

Belimumab Improves Renal Outcomes in Active Lupus Nephritis: a Phase 3 Randomized, Placebo-Controlled Trial

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**At the time of study*



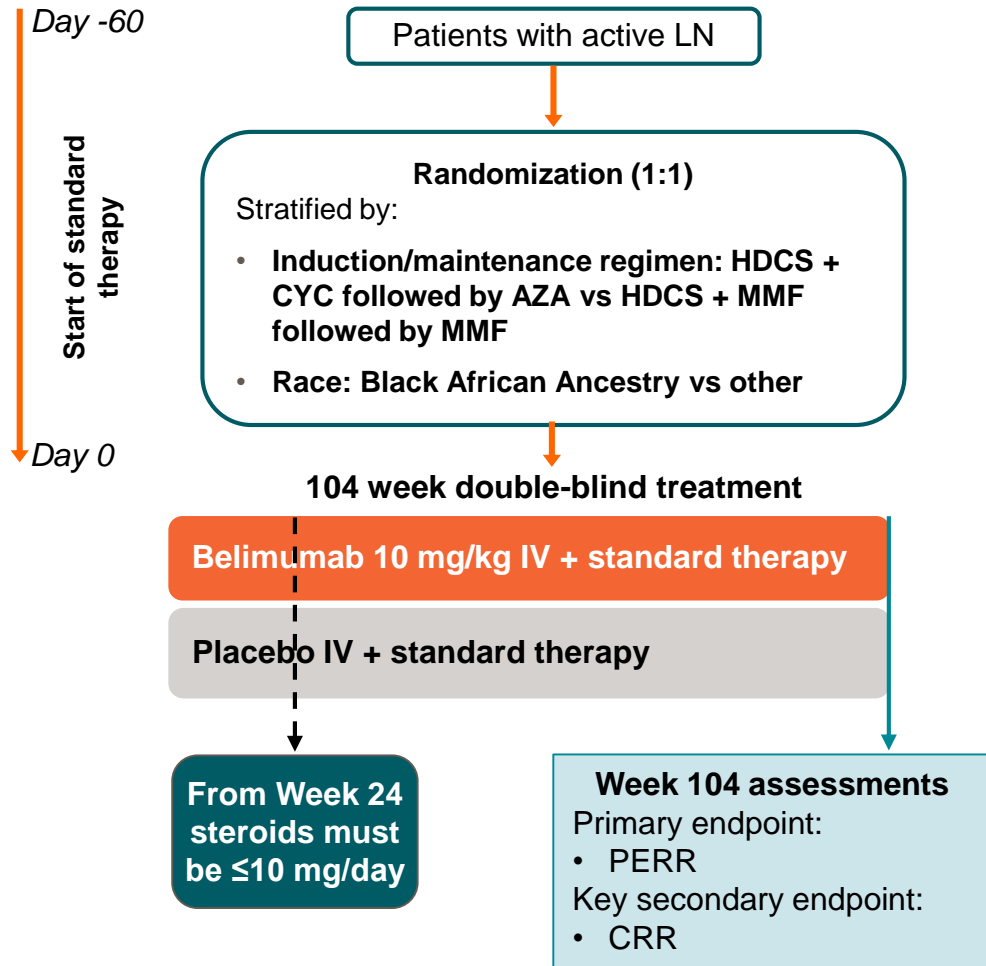
Disclosures

- **BHR** has received consultancy fees from AstraZeneca, Aurinia Pharmaceuticals, Bristol Myers Squibb, Calliditas Therapeutics, ChemoCentryx, EMD Serono, GSK, Janssen Pharmaceutica, MorphoSys, Novartis, Omeros and Retrophin
- **FH** has received consultancy fees from GSK, and research funding from UCB
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- **A Malvar** has received consultancy fees from GSK and Roche
- **YKOT** has received consultancy fees from GSK, Aurinia Pharmaceuticals and Novartis, and research funding from GSK
- **CCM** reports no conflicts of interest
- **GC** has received consultancy fees and research funding from Genentech and Merck
- **XY** has received consultancy fees from Baxter and AstraZeneca, and research funding from Baxter, Kyowa Kirin and Wanbang Biopharmaceuticals
- **SD** has received consultancy fees from Bristol Myers Squibb
- **BJ, SM, A Madan, JG, YG and DAR** are employees of GSK and hold stocks and shares in the company
- **CK** was an employee of GSK and held stocks and shares in the company at the time of study

