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A Randomized Phase 2 Study of MAU868 vs Placebo to Treat BK Viremia in Kidney Transplant Recipients

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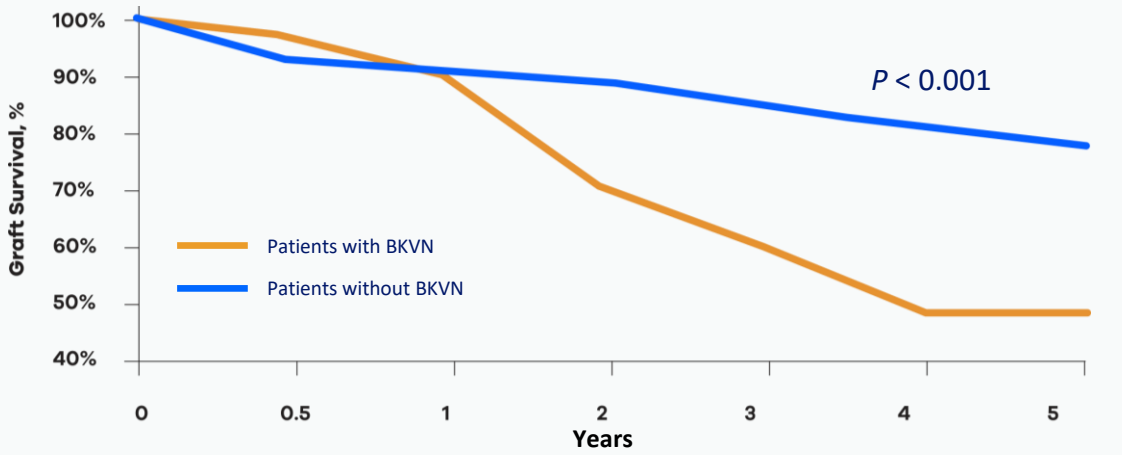
I have financial relationship(s) with:
Grant/ Research: Vera Therapeutics
Consultant: Vera Therapeutics
Advisory Board: Vera Therapeutics

AND

My presentation does include discussion of investigational use: use of MAU868 (IgG monoclonal antibody against BKV) for treatment of BK Viremia and Nephropathy

Kidney Transplants: BKV Nephropathy is a Leading Cause of Allograft Loss

Graft Survival in Kidney Transplant Patients is Worse with BKV Nephropathy



Vasudev, B et al. Kidney International 2005

- Poor Transplant Outcomes with BKV Reactivation
  - BKV viremia is associated with reduction in renal function and allograft survival
  - BKV nephropathy is associated with allograft loss
- Current Treatment for BKV in Renal Transplant: Reduce Immunosuppression, with risk of allograft rejection

