

# Phase I Placebo-Controlled Safety, PK, and PD Study of MB66 Anti-HIV and Anti-HSV Film

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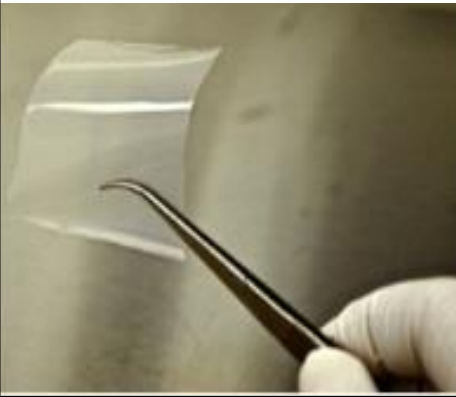
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# Background and Objectives:

- HIV-1 and HSV-2 are associated with significant morbidity, HSV-2 increases the risk of HIV-1 acquisition
- To date, there are no effective vaccines to prevent transmission of HIV and HSV
- Monoclonal antibodies (mAbs) show promise as microbicides because of their specificity, flexibility, and safe profile
- Two pilot Phase I clinical trials conducted in Europe of vaginally applied HIV antibodies were shown to be safe for women
- We recently completed a Phase I clinical study of repeated dose vaginal application of film containing HIV and HSV monoclonal antibodies
- We report the first-in-human Phase I clinical trial of a repeated dose antibody-based multipurpose prevention technology (MPT) vaginal film against HIV and HSV
- **Objectives:** To assess the safety, pharmacokinetics (PK) and *ex vivo* efficacy of repeated doses of MB66 film delivered vaginally to women

