



**KIDNEY
WEEK** 20
26

HLX79 (E-602) Plus Rituximab Produces Fast and Durable Responses in Patients with Membranous Nephropathy

Brad Rovin

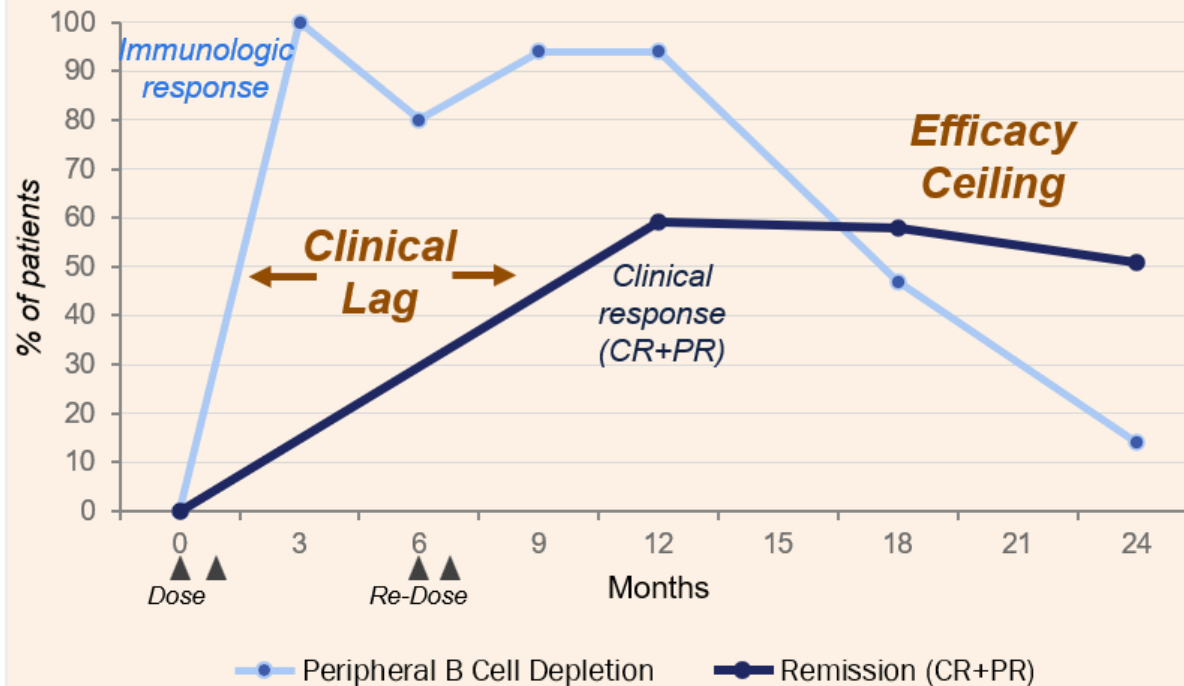
The Ohio State University,
Wexner Medical Center

Unmet Needs in Primary Membranous Nephropathy

Anti-CD20 B Cell Depletion in pMN:

Immunologic vs. Clinical Response

Obinutuzumab – ADCC-enhanced anti-CD20



Source: MAJESTY study Phase 3 data in pMN (Fervenza, NEJM, 2026)

