A Randomized Phase 2 Study of MAU868 vs Placebo for BK Viremia in Kidney Transplant Recipients: BK Viral Kinetics and Outcomes in Two Dosing Cohorts

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I have financial relationship(s) with:
Consultation fees & grants, Vera Therapeutics
Consultation fees & grants, CareDx
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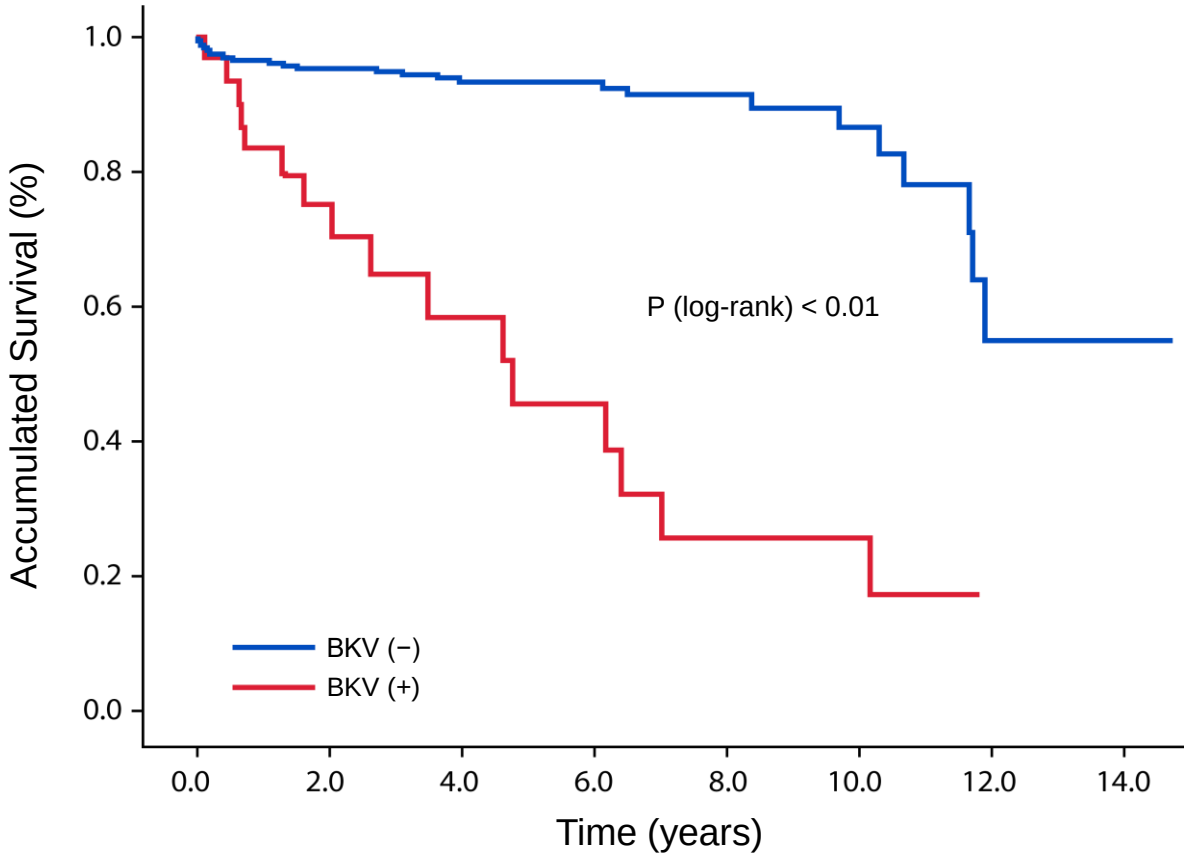
Consultation fees, Argnex
Consultation fees & grants, Hansa Biopharma
Consultation fees & grants, CSL Behring
IP and stock options, CSL Behring
Consultation fees, Genentech

