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

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Disclosures

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Transplant Immunotherapy Program

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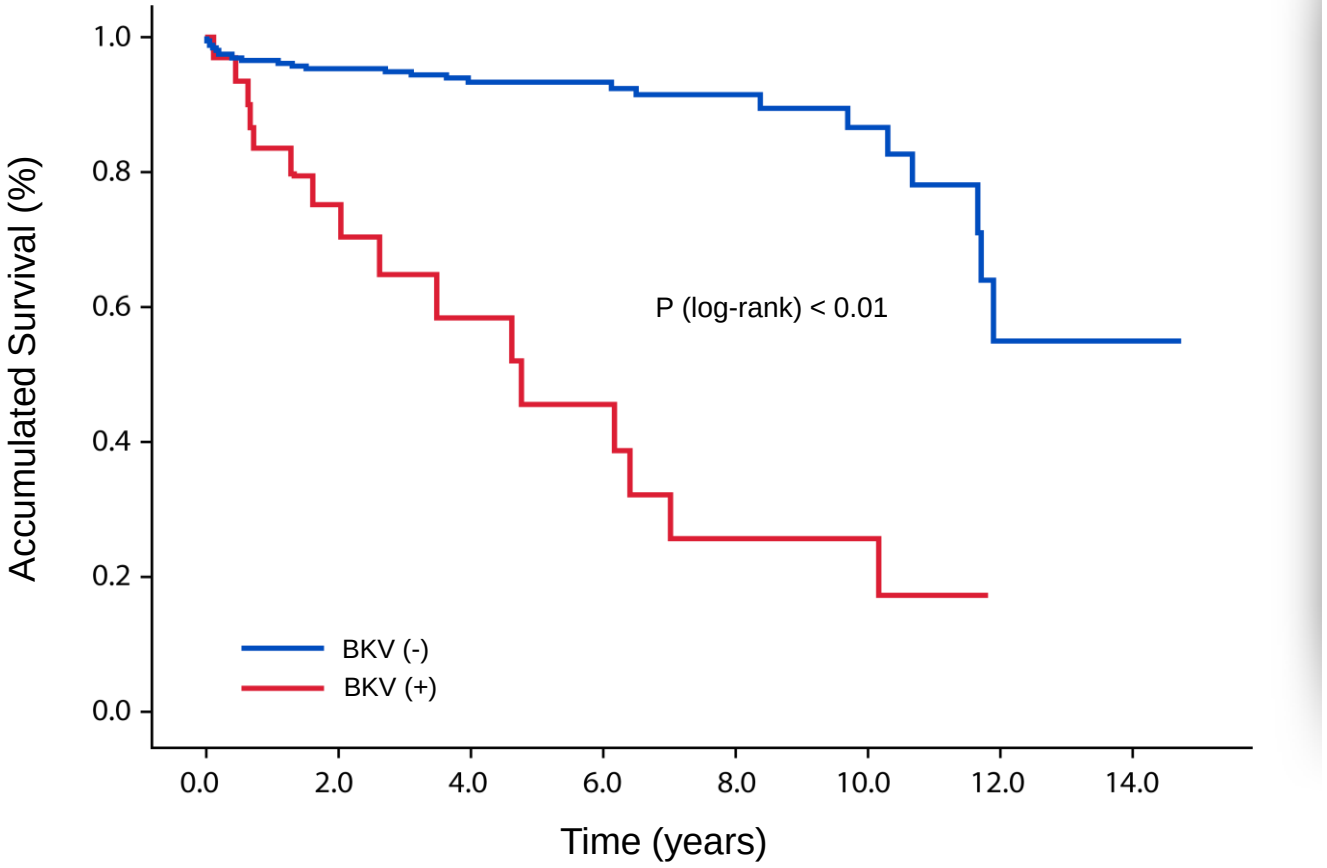
Kidney Transplants: BKV Nephropathy is a Leading Cause of Allograft Loss

The median allograft survival was ~6 years shorter in patients who developed BK viremia



- 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
- Mainstay of current management is the reduction of immunosuppression which increases the risk of allograft rejection
- No effective or specific therapies for BK Virus
- New therapeutic approaches in clinical development