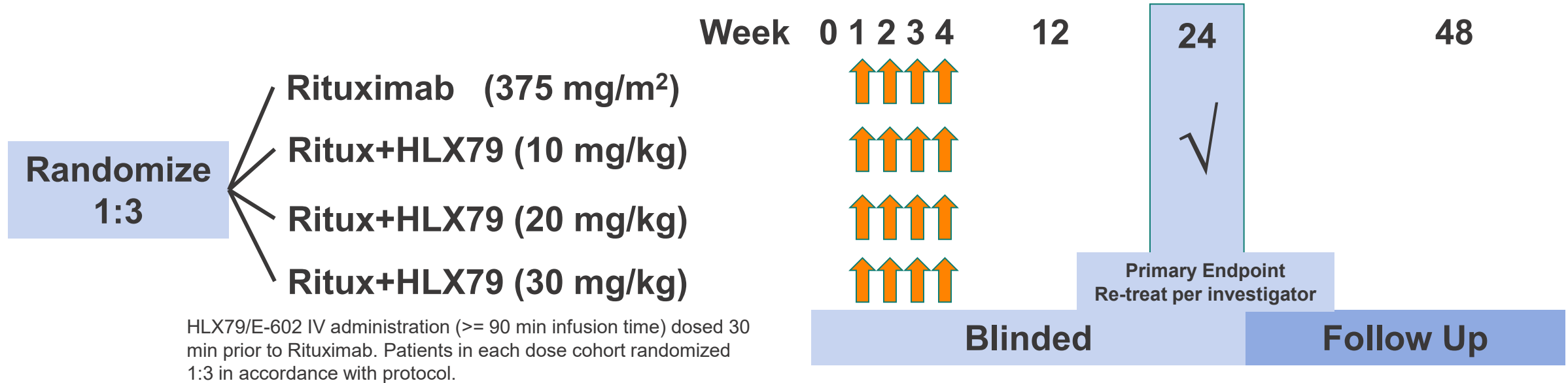
- Even with highly effective B cell depletion therapy there is a significant delay between immunologic response and clinical response in PMN and responses occur in only about half the patients
- It would be ideal to decrease the length of time between immunologic and clinical responses in PMN
- It would be ideal to increase the % of patients who respond to treatment

This trial was undertaken to determine if adding HLX79/E-602 to rituximab therapy in PMN can address these unmet needs

HLX79/E-602: First-in-Class Human Sialidase

- **We know CD163+ macrophages have a role in autoimmune diseases**
- **We know B cells and memory B cells have a role in autoimmune disease**
- **We postulated that the addition of HLX79/E-602 to B cell depleting therapy in primary membranous nephropathy would improve time to response and proportion of responses**

Phase IIA Study Design of HLX79/E-602 in Moderate-Severe Primary Membranous Nephropathy (NCT07038382)



ENDPOINTS

Efficacy, safety, tolerability at week 24 (blinded) with follow-up to week 48

RESPONSE CRITERIA

CR: proteinuria <0.3 g/d, blood albumin > 3.5 g/dL

PR: proteinuria reduction $\geq 50\%$ of baseline and to a level between 0.3 and 3.5 g/d

Baseline Characteristics

	Rituximab (n=6)	HLX79 10 mg/kg (n=6)	HLX79 20 mg/kg (n=7)	HLX79 30 mg/kg (n=7)
Age (years)	54.8	53.3	56.1	55.7
% Male	67	83	71	43
Median Proteinuria (g/d)	6.6	11	8.6	4.7
Median eGFR (ml/min/1.73m ²)	102	84	95	90
Median Serum Albumin (g/L)	27	25	30	31
Median Anti-PLA2R (RU/ml)*	8.5	38	65	11

*Euroimmune ELISA

Limit of detection 1.72 RU/mL

Phase IIA Safety Summary (n=26)

Adverse Events	Rituximab (n=6)	HLX79 10 (n=6)	HLX79 20 (n=7)	HLX79 30 (n=7)
Any TEAE	83%	83%	86%	57%
TEAE related to HLX79/Placebo	50%	67%	57%	43%
TESAE	33%	0	0	0
TEAE leading to tx interruption	50%	33%	0	29%
TEAE leading to tx discontinuation	33%	0	0	0
Death	0	0	0	0

Notable TEAS: infusion related reactions (n = 7), administration site reactions (n = 7), infection (n = 9). No thromboembolism observed. Two patients in the rituximab control group discontinued due to AEs (dialysis initiation, infusion reaction) and one patient in the rituximab control group experienced an SAE of lung infection.