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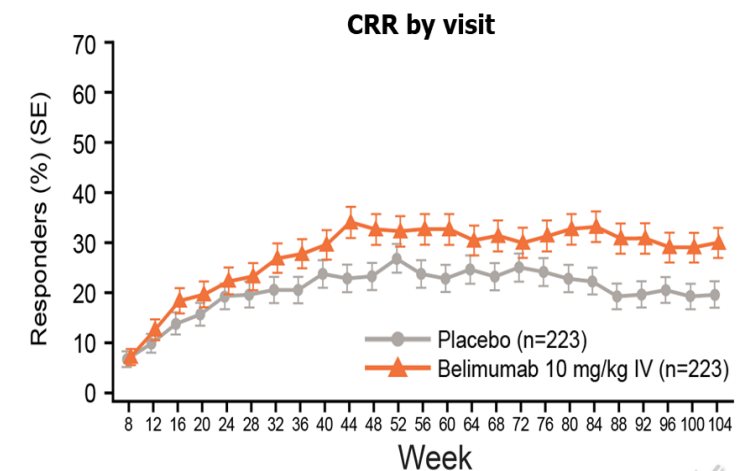
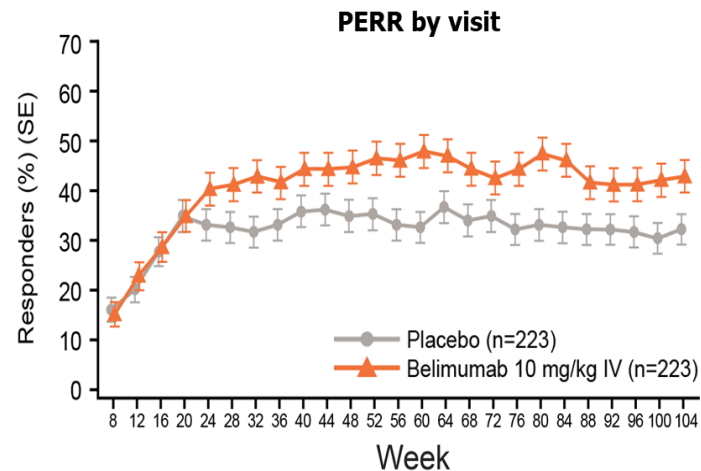


BLISS-LN study design



	Primary Efficacy Renal Response	Complete Renal Response
uPCR	≤0.7	<0.5
eGFR (ml/min/1.73m ²)	≥60	≥90
eGFR (% below pre-flare)	20	10
Rescue therapy	No	No

Top Line Results	Patients (%)		OR (95% CI)	p-value
	Placebo n=223	Belimumab 10 mg/kg IV n=223		
PERR at Week 104	72 (32.3)	96 (43.0)	1.55 (1.04, 2.32)	0.0311
CRR at Week 104	44 (19.7)	67 (30.0)	1.74 (1.11, 2.74)	0.0167



1. Furie R, et al, *New Eng J Med.* 2020;383:1117-28

AZA, azathioprine; CI, confidence interval; CRR, Complete Renal response; CYC, cyclophosphamide; eGFR, estimated glomerular filtration rate; HDCS, high-dose corticosteroids; IV, intravenous; LN, lupus nephritis; MMF, mycophenolate mofetil; OR, odds ratio; PERR, Primary Efficacy Renal Response; SE, standard error; uPCR, urinary protein:creatinine ratio