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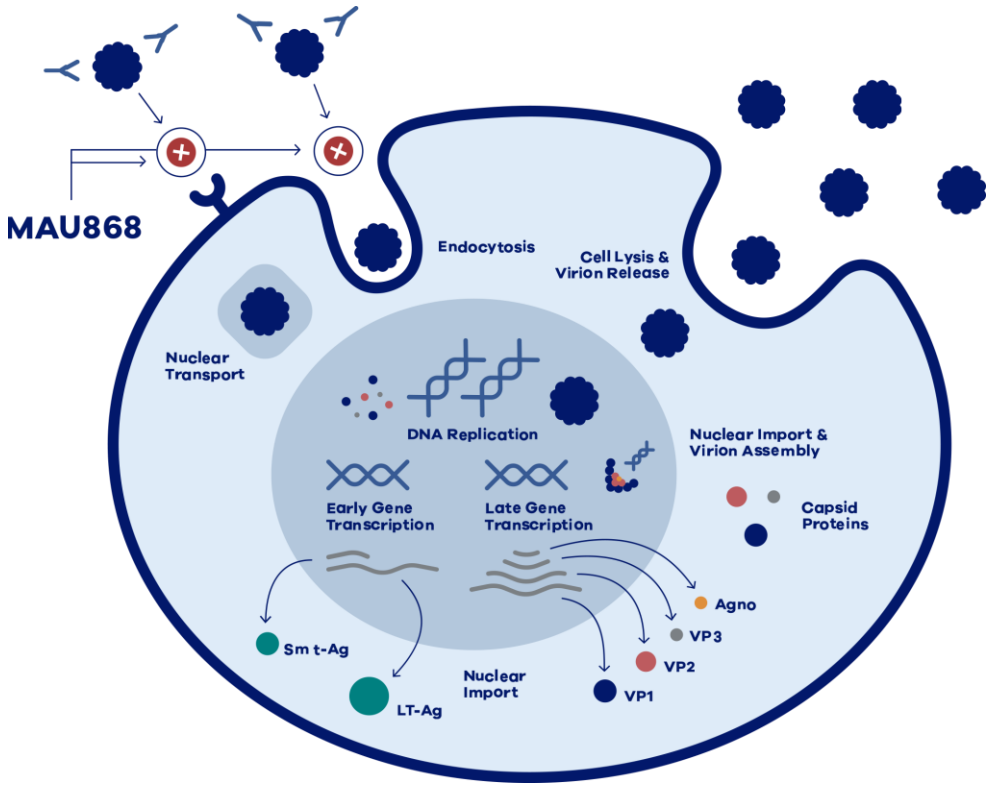
MAU868: First Known Neutralizing Antibody Targeting BK Virus

- **Novel Target:** mAb that neutralizes viral infection by blocking BKV virion binding to host cells
- **Active Against All Genotypes:** Sub-nanomolar potency against all major genotypes
- **Proven Mechanism:** Neutralization of virus infection effective in other approved mAb therapies
- **More Potent than IVIG:** ~10,000 fold more potent *in vitro*

Blocks BKV Virion Binding

Designed to disrupt cell surface binding and to prevent cell entry and spread of infection



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Phase 2 Trial of MAU868 in Kidney Transplant Patients with BK Viremia