HLX79/E-602 + RTX in pMN: Full Dataset Through 36 Weeks

E-602 + Rituximab in pMN: Timing and Magnitude of Clinical Response

Baseline				Time (weeks) since first dose																	
Cohort	Patient	g/Day	anti-PLA2R (RU/mL)	4		8		12		16		20		24		28		32		36	
Rituximab Alone	2008*	4.5	6.5																		
	2005	5.1	2.0																		
	9002	4.1	118.3																		
	15001	8.0	10.6																		
	2003*	14.4	6.2																		
	13001*	18.4	2112.0																		
E-602 10 mg/kg +Rituximab	2002	7.5	27.0																		
	16001	8.5	43.1																		
	1002	10.9	125.8																		
	12001	11.1	23.3																		
	2004	12.7	32.9																		
	2001	22.5	209.3																		
E-602 20 mg/kg +Rituximab	17002*	3.5	< 1.72																		
	9001	3.8	< 1.72																		
	4001	3.9	30.8																		
	8002	8.6	67.9																		
	2007	11.3	153.4																		
	5003	11.4	191.5																		
	16002	14.1	65.3																		
E-602 30 mg/kg +Rituximab	17003	4.2	17.6																		
	3001	4.2	10.6																		
	2010	4.5	15.5																		
	2011*	4.7	< 1.72																		
	2009	6.2	59.7																		
	14002	8.1	3.6																		
	4002	13.6	< 1.72																		
Dosing:				Δ	Δ	Δ	Δ									Δ	Δ	Δ	Δ		

***All subjects re-dosed at 6 months except 2008, 17002, 2011, 2003, 13001**

Patient stratification

Mod risk
High risk

Response Category

↓Proteinuria >50%
Partial response (PR)

PR, <1g/day
Complete response (CR)

x	Withdrew
	non response

High-risk definition: baseline anti-PLA2R antibody >50 RU/mL or 24-hour urine protein >8 g/d.

**Week 24
Response
Rate**

4/6
1CR+3PR
67%

2/6
2PR
33%

5/7
5 PR
71%

6/7
1CR+5PR
86%

**Week 36
Response
Rate**

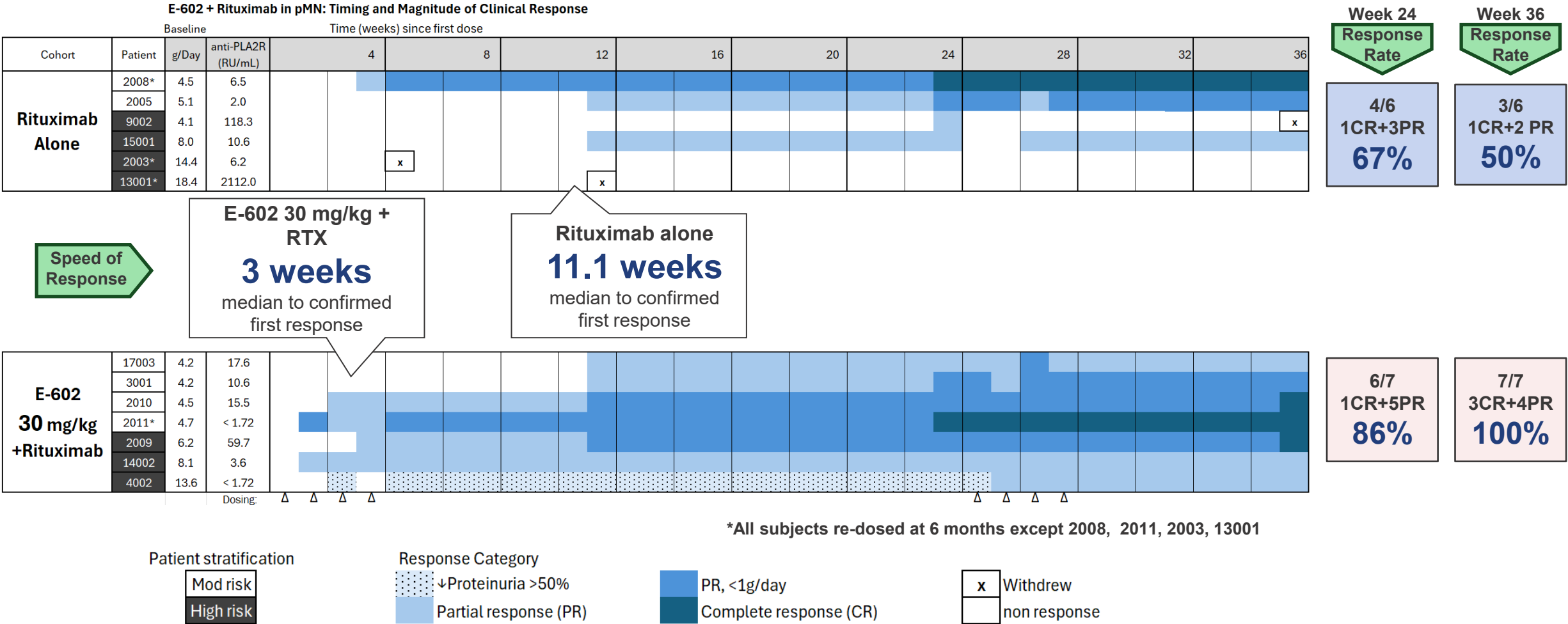
3/6
1CR+2 PR
50%

3/6
3PR
50%

5/7
2CR+3PR
71%

7/7
3CR+4PR
100%

Highlight: Faster and Higher Response Rates at 30 mg Dose vs Rituximab Control



High-risk definition: baseline anti-PLA2R antibody >50 RU/mL or 24-hour urine protein >8 g/d.