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ORIGINAL ARTICLE

Two-Year, Randomized, Controlled Trial of Belimumab in Lupus Nephritis

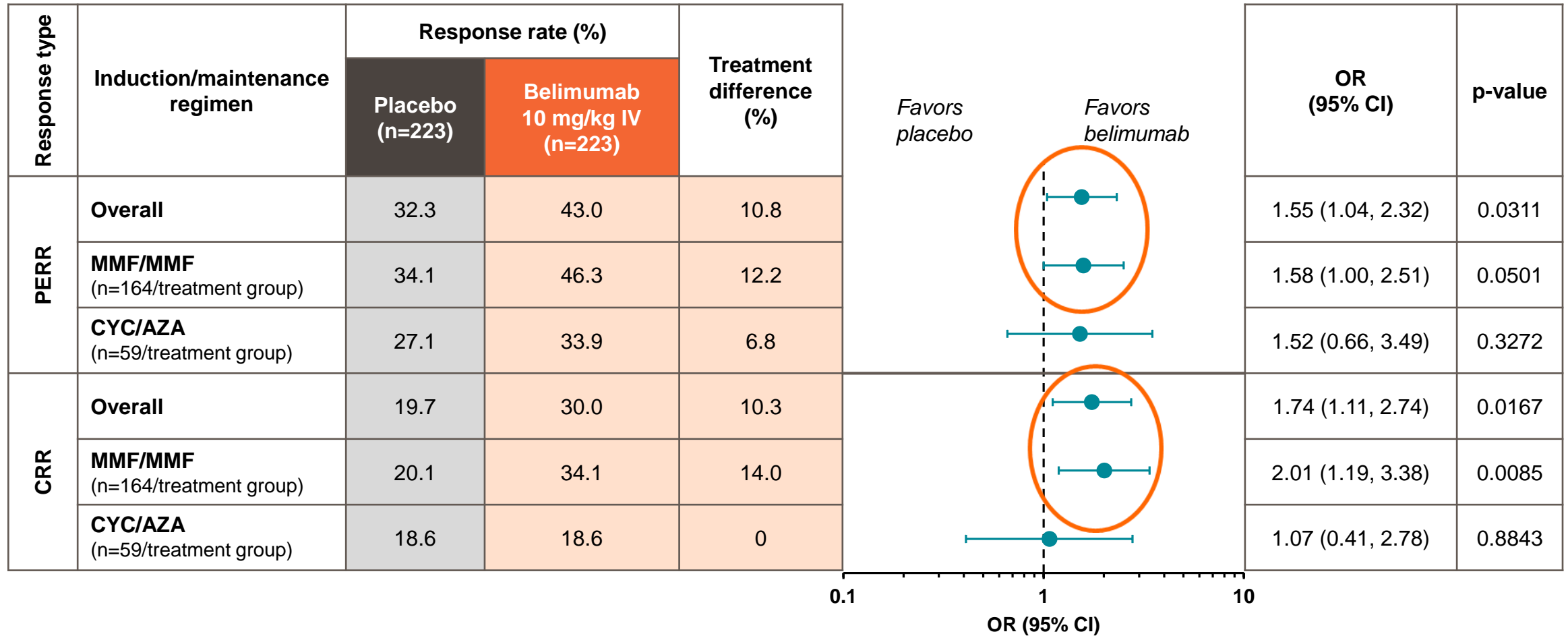
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PERR and CRR at Week 104 by induction/maintenance regimen

