

From Natural History to Post-Approval Evidence: An Integrated Multi-Source Real-World Program Characterizing IgA Nephropathy in the Era of Oral Targeted-Release Formulation of Budesonide

Giancarlo Pesce¹, **Lobat Hashemi**², Ramin Tolouian³, Margaret Helmuth⁴, Artak Khachatryan⁵, Ananth Kadambi⁶, Terri Madison³

¹Certara Italy, Milan, Italy; ²Veloxis, Cary, NC, USA; ³Calliditas Therapeutics, New York, NY, USA; ⁴University of Michigan, Ann Arbor, MI, USA; ⁵Certara UK, London, UK; ⁶Certara USA, Radnor, PA, USA.

BACKGROUND

Immunoglobulin A nephropathy (IgAN) is a rare, heterogeneous kidney disease with limited real-world evidence on treatment effectiveness and safety. With the approval by the FDA of oral targeted release budesonide therapy (Tarpeyo®), the integration of multiple real world data sources provides an opportunity to characterize unmet need, delineate treatment patterns prior to approval, and evaluate early clinical outcomes following its introduction into clinical practice.

OBJECTIVES

The objective of the project is to understand IgAN natural history, evaluate the safety and economic burden of systemic glucocorticoids (SGC), and generate early post-approval effectiveness data. Due to the rarity and heterogeneity of IgAN, no single data source was sufficient. A multi-source real-world data approach including integrating registry, electronic health records (EHR), and chart-review data was used to generate complementary insights across natural history, pre-approval care, and early post-approval treatment to support clinical, regulatory, and payer decision-making.

METHODS

Three independent US-based observational studies were conducted (Table 1 and Figure 1):

- CureGN registry:** an ancillary observational study using prospectively collected CureGN data to describe disease characteristics, treatment patterns, and renal outcomes among 653 biopsy-confirmed US patients with IgAN enrolled from 2015 to 2024.
- TriNetX HER study:** a retrospective cohort study using the TriNetX Dataworks network (2011–2022) comparing adverse events (AEs), healthcare resource utilization (HCRU), costs, and kidney failure among 1:1 propensity score-matched patients with IgAN who initiated systemic glucocorticoids (SGC) versus those not treated with SGC. Matching was based on characteristics at diagnosis; the index date was SGC initiation, and matched non-SGC patients were assigned a pseudo-index date.
- CKC chart review:** a retrospective case series of 45 Asian-American adults with IgAN treated with delayed-release budesonide (Tarpeyo®/Nefecon) at Chinatown Kidney Care (CKC), New York, during 2022–2023. Outcomes included changes in estimated glomerular filtration rate (eGFR), urine protein-creatinine ratio (UPCR), and AEs up to 12 months after treatment initiation.

RESULTS

CureGN Registry

- 653 patients with IgAN, with median follow-up of 5.8 years in the renal outcomes analysis; participants were more often male (59%), White (80%), and non-Hispanic (85%) (Madison 2025 and Khalid 2025)
- Adolescents aged 13–17 years had a higher risk of kidney failure versus adults aged 18–44 years (HR 2.41; 95% CI 1.13–5.13), while older adults had lower relative risk
- In the adult therapies analysis, systemic corticosteroids were the most frequently used immunosuppressive therapy after biopsy (61.2%), yet use of traditional immunosuppressive therapy was not associated with a significantly lower risk of kidney failure after adjustment for eGFR and UPCR.

TRINETX EHR

- The final TriNetX analysis included 802 propensity score-matched patients with IgAN (401 SGC and 401 non-SGC), with median follow-up of 3.5 and 3.1 years, respectively (Pesce et al. 2025).
- SGC treatment was associated with higher rates of multiple AEs, including severe infections requiring hospitalization (3.5% vs 0.3%), peripheral/face edema (14.7% vs 4.2%), and dyspnea (27.2% vs 11.5%).
- In patients initiating SGCs, adjusted kidney failure risk was higher at 1 year (aHR 2.33) and 2 years (aHR 1.84) but similar at 5 years (aHR 1.335), with no clear evidence of kidney-function preservation benefit.
- Annualized total HCRU costs were nearly threefold higher in patients initiating SGCs (Figure 3).

CKC Case-Series

- Among 45 patients treated with Tarpeyo®, mean treatment duration was 9.3 months and n=30 (67%) completed at least one 9-month course (Table 2) (Ngai 2024).
- Overall eGFR remained stable after 9 months of treatment; patients treated for at least 9 months had a mean increase of 3.6 mL/min/1.73 m², whereas those treated for less than 9 months had a mean decrease of 3.5 mL/min/1.73 m².
- UPCR decreased by 19% overall and by 26% among patients treated for at least 9 months
- AEs were mostly mild or moderate with no severe or unexpected events reported.