Highlight: Faster and Higher Response Rates in High-Risk Patients

E-602 + Rituximab in pMN: Timing and Magnitude of Clinical Response

Baseline				Time (weeks) since first dose																		
Cohort	Patient	g/Day	anti-PLA2R (RU/mL)	4		5	8		12		16		20		24		28		32		36	
Rituximab Alone	9002	4.1	118.3																			x
	15001	8.0	10.6																			
	2003*	14.4	6.2			x																
	13001*	18.4	2112.0						x													
E-602 10 mg/kg + RTX	16001	8.5	43.1																			
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	14002	8.1	3.6																			
	4002	13.6	< 1.72																			
Dosing:				Δ	Δ	Δ	Δ										Δ	Δ	Δ	Δ		

***All subjects re-dosed at 6 months, except: 2003, 13001**

Week 24
Response
Rate

2/4
50%

1/5
20%

3/4
75%

2/3
67%

Week 36
Response
Rate

1/4
25%

3/5
60%

3/4
1 CR+2PR
75%

3/3
1CR+2PR
100%

Patient stratification

Mod risk
High risk

Response Category

↓Proteinuria >50%
Partial response (PR)

PR, <1g/day
Complete response (CR)

x	Withdrew
	non response

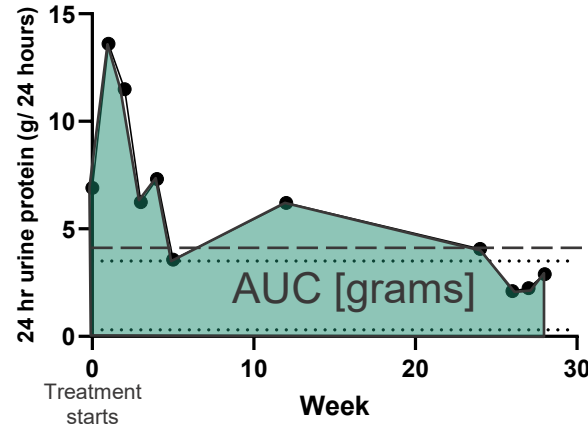
High-risk definition: baseline anti-PLA2R antibody >50 RU/mL or 24-hour urine protein >8 g/d.

Post Hoc Analysis: Proteinuria Burden Trends Lower with Increasing Dose

- **Proteinuria burden – Time-Weighted AUC (TWAUC)**

- Area under the proteinuria curve (AUC) ÷ days
- Represents average daily proteinuria (g/day)
- Baseline-adjusted for this cohort
- Uses every measurement collected, not a single timepoint
- Cumulative proteinuria predicts long-term loss of kidney function

