION

This study is the first to evaluate the efficacy and safety of telitacicept as an add-on therapy for pediatric patients with refractory IgAN and IgAVN, most of whom had persistent proteinuria despite previously aggressive treatment with immunosuppressant drugs. Our findings indicate that proteinuria improved sustainably over time in these patients, accompanied by a reduction in the daily dosage of glucocorticoids.

Telitacicept reduced proteinuria in pediatric patients with refractory IgAN or IgAVN, with 24-hour UP decreasing by 48% to 79% and UPCR by 47% to 78%. This efficacy parallels adult studies showing 25% to 49% proteinuria reduction with 160 to 240 mg telitacicept over 24 weeks.[5] Similarly, atacicept,

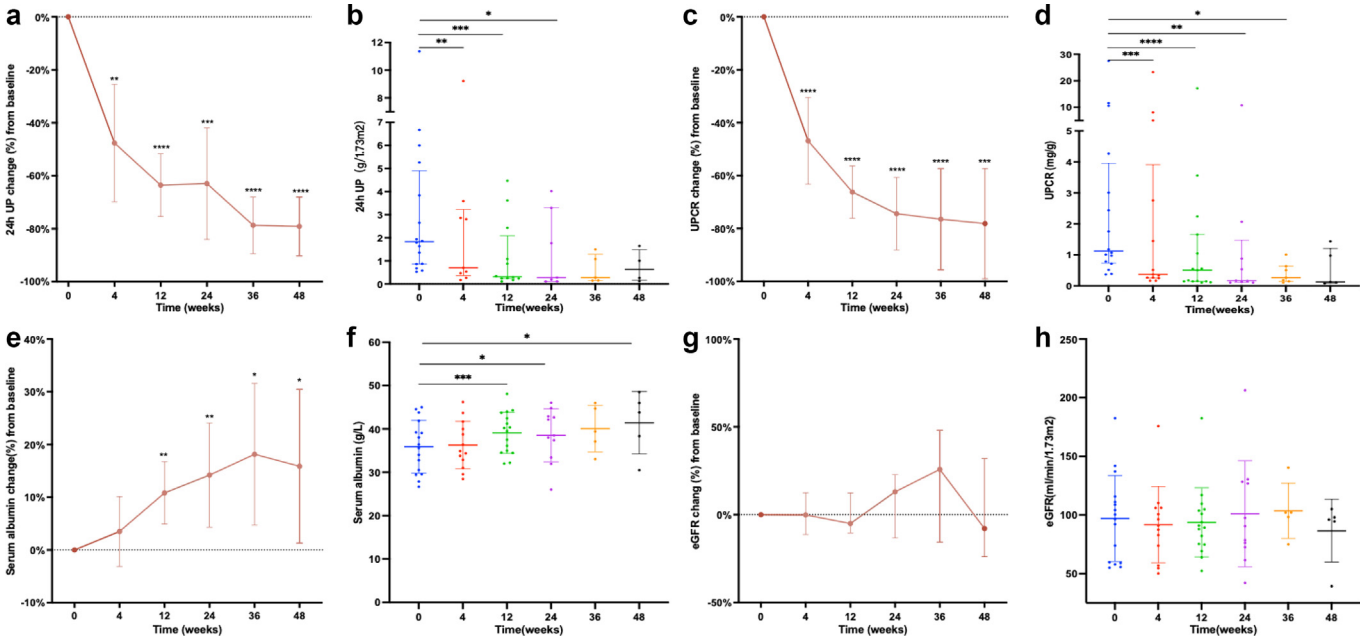

Figure 1. Changes in (a, b) 24-hour UP, (c, d) UPCR, (e, f) serum albumin, and (g, h) eGFR during treatment with telitacicept. The error bars indicate (a, c, e, g) the 95% confidence interval, (b, d, h) interquartile range, or (f) SD. eGFR, estimated glomerular filtration rate; UP, urinary protein; UPCR, urine protein-to-creatinine ratio. $^{*}P < 0.05$, $^{**}P < 0.01$, $^{***}P < 0.001$, $^{****}P < 0.0001$.

another B cell lymphocyte stimulator or a proliferation-inducing ligand inhibitor, achieved 24% to 25% reduction in 24-hour proteinuria in patients with IgAN at 24 weeks.[7] Furthermore, 62.5% of them achieved complete remission during a median follow-up of 24 weeks. Despite prednisolone or mycophenolate mofetil treatment in over 90% of patients, most remained refractory with persistent proteinuria. After adding telitacicept, 10 patients (62.5%) achieved complete remission while reducing glucocorticoid doses. Although these results suggest telitacicept's effectiveness in pediatric refractory IgAN or IgAVN, further studies are needed to evaluate potential drug interactions and establish its definitive therapeutic role. Subgroup analysis revealed that patients with IgAVN also responded well to telitacicept, with a median reduction in 24h UP of 83% and in UPCR 72% after 12 weeks of treatment. Further studies are needed to validate whether telitacicept could be a new favorable treatment option for patients with IgAVN.