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

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

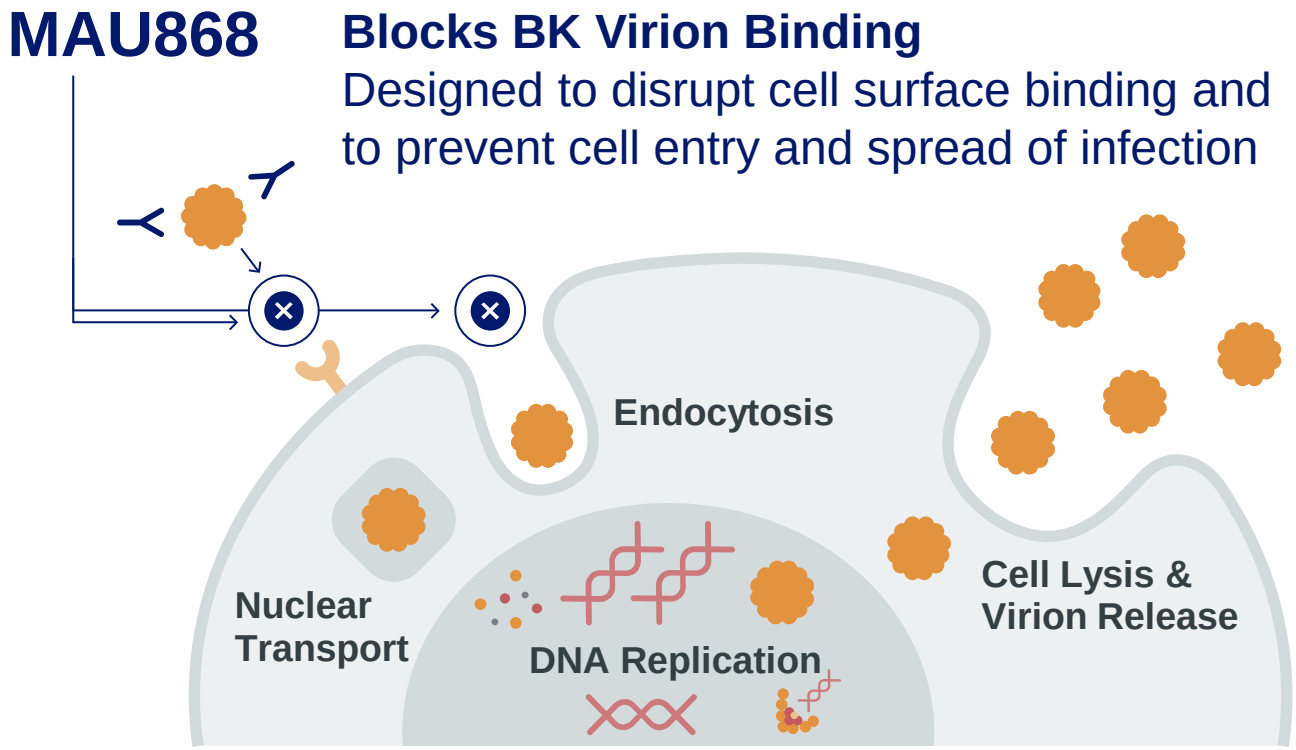


- Poor transplant outcomes with BKV reactivation
  - BK viremia is associated with reduction in renal function and allograft survival
  - BKV nephropathy is associated with allograft loss
- Mainstay of current management is the reduction of immunosuppression which increases the risk of allograft rejection
- No effective or specific therapies for BKV
- New therapeutic approaches in clinical development

Moura EB, et al. An Acad Bras Cienc 2017 May;89(1 Suppl 0):675-684.

MAU868: First Known Neutralizing Antibody Targeting BK Virus

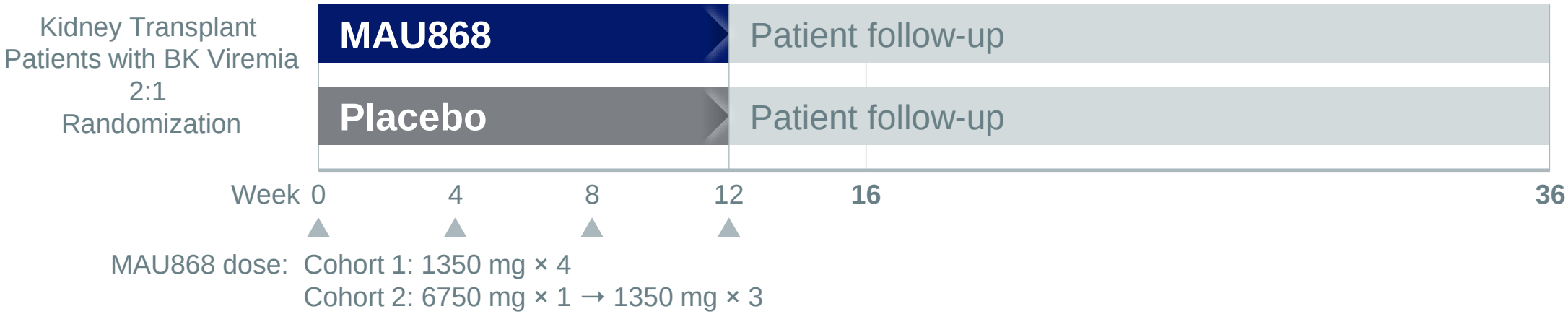
- Novel target: mAb that neutralizes viral infection by blocking BK virion binding to host cells
- Activity shown against all genotypes: sub-nanomolar potency against all major genotypes
- Proven mechanism: neutralization of virus infection effective in other approved mAb therapies
- ~10,000 fold more potent than IVIG *in vitro*