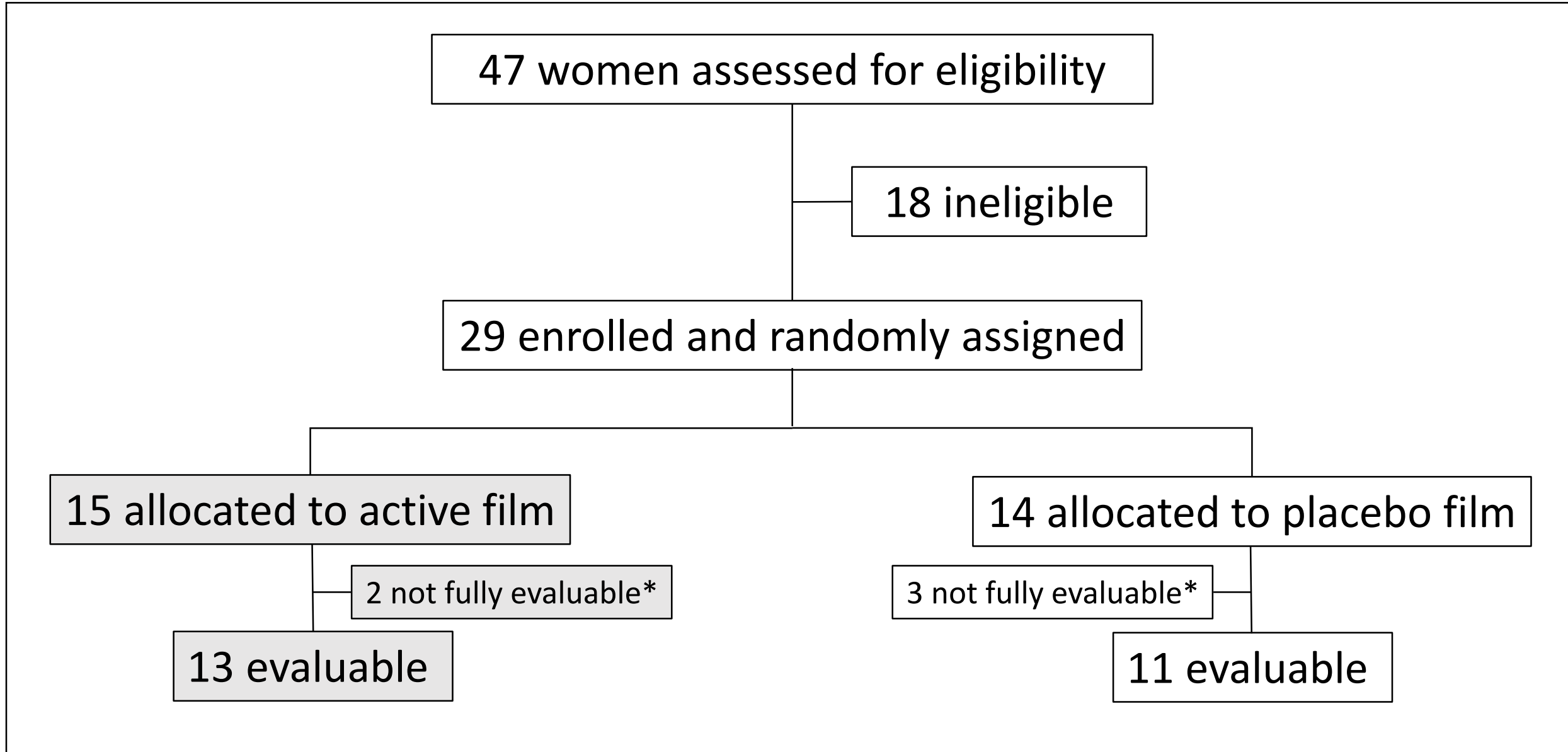
# Study Product and Design

## MB66-01 Study Schema with Target Enrollment

MB66 Film	
	
Composition	
Component	% (wt/wt)
PVA 8-88	60
Maltitol	25
Histidine	0.1
Polysorbate 20	0.01
HSV8-N	5
VRC01-N	5
Water	5
<b>Total</b>	<b>100</b>

Visit 1 Screening	Visit 2 Enrollment And Dosing	Visit 3 Clinical Evaluation	Telephone Safety Contact	Visit 4 Clinical Evaluation	Visit 5 Clinical Evaluation
<i>Up to Day-45</i>	<i>Day 0</i>	<i>Day 1</i>	<i>Day 3-4</i>	<i>Day 7-8</i>	<i>Day 12-16</i>
<b>Arms and dosing:</b>					
15 women: 1 active film/d for 7 d	■	■	■ ■ ■ ■ ■		
15 women: 1 placebo film/d for 7 d	□	□	□ □ □ □ □		
<b>Sampling:</b>					
	PK at 0, 1, 4 hr	PK at 24 hr		PK at 1wk	PK at 2wk
Immune Modulators		Immune Modulators		Immune Modulators	Immune Modulators
	Microbial Environment	Microbial environment		Microbial environment	Microbial environment
<hr/>					
<i>Day -5</i>	<i>Visit 4</i>				<i>Day 28</i>
-----Abstinence-----  --Condom use---					