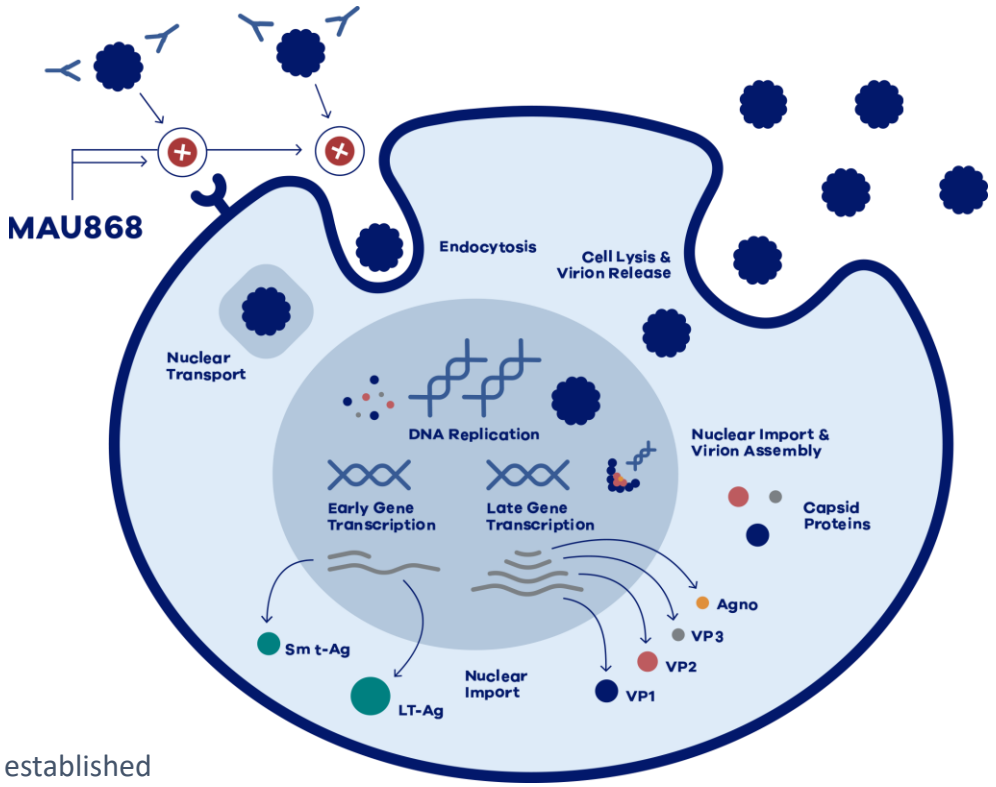
Moura et al. 2017

MAU868: First Known Neutralizing Antibody Targeting BK Virus

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

MOA: Blocks BK Virion Binding

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



MAU868 is an investigational compound, and the safety and efficacy of MAU868 have not been established