mITT population*

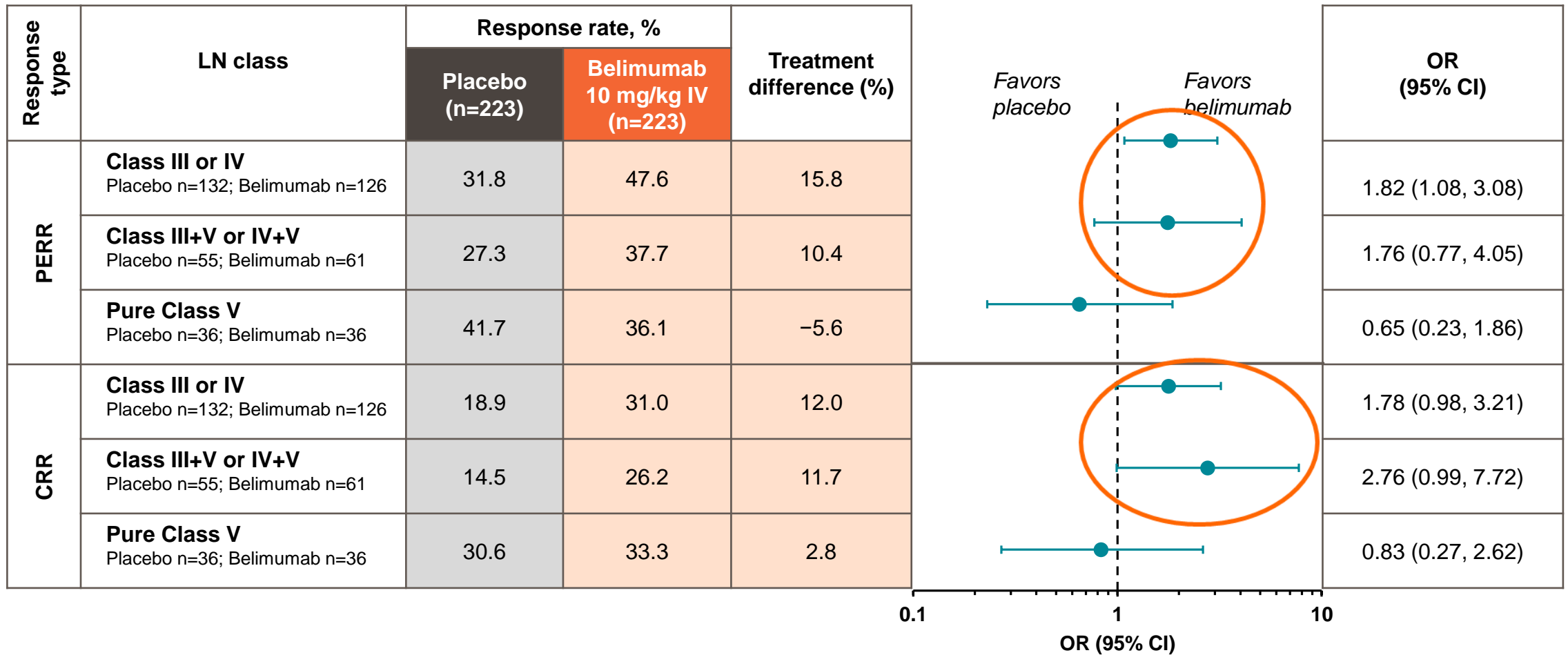


*Defined as all randomized patients who received ≥1 dose of investigational treatment, excluding 2 patients (N=446)



PERR and CRR at Week 104 by LN class

mITT population*



*Defined as all randomized patients who received ≥ 1 dose of investigational treatment, excluding 2 patients (N=446)



Change in kidney function between 24 and 104 weeks (*post hoc*)

mITT population*

	On-treatment		On-Study (some no longer on study treatment)	
	Placebo (n=223)	Belimumab 10 mg/kg IV (n=223)	Placebo (n=223)	Belimumab 10 mg/kg IV (n=223)
Patients at any visit, n	198	196	198	196
Patients at Week 104, n	128	140	163	173
Mean eGFR (SE) at Week 24 [†]	106.6 (2.49)	109.4 (2.36)	106.8 (2.55)	109.5 (2.39)
eGFR slope (ml/min/1.73m²/year) (SE)[†]	-3.18 (1.10)	-0.99 (0.77)	-5.72 (1.47)	-2.12 (0.97)
eGFR slope difference vs placebo (SE) [†]	-	2.19 (1.34)	-	3.61 (1.76)
95% CI	-	(-0.45, 4.84)	-	(0.15, 7.06)
p-value	-	0.1041	-	0.0407

*Defined as all randomized patients who received ≥1 dose of investigational treatment, excluding 2 patients (N=446); [†]statistics are from a linear mixed model consisting of treatment group (belimumab vs placebo), analysis visit (weeks), and their interaction, and random intercept and slope at the patient level. Covariance structure for random intercept and slope is unstructured and heterogeneous for treatment groups



Time to first decline in eGFR by 30% and 40% (*post hoc*)

	Censored at withdrawal or treatment discontinuation		Censored at withdrawal	
	Placebo (n=223)	Belimumab 10 mg/kg IV (n=223)	Placebo (n=223)	Belimumab 10 mg/kg IV (n=223)
Patients with 30% decrease in eGFR	12.6%	6.7%	17.0%	8.5%
30% decrease in eGFR, HR 95% CI p-value		0.52 (0.28, 0.98) 0.0429		0.47 (0.27, 0.83) 0.0084
Patients with 40% decrease in eGFR	6.7%	2.7%	11.7%	4.5%
40% decrease in eGFR, HR 95% CI p-value		0.38 (0.15, 0.98) 0.0457		0.35 (0.17, 0.74) 0.0056



Time to first renal flare after week 24 (*post hoc*)

Renal Flare Definitions

- **Week 24 uPCR and eGFR values were used as baseline:**
 - Reproducible increase in uPCR to >1 g if the baseline value (Week 24) was <0.2 g, to >2 g if the baseline value (Week 24) was between 0.2 g and 1 g, or more than twice the value at baseline if the baseline value (Week 24) was >1 g
- **AND/OR**
 - Reproducible decrease in GFR of >20%, accompanied by proteinuria (>1 g), and/or RBC and/or WBC cellular casts
- **AND/OR**
 - Renal-related treatment failure

	Placebo* (n=223)	Belimumab* 10 mg/kg IV (n=223)
Total patients (n)	196	194
Patients who flared, n (%)	51 (26.0)	28 (14.4)
HR		0.45
95% CI	-	(0.28, 0.72)
p-value		0.001