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

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

MAU868-201: Randomized, Double-blind, Placebo-controlled Phase 2 Study



Study Population

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

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

Study Endpoints

- **Primary:** safety, tolerability
- **Secondary:** BKV-related outcomes including:
  - Viremia
  - Nephropathy
  - Graft function
  - Allograft rejection

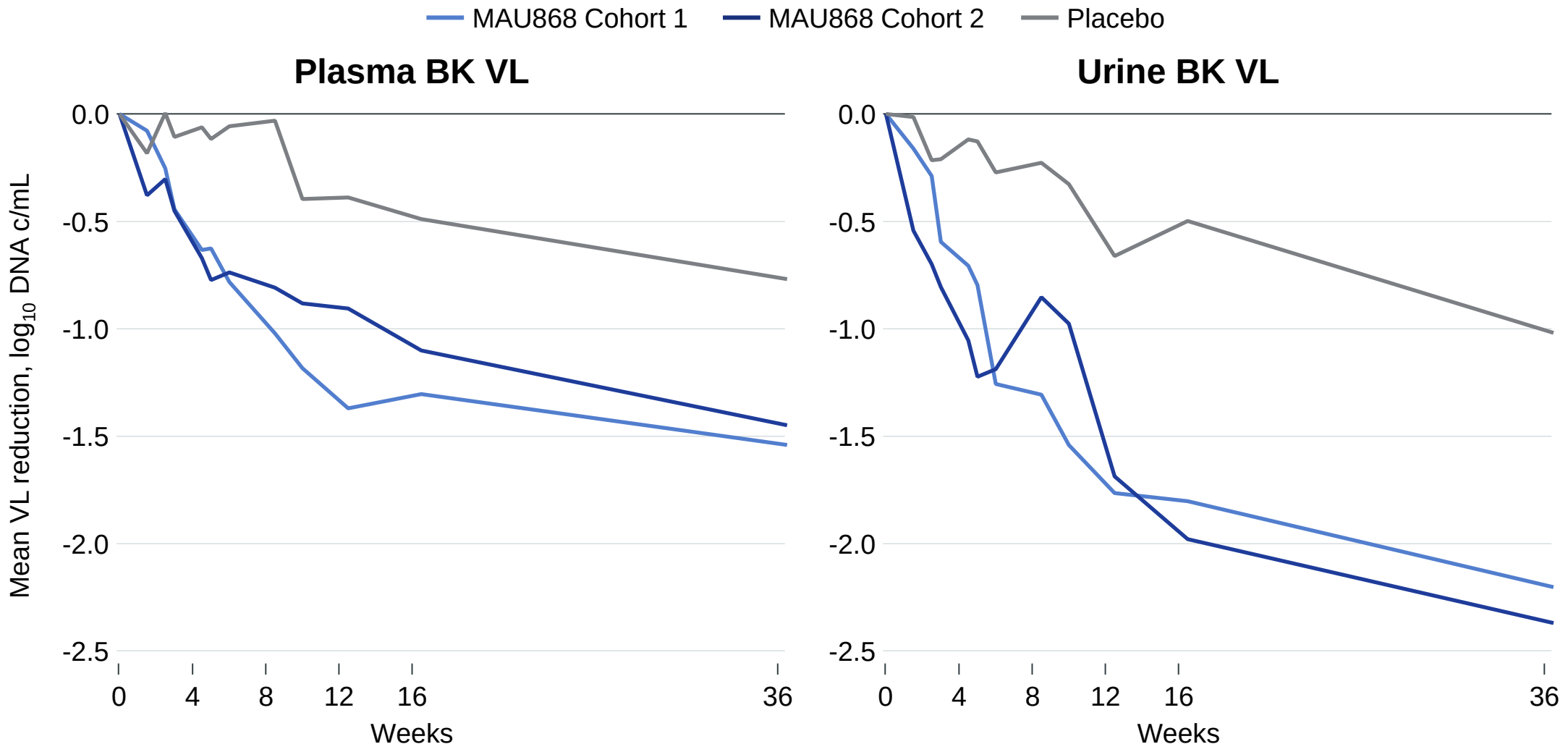
Starting at baseline, all viral load assays performed at a central laboratory by blinded personnel. Clinicaltrials.gov NCT04294472