Sathe A. et al, Kidney Week 2020; Kovacs S. et al, Kidney Week 2020

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

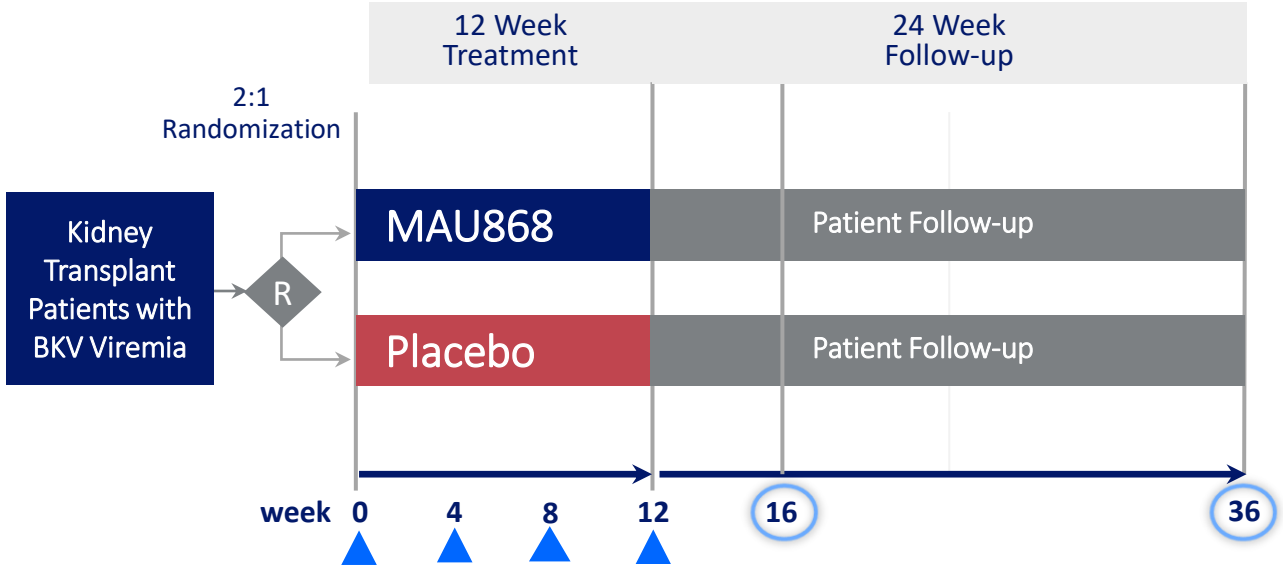
MAU868-201 Trial Design

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
  - consecutive positive VLs if most recent is ≥ 10^3 DNA copies/ml
- Excluded patients with BK viral load ≥ 10^7 DNA copies/ml and/or a viral load that exceeded 10^3 copies/mL for >4 months

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

Study Endpoints

Primary

- Safety, tolerability

Secondary

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

Starting at baseline, all viral load assays performed at a central laboratory by blinded personnel

Clinicaltrials.gov Identifier: NCT04294472

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Patient Demographics

Baseline characteristics and data were comparable between groups

	ALL MAU868 (n=20)	Placebo (n=8)
Age (mean)	58	53
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 Did Not Differ Between Groups

	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 (10%)	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)	151 (86, 317)

*per medical history and biopsy

Baseline Characteristics (Cont.) Did Not Differ Between Groups

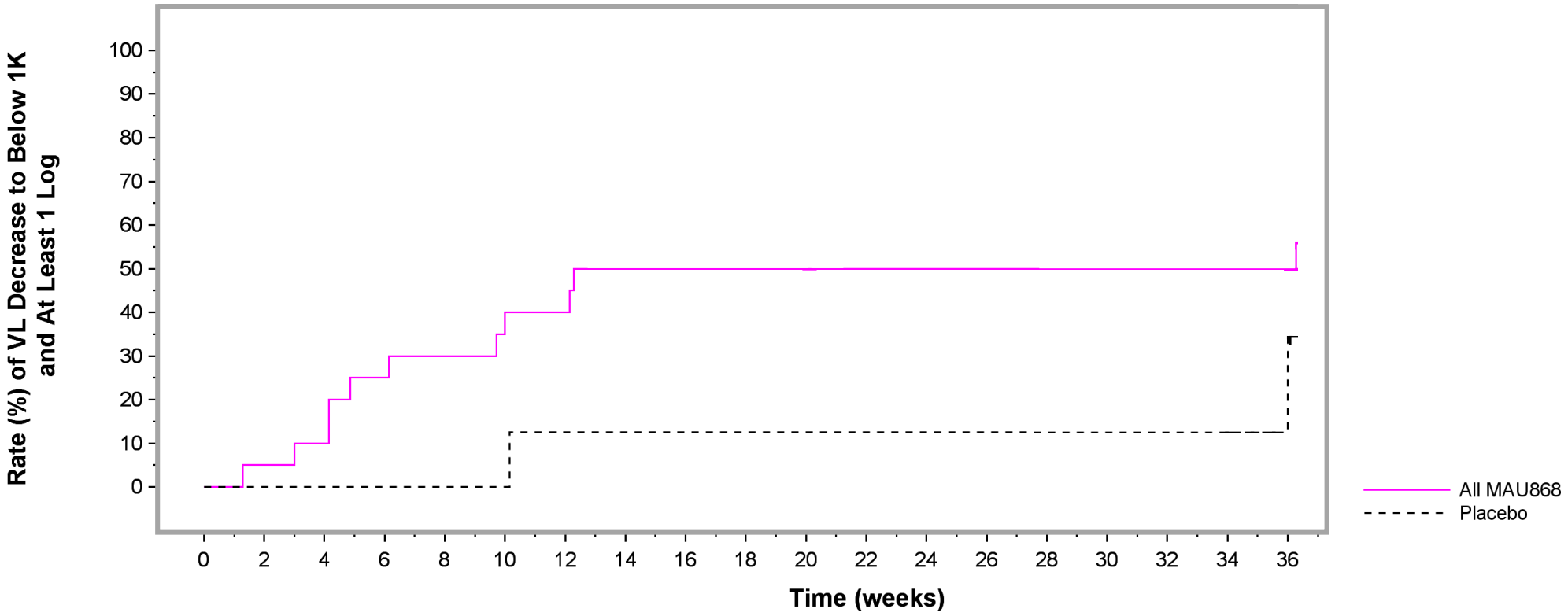
	MAU868 (n=20)	Placebo (n=8)
Baseline BK viremia		
Mean ± SD in DNA copies/ml	54.9 K ± 112.0 K	315.1 K ± 620.6 K
Median (min, max)	16.6 K (1.6K, 491K)	41.8 K (1.2K, 1800K)
Mean ± SD in Log	4.20 ± 0.69	4.52 ± 1.15
Median (min, max)	4.19 (3.2, 5.7)	4.46 (3.1, 6.3)
Duration of BK Viremia (days)		
Mean (SD)	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%)
III	0	1 (13%)
IVc-2	1 (5%)	0