Illustrative Patient Example

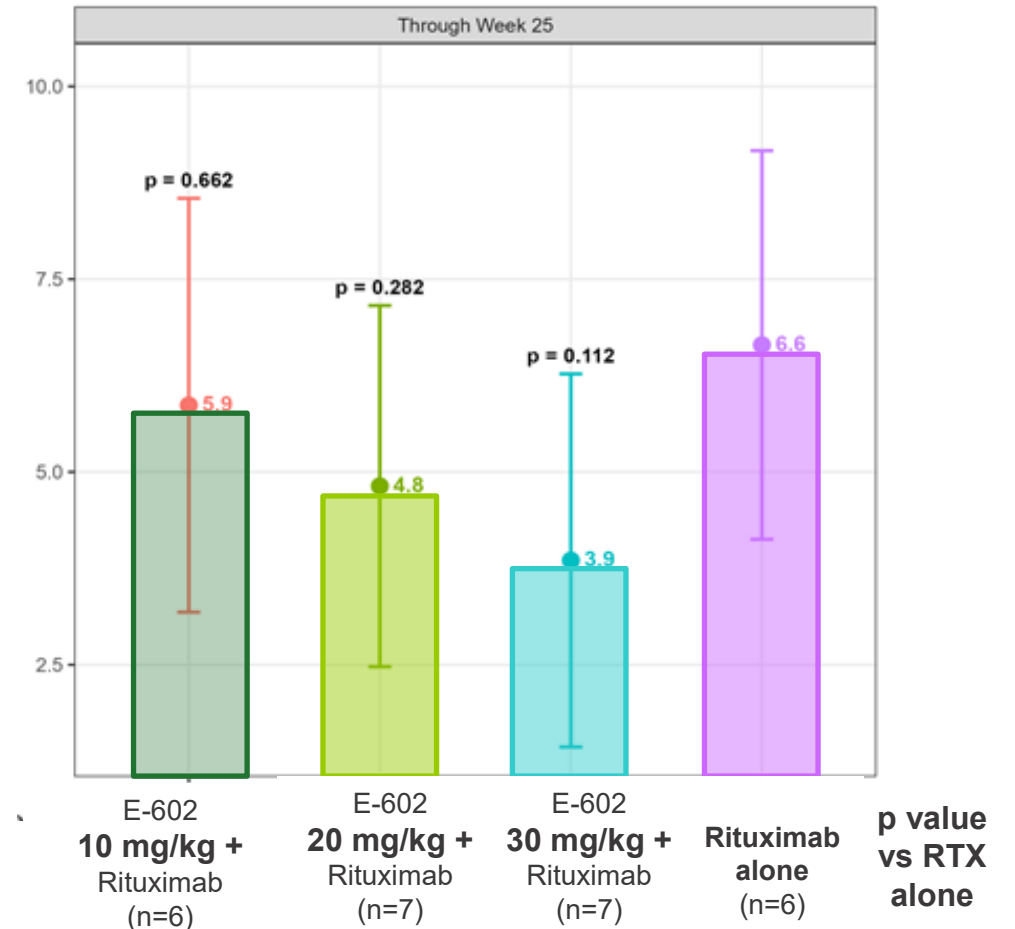


$$\text{TWAUC} = \text{AUC/Days} \text{ [g/day]}$$

Phase IIA Results: Baseline Adjusted TWAUC

Baseline-adjusted TWAUC by Treatment

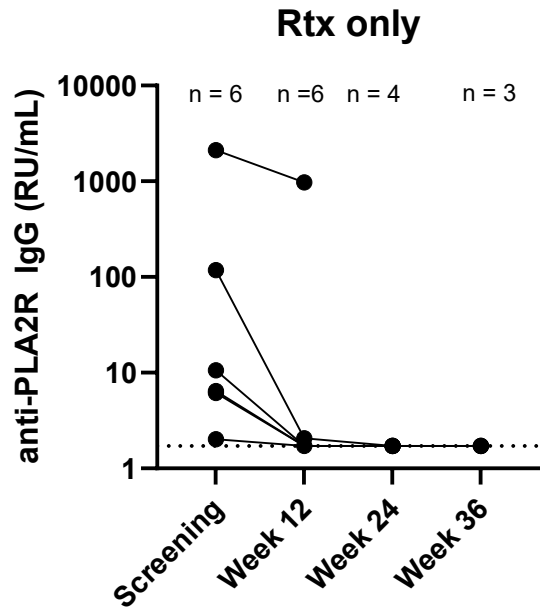
Adjusted least-squares means and two-sided 95% confidence intervals; values are LS means



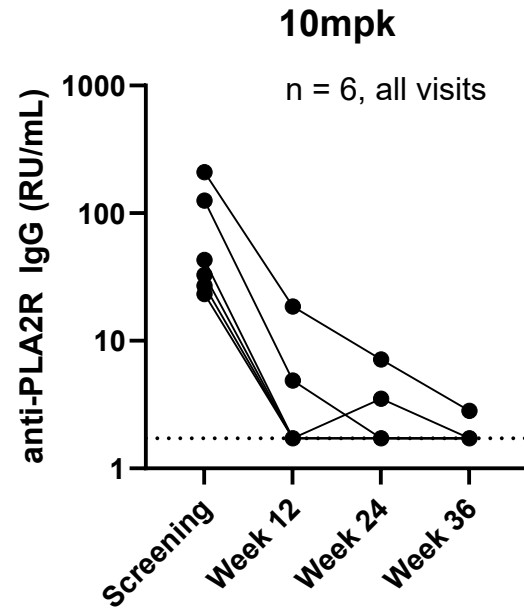
Directional trend, not statistically significant (unpowered exploratory analysis). Baseline adjusted across all 26 patients

