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Association of baseline absolute lymphocyte count (ALC) with change in BK viral load (VL) in a randomized placebo-controlled study of MAU868 in kidney transplant recipients

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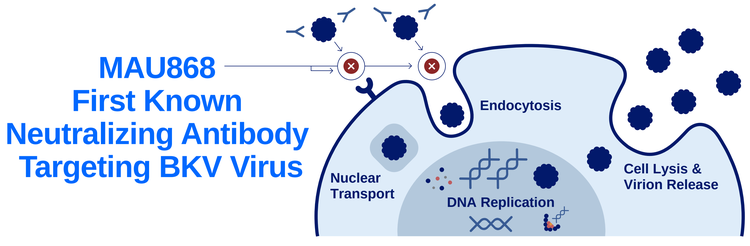
Introduction

- BK virus (BKV) is an important cause of renal allograft dysfunction and loss in kidney transplant recipients (KTR)
- Impaired cellular immunity, assessed as lymphopenia, is considered a risk factor for BKV replication and nephropathy



- MAU868 binds to a novel target that neutralizes viral infection by blocking BK virion binding to host cells
  - *In-vitro* activity demonstrated against all major genotypes at subnanomolar potency
  - ~10,000 fold more potent than IVIG *in vitro*
- A phase 2 randomized, placebo-controlled, double-blind study in adult KTRs with BK viremia demonstrated that MAU868 had a greater virologic response than placebo[1]
- The objective of this analysis was to assess the relationship of baseline ALC with change in BK VL

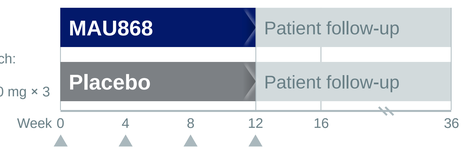
Methods

- The relationship of baseline ALC to the maximum BK VL reduction from baseline through week 36 was assessed with linear regression modeling among participants in a randomized study comparing efficacy and safety of MAU868 vs placebo in KTRs with BK viremia
- Bivariate analysis for each treatment arm was performed with the maximum reduction in BK VL as a dependent variable and the following baseline factors: log BK VL, estimated glomerular filtration rate, age, body mass index, race, ethnicity, and ALC
- A multivariable model was then constructed with the maximum reduction in BK VL as a dependent variable and baseline log BK VL and ALC as independent variables
- A human BKV, quantitative real-time PCR assay performed by Eurofins Viracor BioPharma Services was used
  - The lower limit of detection was recalculated as 26 DNA copies (c)/mL and lower limit of quantification was recalculated as 39 DNA c/mL

Study Schema

KTRs with BK Viremia
2:1 Randomization

Dose cohorts, n=12 each:
1) 1350 mg × 4
2) 6750 mg × 1 → 1350 mg × 3



Starting at baseline, all VL assays performed at a central laboratory by blinded personnel.
Clinicaltrials.gov NCT04294472.

Results

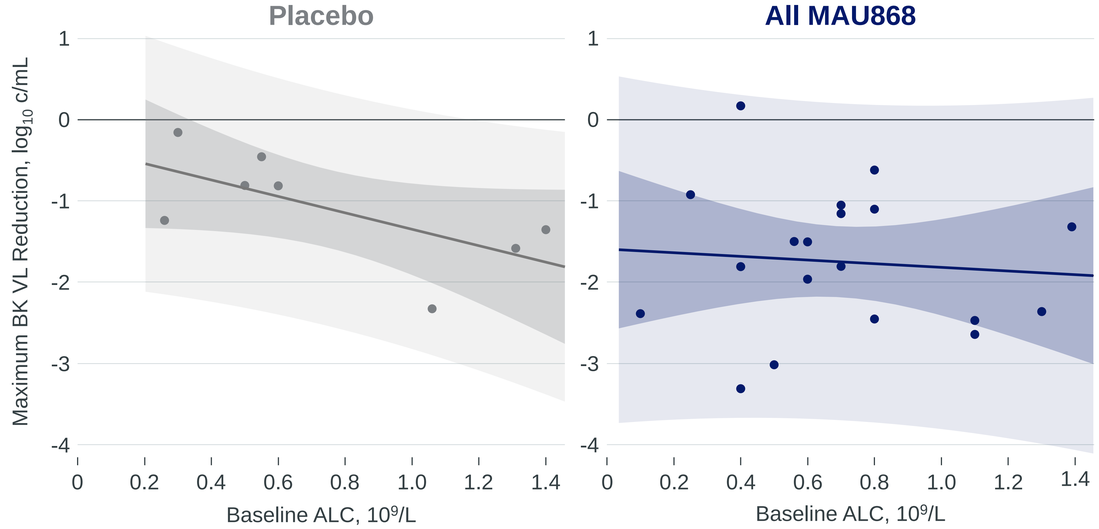
Baseline Characteristics

		ALL MAU868 n=20	Placebo n=8
Age, mean ± SD		58.2 ± 11.17	53.5 ± 16.85
Male, n (%)		18 (90)	5 (63)
Race, n (%)	African-American	5 (25)	4 (50)
	White	11 (55)	3 (38)
	Other	4 (20)	1 (13)
BK viremia, mean ± SD $\log_{10}$ c/mL		4.20 ± 0.69	4.52 ± 1.15
BKV genotype, n (%)	Ia	4 (20)	3 (38)
	Ib-1	3 (15)	2 (25)
	Ib-2	12 (60)	2 (25)
	III	0	1 (13)
	IVc-2	1 (5)	0
ALC, mean ± SD ×10^9/L		0.695 ± 0.341	0.748 ± 0.447
Prior immunosuppression decrease for BKV, n (%)		13 (65)	5 (63)

MAU868 Demonstrated Greater Virologic Response than Placebo

	Week 16		Week 36	
	MAU868 n=20	Placebo n=8	MAU868 n=20	Placebo n=8
BK VL reduction, median (min, max) $\log_{10}$ DNA c/mL	-0.97 (-2.6, 0.8)	-0.38 (-2.3, 0.5)	-1.31 (-3.3, 0.6)	-0.85 (-2.3, 1.3)
Patients, n (%)				
VL decreased ≥1 $\log_{10}$ DNA c/mL from baseline	8 (40)	1 (13)	15 (75)	4 (50)
VL <lower limit of detection	3 (15)	0	6 (3)	0
VL <10^3 DNA c/mL	10 (50)	0	11 (55)	3 (38)
VL <10^4 DNA c/mL	13 (65)	3 (38)	15 (75)	5 (63)

Baseline ALC vs Maximum Reduction in BK VL



- Baseline ALC was associated with the maximum reduction in BK VL in the placebo but not MAU868 group (R^2=0.435, p=0.08 vs R^2=0.008, p=0.72, respectively)
- In the multivariable model, there was a trend between baseline ALC and decrease in BK VL in placebo but not MAU868 group (p=0.13 vs p=0.73, respectively)

Conclusions

- MAU868 is a potential first-in-class human IgG1 monoclonal high-affinity neutralizing antibody against BK virus evaluated in a Phase 2 study of kidney transplant recipients with BK viremia; those who received MAU868 had a greater virologic response than those receiving placebo, including sustained viral load reduction through 36 weeks
- In this exploratory analysis, higher baseline ALC trended with greater reductions in BK viral load in placebo-treated patients; no similar trend was identified in MAU868-treated patients
- Further investigation of the relationship between ALC and BK viral load response is warranted

References: 1. Jordan SC, et al. ASN Kidney Week 2022, abstr SA-OR43. **Acknowledgments:** We thank all the patients who participated in this study and their families.

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