# Diagram of MB66-01 Enrollment



# Summary of Baseline Characteristics of Enrolled Participants

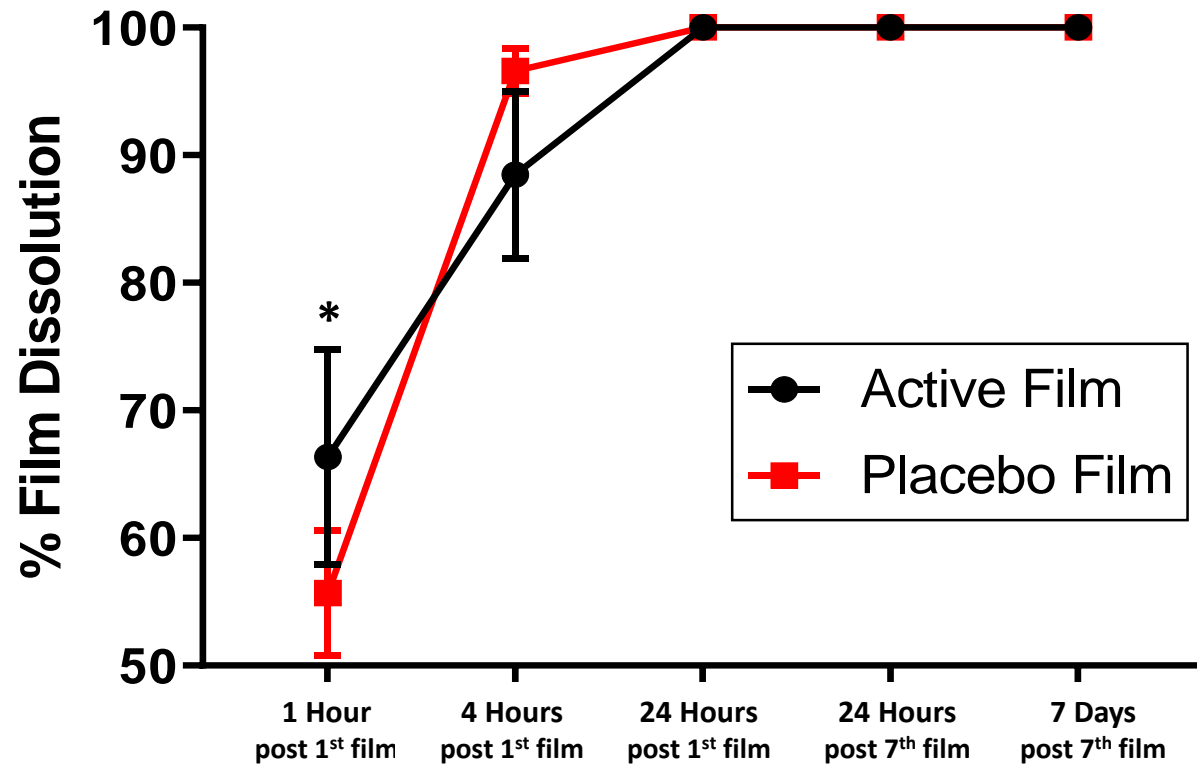
Demographic	Sub-category	Active Film (n=15)	Placebo Film (n=14)	Active vs. Placebo p-value	
Race	White	11 (73.3%)	10 (71.4%)	1.00	Demographics matched those of patients at Miriam Hospital, Providence, Rhode Island.
	African-American	3 (20.0%)	3 (21.4%)	1.00	
	Native American/ Alaska Native	2 (13.3%)	0	0.48	
	Asian	0	0	1.00	
	Native Hawaiian/ Pacific Islander	0	0	1.00	
	Other/Unknown	1 (6.7%)	1 (7.1%)	1.00	
Ethnicity	Latino/Hispanic	2 (13.3%)	3 (21.4%)	0.65	No difference in demographics between Active and Placebo Film Groups
	Other	13 (86.7%)	11 (78.6%)		
Age (Mean ± SD)		28.0 ± 6.9	26.1 ± 7.1	0.47	
Height (in.) (Mean ± SD)		63.9 ± 3.0	64.7 ± 2.1	0.41	
Weight (kg.) (Mean ± SD)		78.0 ± 20.6	76.6 ± 12.1	0.82	
Contraception	Hormone-based	6 (40.0%)	9 (64.3%)	0.27	
	IUDH	4 (26.7%)	3 (21.4%)	1.00	
	IUDC	1 (6.7%)	0	1.00	
	Male Condoms	1 (6.7%)	2 (14.3%)	0.66	
	Vasectomy	0	0	1.00	
	Sterilization	1 (6.7%)	0	1.00	
	Female Partner Only	0	0	1.00	
	Abstinence (at least 60 days)	3 (20.0%)	2 (14.3%)	1.00	