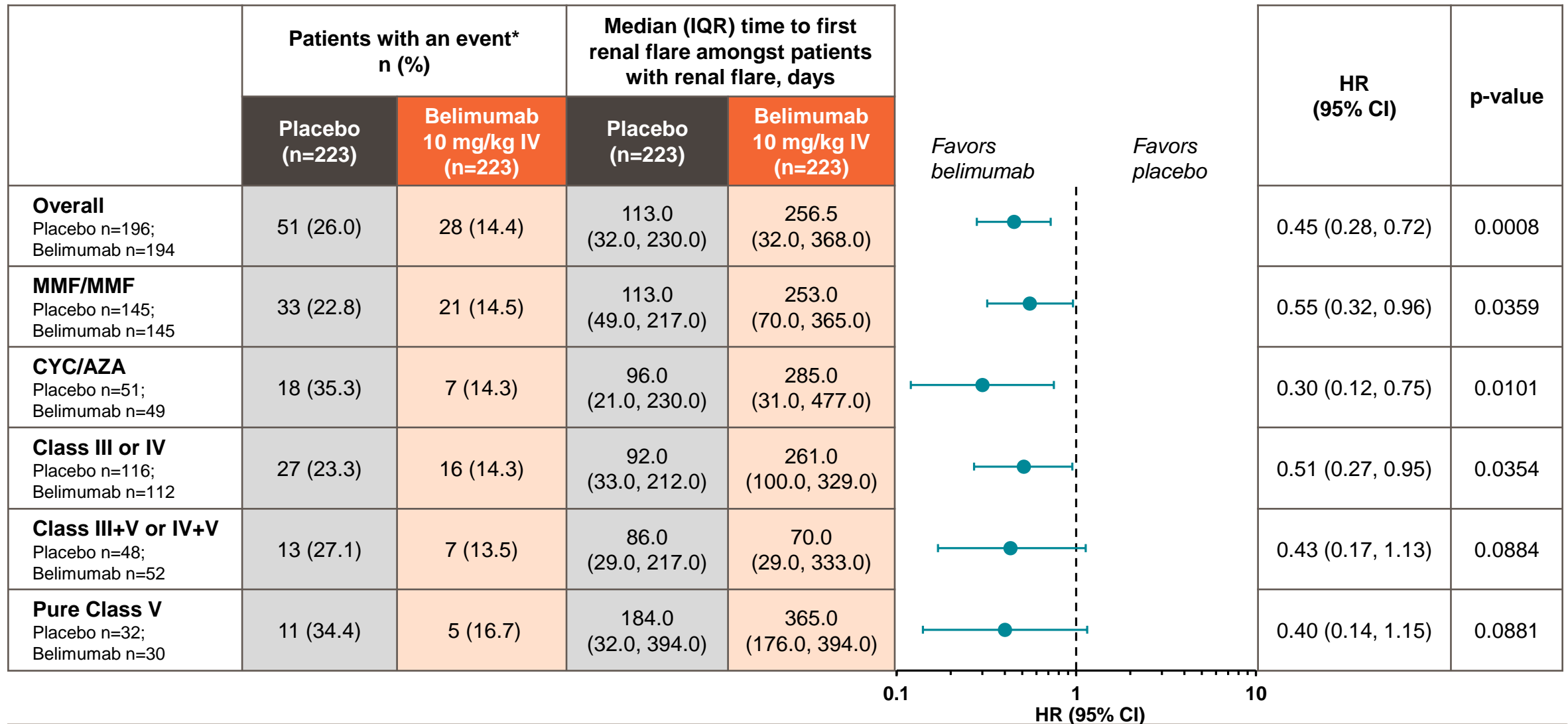
*Censored for treatment discontinuation or withdrawal or treatment failure not related to renal flare

RBC, red blood cell; WBC, white blood cell



Time to first renal flare from Week 24 (*post hoc*)

By induction/maintenance regimen and LN Class



*Censored for treatment discontinuation or withdrawal not related to renal flare
IQR, interquartile range



Conclusions

- In this largest LN study to date, a greater proportion of patients treated with belimumab plus standard therapy achieved PERR and CRR at Week 104 compared with standard therapy alone
 - This was observed overall and in groups stratified by induction/maintenance regimen (MMF/MMF and CYC/AZA)
- Compared with patients treated with standard therapy alone, when analyzed by LN class, more belimumab patients achieved PERR and CRR at Week 104 in all LN classes, except pure Class V
- The rate of eGFR decline from Week 24 was numerically higher in patients treated with standard therapy alone versus belimumab plus standard therapy
- Renal flares occurred less often in patients receiving belimumab plus standard therapy compared with standard therapy alone, across all LN classes and induction/maintenance therapies

Data from BLISS-LN demonstrate that belimumab plus standard therapy improves multiple renal responses in LN versus standard therapy alone



Thank you

Questions?