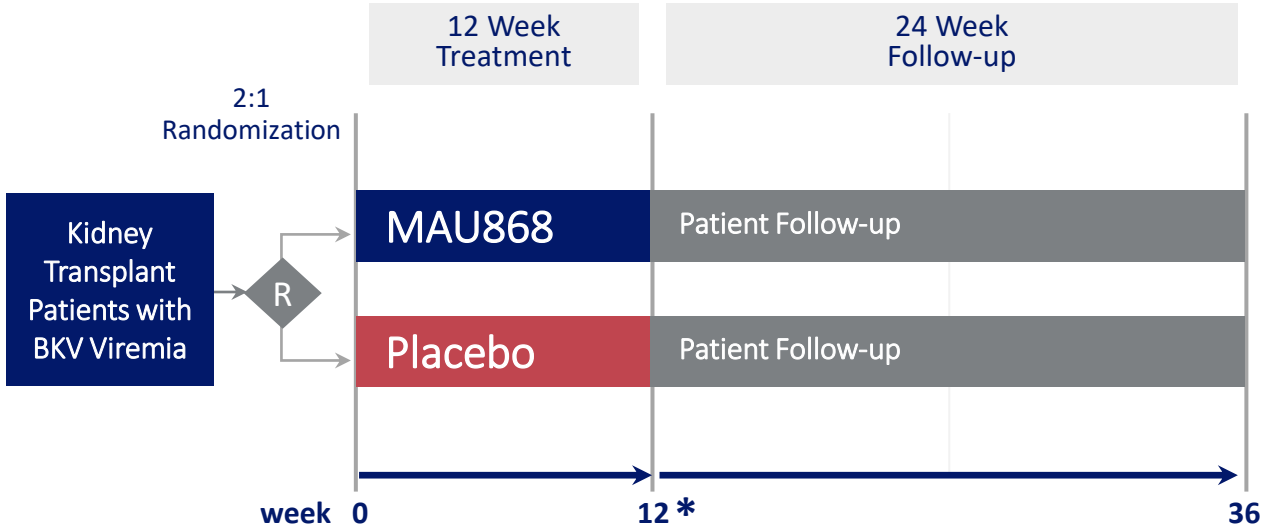
MAU868-201 Trial Design

Study Population

- Kidney transplant within one year of enrollment in the trial
- Documented BKV viremia within 10 days prior to enrollment in the trial
- Plasma BK viral load criteria:
  - VL between ≥ 10^4 DNA copies/ml and ≤ 10^7 DNA copies/ml

  OR
  - VL ≥ 10^3 DNA copies/ml in ≥ 1 of 2 samples 1 to 3 weeks apart

Randomized, Double-blind, Placebo-controlled Phase 2 Study



4 IV doses over 12-wks

Dose Cohorts

Cohort 1 1350 mg x 4
Cohort 2 6750 mg x 1 followed by 1350 mg x3

All viral load assays performed at a central laboratory by blinded personnel

Study Endpoints

Primary

- Safety, tolerability

Secondary

- BKV-related outcomes including:
  - Viremia
  - Renal Function
  - Nephropathy
  - Graft function
  - Allograft Rejection
  - PK

interim analysis at 12 wks

Clinicaltrials.gov Identifier: NCT04294472

Patient Demographics

Baseline characteristics and data were comparable between groups

	ALL MAU868 (n=20)	Placebo (n=8)
Age (mean)	58.2	52.5
Male	18 (90%)	5 (63%)
Race		
Asian	2 (10%)	0
African-American	5 (25%)	4 (50%)
White	11 (55%)	3 (38%)
Other	2 (10%)	1 (13%)
Ethnicity		
Hispanic	5 (25%)	0

Baseline Characteristics

	MAU868 (n=20)	Placebo (n=8)
eGFR (CK-EPI) (mL/min/1.73 m^2)		
Mean (SD)	53 ± 18	60 ± 21
Median (min, max)	51 (21, 85)	62 (23, 84)
15-<30	2 (20%)	1 (13%)
30-<60	11 (55%)	3 (38%)
60-<90	7 (35%)	4 (50%)
Living Donor – Yes	4 (20%)	1 (13%)
Pre-existing BKVAN* – Yes	5 (25%)	2 (25%)
Repeated Renal Transplants – Yes	2 (10%)	2 (25%)
Time from Kidney Transplant (days)		
Mean (SD)	160 ± 91	175 ± 83
Median (min, max)	132 (58, 365)	138 (86, 317)

*per medical history and biopsy

Baseline Characteristics

	MAU868 (n=20)	Placebo (n=8)
Baseline BK viremia		
Mean ± SD	54.9 K ± 112.0 K	315.1 K ± 620.6 K
Median (min, max)	16.6 K (1.6K, 491K)	41.8 K (1.2K, 1800K)
Duration of BK Viremia (days)		
Mean (SD)	49 ± 33	57 ± 26
Median (min, max)	43 (10, 126)	41 (30, 94)
Baseline BKV Genotype		
Ia	4 (20%)	3 (38%)
Ib-1	3 (15%)	2 (25%)
Ib-2	12 (60%)	2 (25%)
II	0	0
III	0	1 (13%)
IVc-2	1 (5%)	0

MAU868 was Well Tolerated

	MAU868 (n=20)	Placebo (n=8)
Patients with any AEs/TEAEs	19 (95%)	8 (100%)
Mild	4 (20%)	3 (38%)
Moderate	8 (40%)	2 (25%)
Severe	5 (25%)	3 (38%)
Life-Threatening	1 (5%)	0
Drug-Related TEAEs	1 (5%)	0
Patients with any SAEs	11 (55%)	2 (25%)
Mild	0	0
Moderate	4 (20%)	0
Severe	5 (25%)	2 (25%)
Life-Threatening	1* (5%)	0
Death	1** (5%)	0