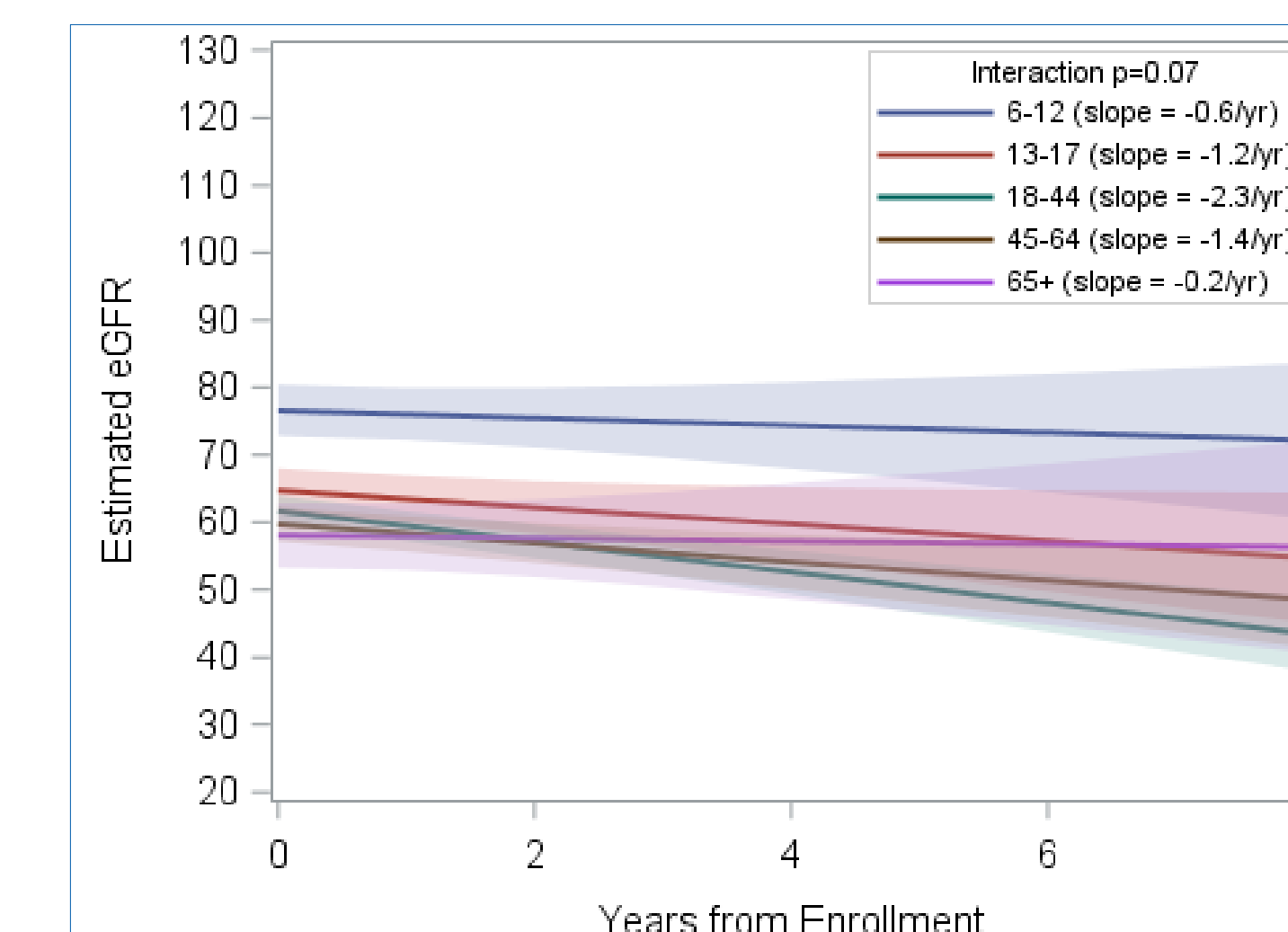


Figure 2: Time periods of the three US-based observational studies on IgAN (Khalid 2025)