Baseline Characteristics

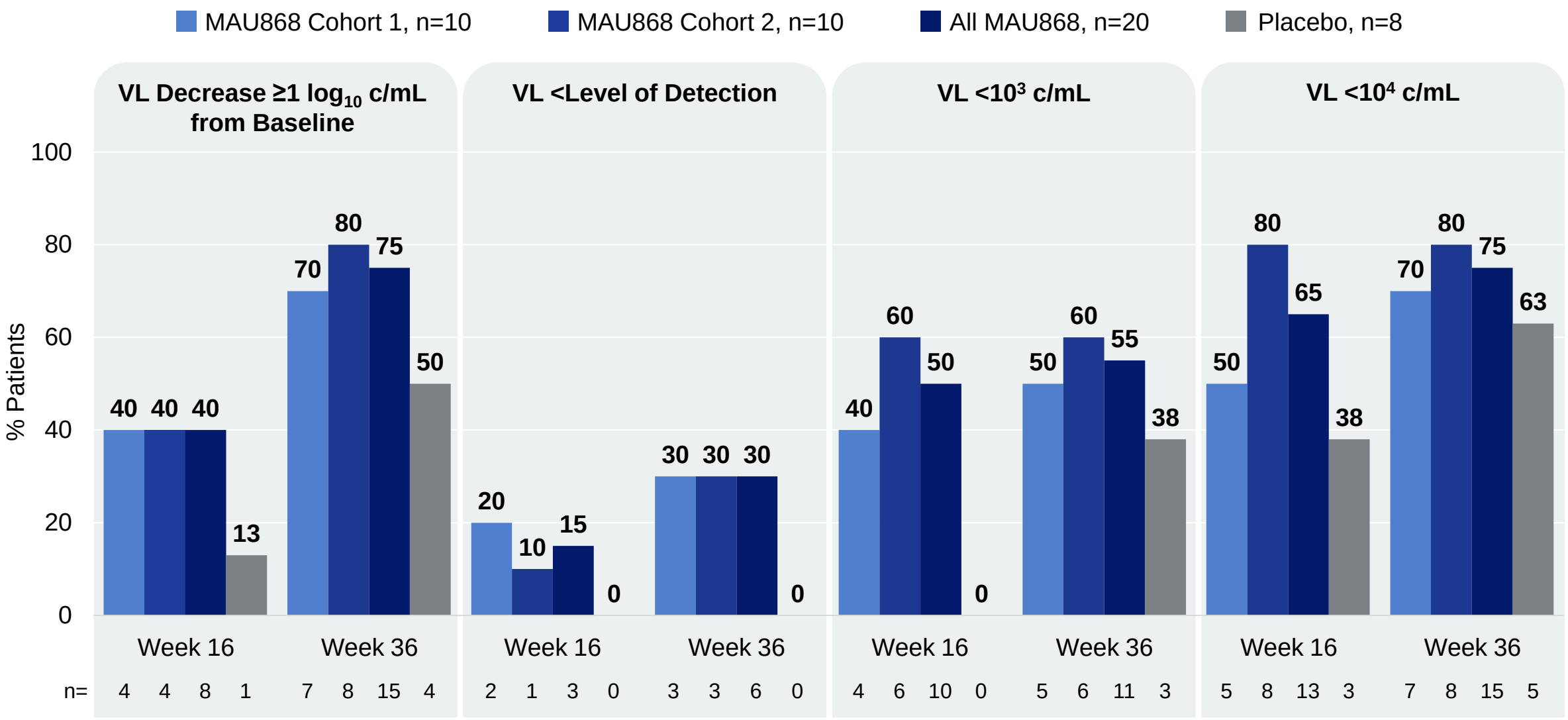
		MAU868			
		Cohort 1, n=10	**Cohort 2**, n=10	**All**, n=20	**Placebo**, n=8
Age, mean		61	56	58	53
Male, n (%)		9 (90)	9 (90)	18 (90)	5 (63)
Race/ethnicity, n (%)	Asian	2 (20)	0	2 (10)	0
	African-American	4 (40)	1 (10)	5 (25)	4 (50)
	White	4 (40)	7 (70)	11 (55)	3 (38)
	Other	0	2 (20)	2 (10)	1 (13)
	Hispanic	3 (30)	2 (20)	5 (25)	0
$eGFR_{CK-EPI}$, mL/min/1.73 m^2	Mean ± SD	54 ± 23	51 ± 12	53 ± 18	60 ± 21
	Median (min, max)	55 (21, 85)	49 (30, 69)	51 (21, 85)	62 (23, 84)
BKVAN prior to baseline, n (%)		3 (30)	1 (10)	4 (20)	2 (25)
Time from kidney transplant, days	Mean ± SD	176 ± 94	144 ± 90	160 ± 91	175 ± 83
	Median (min, max)	139 (82,343)	123 (58, 365)	132 (58, 365)	151 (86, 317)
Baseline BK viremia, log_{10} DNA c/mL	Mean ± SD	4.44 ± 0.69	3.97 ± 0.63	4.20 ± 0.69	4.52 ± 1.15
	Median (min, max)	4.40 (3.4, 5.7)	3.86 (3.2, 5.0)	4.19 (3.2, 5.7)	4.46 (3.1, 6.3)
Duration of BK viremia, days	Mean (SD)	57 ± 40	42 ± 24	49 ± 33	58 ± 23
	Median (min, max)	53 (10, 126)	41 (17, 91)	44 (10, 126)	53 (30, 94)
Baseline BKV genotype, n (%)	I	9 (90)	10 (100)	19 (95)	7 (87)
	III	0	0	0	1 (13)
	IVc-2	1 (10)	0	1 (5)	0