Telitacicept, a dual B cell pathway inhibitor, suppresses B cell differentiation, maturation, and antibody secretion, with hypogammaglobulinemia as its primary adverse effect. We observed decreased IgG, IgM, and IgA levels, with hypogammaglobulinemia in 6 patients (37.5%), 5 of whom had preexisting low levels. Previous studies showed IgG levels decreased by approximately 30% in adult patients with IgAN and reduced immunoglobulin levels in 93% of childhood-onset systemic lupus erythematosus patients.[5,8] Given telitacicept's B lymphocytes–targeting mechanism, regular immunoglobulin monitoring is essential during treatment. A recent study in patients with systemic lupus erythematosus, showed significant decreases in the numbers of total and naive B cells, whereas memory B cells and T cell subsets did not change.[9] Similarly, in our study, the number of CD19+ B cells decreased significantly, which may be due to the effect on the conversion and maturation of B cells.

The limitations of the present study include its observational design, small sample size, lack of a control group, and variability in baseline treatments among patients, which makes it difficult to isolate the effects of concomitant medications. In addition, lack of confirmed pathological tissue improvement is a notable limitation. Future research requires long-term follow-up and larger randomized controlled trials to validate efficacy.

CONCLUSION

To the best of our knowledge, our study is the first to report that telitacicept as an add-on therapy, effectively reduces proteinuria in children with refractory IgAN and IgAVN, thus offering a promising treatment option. Further studies with lager patient numbers and longer observation periods are essential; and the timing and duration of use require additional investigation.

DISCLOSURE

All the authors declared no conflicting interests.

ACKNOWLEDGMENTS

We thank the patients and their families for participating in our study. This study was supported by the National Key R&D Program of China (2021YFC2500202, 2022YFC2705105) and National Natural Science Foundation of China (82200743).

DATA AVAILABILITY STATEMENT

Data and materials were included in the manuscript and Supplementary Material.

AUTHOR CONTRIBUTIONS

JiaoL, XH, XJ, XG, and GL contributed equally. JiaoL and XH contributed to the data collection and drafted the manuscript. XJ, XG, and GL contributed to the data analysis. XF, JC, YZ, JiaIL, YP, JZ, and GZ contributed to patient follow-up. HX and QS contributed to the study design and revised the manuscript for important intellectual content. All the authors have given their approval for the final version of the manuscript to be published. Each author participated sufficiently in the work to be responsible for the content.

SUPPLEMENTARY MATERIAL

Supplementary File (PDF)

Supplementary Methods.

Supplementary References.

Figure S1. Changes in proteinuria during treatment with telitacicept based on primary disease.

Figure S2. Change in immunoglobulin levels and lymphocyte subset during telitacicept treatment.

Table S1. Characteristics of the participants at baseline and indications for telitacicept use.

Table S2. Summary of adverse events reported during the study.

REFERENCES

1. Moldoveanu Z, Wyatt RJ, Lee JY, et al. Patients with IgA nephropathy have increased serum galactose-deficient IgA1 levels. *Kidney Int*. 2007;71:1148–1154. https://doi.org/10.1038/sj.ki.5002185
2. Kiryluk K, Moldoveanu Z, Sanders JT, et al. Aberrant glycosylation of IgA1 is inherited in both pediatric IgA nephropathy and Henoch-Schönlein purpura nephritis. *Kidney Int*. 2011;80:79–87. https://doi.org/10.1038/ki.2011.16
3. Telitacicept DS. Telitacicept: first approval. *Drugs*. 2021;81:1671–1675. https://doi.org/10.1007/s40265-021-01591-1
4. Zan J, Liu L, Li G, et al. Effect of telitacicept on circulating Gd-IgA1 and IgA-containing immune complexes in IgA nephropathy. *Kidney Int Rep*. 2024;9:1067–1071. https://doi.org/10.1016/j.ekir.2024.01.003
5. Lv J, Liu L, Hao C, et al. Randomized Phase 2 trial of telitacicept in patients with IgA nephropathy with persistent proteinuria. *Kidney Int Rep*. 2023;8:499–506. https://doi.org/10.1016/j.ekir.2022.12.014
6. Williams CEC, Lamond M, Marro J, Chetwynd AJ, Oni L. A narrative review of potential drug treatments for nephritis in children with IgA vasculitis (HSP). *Clin Rheumatol*. 2023;42:3189–3200. https://doi.org/10.1007/s10067-023-06781-8
7. Barratt J, Tumlin J, Suzuki Y, et al. Randomized Phase II Janus study of atacicept in patients with IgA nephropathy and persistent proteinuria. *Kidney Int Rep*. 2022;7:1831–1841. https://doi.org/10.1016/j.ekir.2022.05.017
8. Sun L, Shen Q, Gong Y, et al. Safety and efficacy of telitacicept in refractory childhood-onset systemic lupus erythematosus: a self-controlled before-after trial. *Lupus*. 2022;31:998–1006. https://doi.org/10.1177/09612033221097812
9. Ji L, Geng Y, Zhang X, et al. B cell pathway dual inhibition for systemic lupus erythematosus: a prospective single-arm cohort study of telitacicept. *Med*. 2024;5:e515. https://doi.org/10.1002/mco2.515