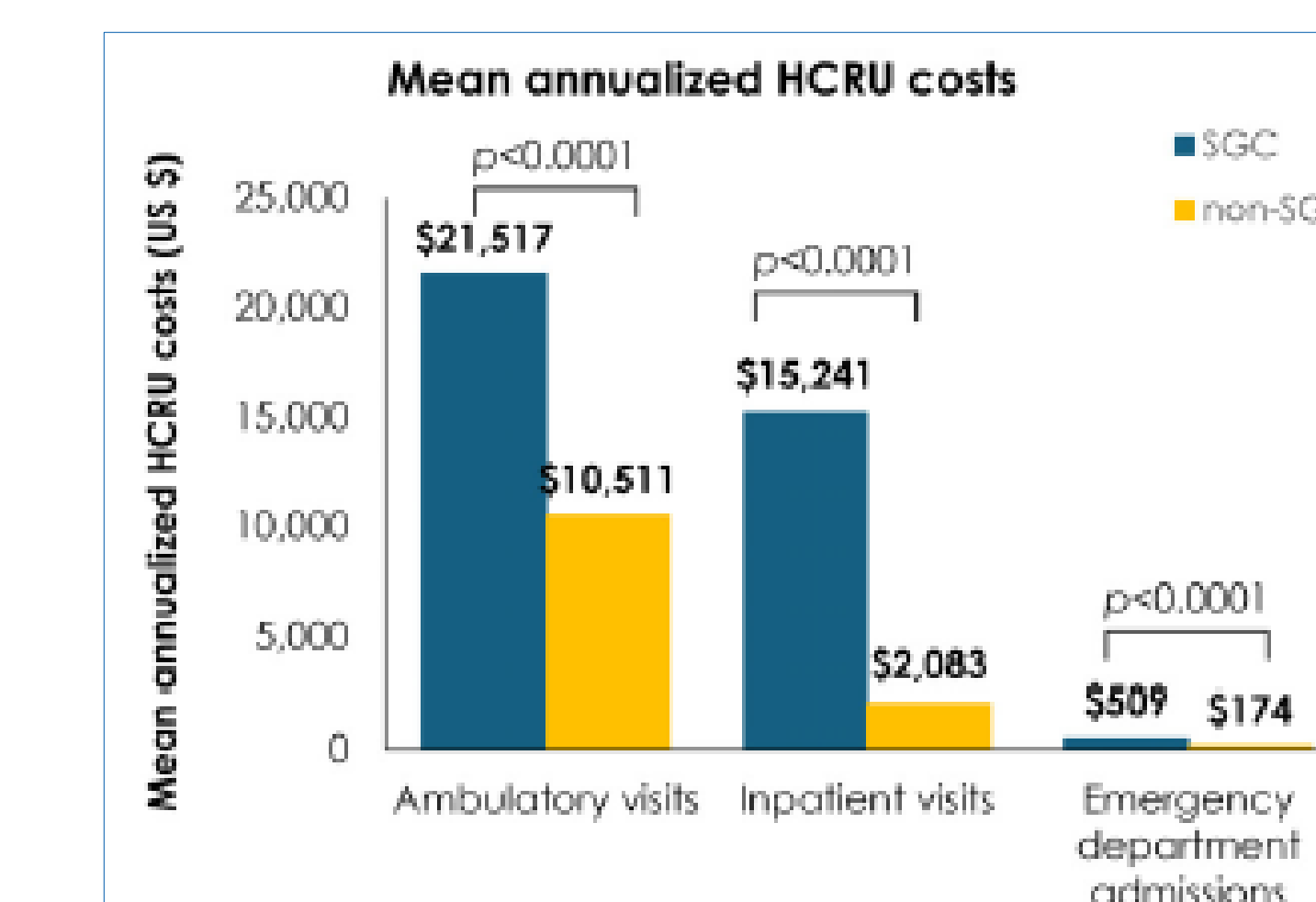


Figure 3: HCRU costs in SGC initiators vs non-SGC cohort (Pesce 2025)

Table 1: Design of three US-based observational studies on IgAN

Data Source	TRINETX EHR	CureGN Registry	Chart Review at CKC
Design	Retrospective Cohort	Retrospective Cohort	Retrospective Case-Series
Population	N=802 PS-matched adult patients with IgAN in the US, including 401 SGC initiators vs 401 non-SGC	N=653 biopsy-confirmed IgAN patients from the US, including both children and adults	N=45 Asian-American adult patients treated with Tarpeyo at a single nephrology center – the Chinatown Kidney Care (CKC) – NY, USA
Period	2011-2022	2015-2024	2022-2023
Endpoints	- Adverse Events - Kidney Failure - Healthcare utilization and costs	- Disease characteristics, - Treatment patterns, - Renal outcomes	- Change in eGFR and UPCR up to 12 months - AEs

Table 2: Clinical outcomes in patients with IgAN treated with Nefecon at the CKC.