Rapid and Sustained Decrease in Viral Load with MAU868

Loading Dose Did Not Appear to Increase Response to Therapy as Measured by Viral Load in Plasma and Urine



Both MAU868 Dosing Cohorts Demonstrated a Similar Plasma Virologic Response Greater than Placebo



Both MAU868 Dosing Cohorts Were Well Tolerated

Patients, n (%)	MAU868			Placebo, n=8
	Cohort 1, n=10	**Cohort 2**, n=10	**All**, n=20	
Any AEs/TEAEs	10 (100)	9 (90)	19 (95)	8 (100)
Mild	1 (10)	1 (10)	2 (10)	2 (25)
Moderate	4 (40)	4 (40)	8 (40)	3 (38)
Severe	3 (30)	3 (30)	6 (30)	3 (38)
Life-threatening	1 (10)	0	1 (5)	0
Drug-related TEAEs	1 (10)	1 (10)	2 (10)[a]	0
Any SAEs	6 (60)	6 (60)	12 (60)	2 (25)
Mild	0	0	0	0
Moderate	1 (10)	2 (20)	3 (15)	0
Severe	3 (30)	3 (30)	6 (30)	2 (25)
Life-threatening	1 (10)	0	1 (5)[b]	0
Death	1 (10)	1 (10)	2 (10)[c]	0

- No AEs or TEAES led to discontinuation of study drug
- No SAEs were deemed related to study drug

AE = adverse event; SAE = serious adverse event; TEAE = treatment-emergent adverse event.
[a]All deemed mild or moderate: nausea, GGT increase, headache (n=1) and injection site swelling (n=1)
[b]Diabetic ketoacidosis
[c]Acute respiratory failure, pneumonia viral acute hypoxic respiratory failure due to COVID-19 pneumonia

SAEs were Consistent with Renal Transplant Patients

	MAU868 Cohort 1 n=10	MAU868 Cohort 2 n=10	Placebo n=8
Patients with SAEs, n (%)	6 (60)	6 (60)	2 (25)
	• Diarrhea, hypotension, urinary tract infection • Sepsis from UTI • Acute myocardial infarction, diabetic ketoacidosis • COVID-19 infection/pneumonia, hypoxic respiratory failure • Bone marrow failure • Diabetic ketoacidosis	• Hernia, COVID-19 pneumonia, acute respiratory syndrome • Post-operative wound infection, incision site hematoma • Acute T cell rejection • COVID-19 infection, diabetic ketoacidosis • Graft pyelonephritis • E. faecalis urosepsis	• Severe transaminitis • Worsening hypercalcemia, esophageal candidiasis

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

UTI = urinary tract infection.

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 loading dose did not appear to increase response to therapy as measured by viral load in plasma and urine
- In both dosing cohorts, 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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