MAU868 Demonstrated Greater Virologic Response than Placebo

	Week 16		Week 36	
	MAU868 (n=20)	Placebo (n=8)	MAU868 (n=20)	Placebo (n=8)
Patients (pts) VL decreased by ≥1 log_{10} BKV DNA copies/ml vs. baseline	8 (40%)	1 (13%)	15 (75%)	4 (50%)
Pts with VL < lower limit of detection (LOD)	3 (15%)	0	6 (30%)	0
Pts with VL <10^3 BKV DNA copies/ml	10 (50%)	0	11 (55%)	3 (38%)
Pts with VL <10^4 BKV DNA copies/ml	13 (65%)	3 (38%)	15 (75%)	5 (63%)
BKV VL reduction - median log_{10} BKV DNA copies/ml (Min, Max)	-0.97(-2.6, 0.8)	-0.38 (-2.3,0.5)	-1.31 (-3.3,0.6)	-0.85 (-2.3,1.3)
Change in estimated glomerular filtration rate (eGFR)- median ml/min/1.73m^2 (Min,Max)	-2.0 (-28.0,13.0)	-6.0 (-11,2.0)	-2.5 (-51.0,25.0)	-5.5 (-27,12)

MAU868 Demonstrated Faster Time to Viral Response than Placebo

Decrease of BK Plasma Viral Load to < 1K DNA copies/ml and by at least 1 Log Reduction from Baseline



Number at Risk:																			
All MAU868:	20	19	18	15	14	13	12	10	10	10	10	9	9	9	9	9	9	9	9
Placebo:	8	8	8	8	8	8	7	7	7	7	7	7	7	7	7	7	7	7	4

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

Patients with immunosuppression changes	Within 4 weeks	Within 16 weeks	Within 36 weeks*
MAU868 (N=20)	0	5 (25%)	6 (30%)
PBO (N=8)	0	1 (13%)	2 (25%)

*all but 1 patient had VL >10^4 at time of change

MAU868 was Well Tolerated

	MAU868 (n=20)	Placebo (n=8)
Subjects with any AEs/TEAEs	19 (95%)	8 (100%)
Mild	2 (10%)	2 (25%)
Moderate	8 (40%)	3 (38%)
Severe	6 (30%)	3 (38%)
Life-Threatening	1 (5%)	0
Drug-Related TEAEs	2 (10%)*^	0
Subjects with any SAEs	12 (60%)	2 (25%)
Mild	0	0
Moderate	3 (15%)	0
Severe	6 (30%)	2 (25%)
Life-Threatening	1 (5%)¥	0
Death	2 (10%)**	0

drug related TEAEs deemed mild or moderate: *nausea, GGT increase, headache; ^injection site swelling

¥ diabetic ketoacidosis

**acute respiratory failure, pneumonia viral acute hypoxic respiratory failure due to COVID-19 pneumonia

- 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

SAEs were Consistent with Renal Transplant Patients

	MAU868 (n=20)	PBO (n=8)
# (%) Pts with SAEs	12 (60%)	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

Conclusions

- MAU868 is a potential first-in-class human IgG1 monoclonal high-affinity neutralizing antibody against BK virus
- Post-renal transplant patients with BK viremia who received MAU868 had a greater virologic response than those receiving placebo
  - A greater percentage of patients who received MAU868 had sustained viral load reduction vs. placebo through 36 weeks
  - Patients who received MAU868 exhibited a faster time to viral reduction
- MAU868 was well-tolerated and adverse events observed were generally consistent with the renal transplant setting
- The demonstrated safety and clinically meaningful changes to viremia warrant further investigation of MAU868 for the treatment of BKV infection

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