	All patients (N=45)	Received Nefecon for ≥9 months (N=30)	Received Nefecon for <9 months (N=15)
Follow-up time, months, mean (SD)	14.9 (3.3)	14.4 (3.3)	15.8 (3.2)
Total follow-up, person-months	669	432	237
Kidney failure, n (%)	1 (2.2)	0	1 (6.7)
30% eGFR reduction, n (%)	6 (13.3)	2 (6.7)	4 (26.7)
40% eGFR reduction, n (%)	3 (6.7)	1 (3.3)	2 (13.3)
50% eGFR reduction, n (%)	2 (4.4)	1 (3.3)	1 (6.7)

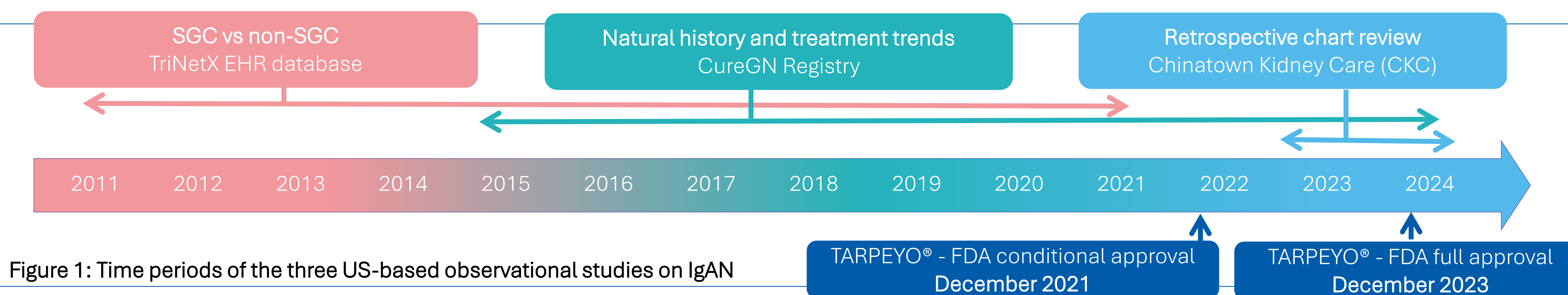


Figure 1: Time periods of the three US-based observational studies on IgAN

CONCLUSIONS

Registry and EHR analyses highlighted unmet needs and the limitations of systemic corticosteroids, while chart-level data demonstrated the favorable real-world effectiveness and tolerability of oral targeted-release formulation of budesonide.

- CureGN registry study shows substantial long-term progression despite supportive care, particularly in younger/high risk patients.
- The EHR study demonstrates that real world SGC use is associated with serious AEs and greater HCRU costs, without clear functional benefit – although residual indication bias cannot be completely ruled out.
- The CKC case series suggests that a targeted, oral targeted-release budesonide formulation can stabilize eGFR and reduce proteinuria with acceptable tolerability when used for the recommended 9-month course.

Taken together, these complementary real-world data sources provide an integrated picture of IgAN across the pre- and post-approval landscape and support clinical, regulatory, and payer decision-making in rare kidney disease.

Contact: Please contact **Lobat Hashemi** (lhas@veloxis.com)
Funding/Disclosure: Calliditas Therapeutics AB sponsored the study. Calliditas and Veloxis Pharmaceuticals work together as part of the Asahi Kasei Healthcare sector. LH (Veloxis), RT and TM (Calliditas) are employees of the Asahi Kasei Group. GP, MH, ArK, AnK report study and medical writing funding provided to their institution by Calliditas during the conduct of the study.

References:

- Khalid M, et al. (2025) Kidney Outcomes in IgAN Across the Age Spectrum in the Cure Glomerulopathy Network (CureGN): SA-PO0804. Journal of the American Society of Nephrology 36(10S):10.1681/ASN.2025gt4zxcrc, DOI: 10.1681/ASN.2025gt4zxcrc
- Madison, T, et al. (2025) Therapies for IgAN in the Cure Glomerulonephropathy Network (CureGN): SA-PO0840. Journal of the American Society of Nephrology 36(10S):10.1681/ASN.2025d2zef6w2, DOI: 10.1681/ASN.2025d2zef6w2
- Ngai C, et al. (2024) Results from a Real-World Case Series of Patients with IgAN Who Received at Least 9 Months of Tarpeyo: FR-PO866. Journal of the American Society of Nephrology 35(10S):10.1681/ASN.2024adbxc6, DOI: 10.1681/ASN.2024adbxc6
- Pesce G, et al. (2025) Real-world challenges associated with the use of four common systemic glucocorticoids in a United States IgAN cohort. Front. Nephrol. 5:1574239. doi: 10.3389/fneph.2025.1574239