Trend Towards Dose Dependent Anti-PLA2R Antibody Reduction

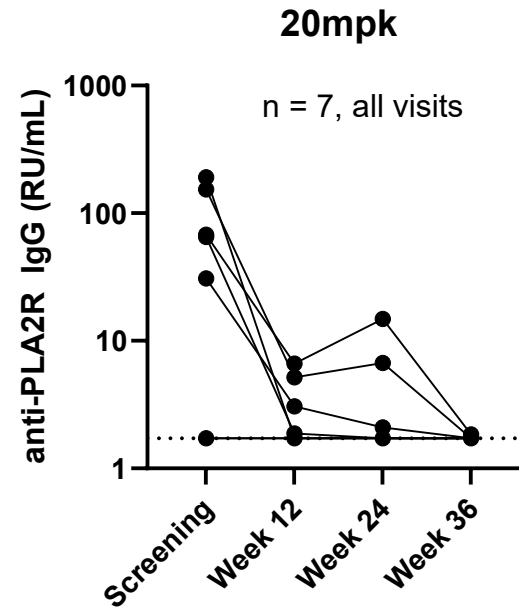
Rituximab Only



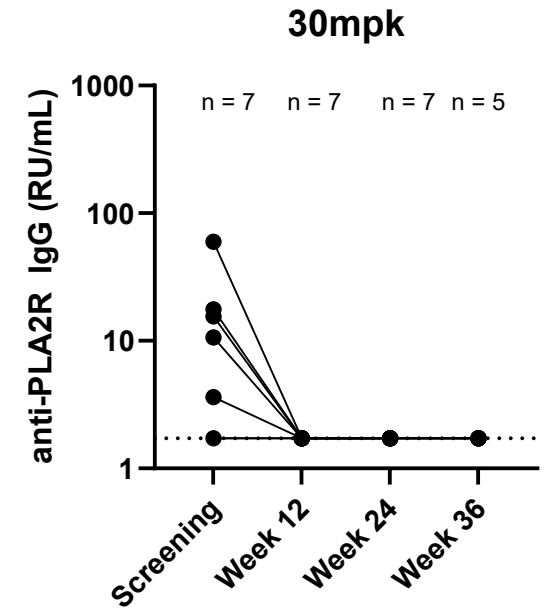
10 mg/kg



20 mg/kg



30 mg/kg



--- Limit of detection of assay = 1.72 RU/mL

Conclusions

- **HLX79/E-602: first-in-class glycan-editing therapy for autoimmune kidney disease**
- **Well-tolerated as an add-on to rituximab, with no additional safety signals**
- **Early efficacy signal vs an active comparator (rituximab)**
 - Faster response: median time to first response 3 vs 11 weeks
 - Higher response rate: 86% vs. 67% at week 24, 100% vs. 50% at week 36
 - Proteinuria burden trends lower as dose increases
- **Next steps: Randomized Phase 2b in pMN and expansion into other indications**

Study Sites, PI, and Industry Sponsors

Study Sites

Guangdong Provincial People's Hospital

Shanghai General Hospital

Xiangya Hospital Central South University

Peking University People's Hospital

The First Affiliated Hospital of Xiamen University

Sun Yat-sen Memorial Hospital, Sun Yat-sen University

Beijing Tsinghua Changgung Hospital

The First Affiliated Hospital of Nanchang University

The First Affiliated Hospital of Anhui Medical University

Northern Jiangsu People's Hospital

Zhongda Hospital Southeast University

Jiangsu Provincial People's Hospital

Jiangxi Provincial People's Hospital

Renmin Hospital of Wuhan University

The First Affiliated Hospital of Xi'an Jiaotong University

The First Affiliated Hospital, Zhejiang University School of Medicine

The First Affiliated Hospital of Henan University of Science and Technology



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GUANGDONG ACADEMY OF MEDICAL SCIENCES
广东省人民医院
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