- No adverse events (AE) or treatment emergent adverse events (TEAES) led to discontinuation of study drug
- No serious adverse events (SAEs) were deemed related to study drug
- There were no infusion reactions

*diabetic ketoacidosis
**acute hypoxic respiratory failure due to COVID-19 pneumonia

SAEs were Consistent with Renal Transplant Patients

	MAU868 (n=20)	PBO (n=8)
# (%) Pts with SAEs	11 (55%)	2 (25%)
	• Hernia • Right subcutaneous hematoma at incision site • Acute T cell-mediated rejection • Acute onset of fever, graft pyelonephritis • Urosepsis secondary to enterococcus faecalis • Hypotension, diarrhea, UTI • Sepsis from UTI x 2 • Diabetic ketoacidosis • *COVID-19 infection, acute hypoxemic resp failure, COVID-19 pneumonia, worsening of acute hypoxic resp failure • Multilineage bone marrow suppression x 3 • Acute diabetic ketoacidosis	• Severe transaminitis • Worsening hypercalcemia, esophageal candidiasis

No SAE led to discontinuation of study drug; no drug-related SAE

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Antiviral Effect and Renal Effect of MAU868 vs Placebo at Week 12

	MAU868 (n=20)	Placebo (N=8)	P-value
Log reduction in BK viremia- median (interquartile range [IQR]) DNA copies/ml	-1.14 (-1.88,-0.50)	0.37 (-0.72,0.04)	0.051
Proportion of patients with a reduction of BK plasma viral load- n (%)			
by ≥ 1 log	11 (55%)	1 (13%)	0.040
to < lower limit of quantification (LLOQ)	4 (20%)	0	0.172
to < 10^4 DNA copies/ml	15 (75%)	3 (38%)	0.061
Change in estimated glomerular filtration rate [eGFR (CK-EPI)]- median (IQR) mL/min/1.73m^2	2.0 (-5.0,4.0)	-6.0 (-8.5,-0.5)	0.217

Post Randomization Immunosuppression Changes were Uncommon

- Prior to randomization, immunosuppressive could be decreased or altered per the institution's standard of care
- In the first 4 weeks after randomization, investigators encouraged to refrain from additional changes and/or rescue medication (e.g. IVIG) unless specific criteria were met
- Within 4 weeks:
  - No patients had immunosuppression changes
  - No patients received rescue antiviral therapy
- Within 12 weeks:
  - 3 patients had immunosuppression decreased or discontinued
  - No patients received rescue therapy

3 patients had immunosuppression decreased or discontinued between baseline and week 12 (Day 84)				
Treatment	**Immuno-suppression (Study day)**	**Baseline VL (log)**	**VL at decrease (log)**	**VL at week 12 (log)**
MAU868	MMF stopped (day 29)	5.3	4.6	3.9
MAU868	MMF by 50% (day 48) MMF stopped (day 61)	3.4	3.3 3.1	2.8
PBO	MMF stopped (day 43)	5.7	6.2	4.2

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Conclusions

- MAU868 is a potential first-in-class human IgG1 monoclonal high affinity neutralizing antibody against BK virus
- MAU868 was well-tolerated and adverse events observed were generally consistent with the renal transplant setting
- Post-renal transplant patients with BK viremia who received MAU868 had greater virologic response than those receiving placebo at 12 weeks
  - Significantly more patients who received MAU868 had a viral load reduction by ≥1 log vs. placebo (55% vs. 13%)
  - Most patients (75%) who received MAU868 had antiviral suppression of $<10^4$ DNA copies/ml [compared to placebo (38%)]
- There were clinically meaningful changes to viremia that warrants further investigation of MAU868 for the treatment of BKV infection

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