# Distribution and Nature of Adverse Events by Study Arm

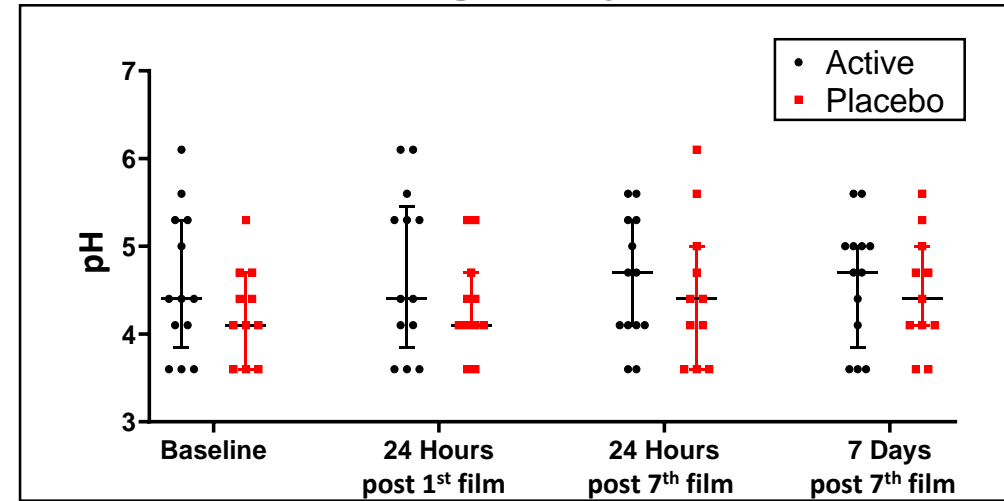
	Active Film		Placebo Film		Active vs. Placebo	
	(n=15)		(n=14)		p-value	
	Total	Related	Total	Related	Total	Related
No. of AEs	27	10	18	9	-----	-----
No. of AEs per Participant	1.80 ± 0.34	0.67 ± 0.23	1.29 ± 0.24	0.64 ± 0.20	0.29	0.95
Maximum AE Grade per Participant	1.13 ± 0.17	0.33 ± 0.13	1.14 ± 0.21	0.57 ± 0.17	0.96	0.38
No. of Participants with AE	13 (86.7%)	7 (46.7%)	12 (85.7%)	7 (50.0%)	1.00	1.00
AEs ≥ Grade 2	4 (26.7%)	2 (13.3%)	4 (28.6%)	1 (7.1%)	1.00	1.00
<b>AE Category</b>						
<b>Genitourinary</b>						
UTI	1 (6.7%)	0	1 (7.1%)	1 (7.1%)	1.00	0.48
Uterine Cramping	2 (13.3%)	2 (13.3%)	0	0	0.48	0.48
Vaginal Spotting	2 (13.3%)	1 (6.7%)	4 (28.6%)	2 (14.3%)	0.39	0.60
Vaginal Discharge	2 (13.3%)	2 (13.3%)	2 (14.3%)	2 (14.3%)	1.00	1.00
Vaginal Itching	0	0	1 (7.1%)	1 (7.1%)	0.48	0.48
Vaginal Odor	3 (20%)	2 (13.3%)	1 (7.1%)	1 (7.1%)	0.60	1.00
Labial Abrasions	-----	-----	-----	-----	-----	-----
Asymptomatic Microscopic Hematuria	7 (46.7%)	2 (13.3%)	4 (28.6%)	1 (7.1%)	0.45	1.00
Proteinuria	2 (13.3%)	1 (6.7%)	3 (21.4%)	1 (7.1%)	0.65	1.00

No difference in  
AE ≥ Grade 2  
related to product

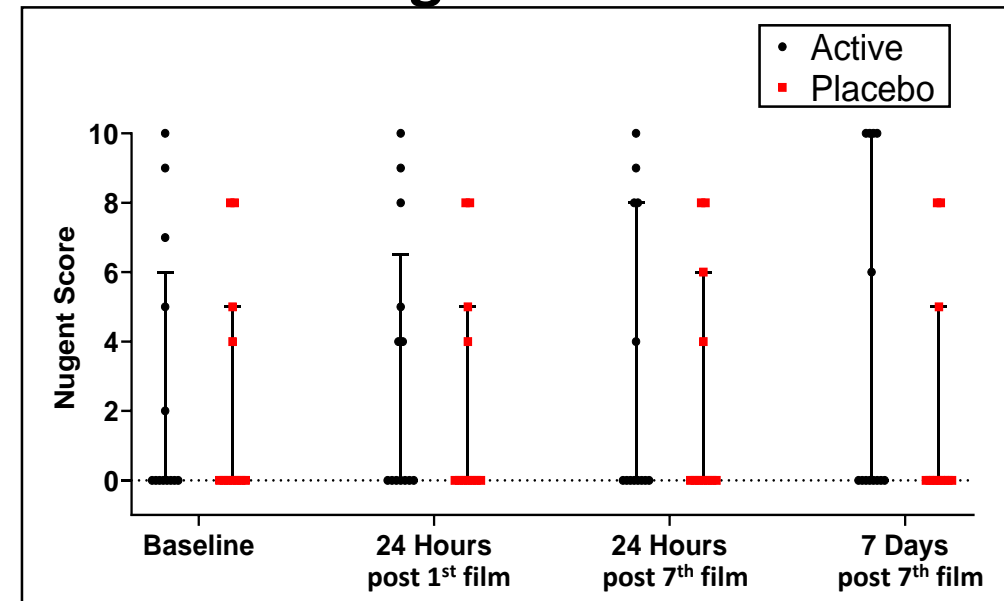
# MB66 Film Dissolution



# Vaginal pH

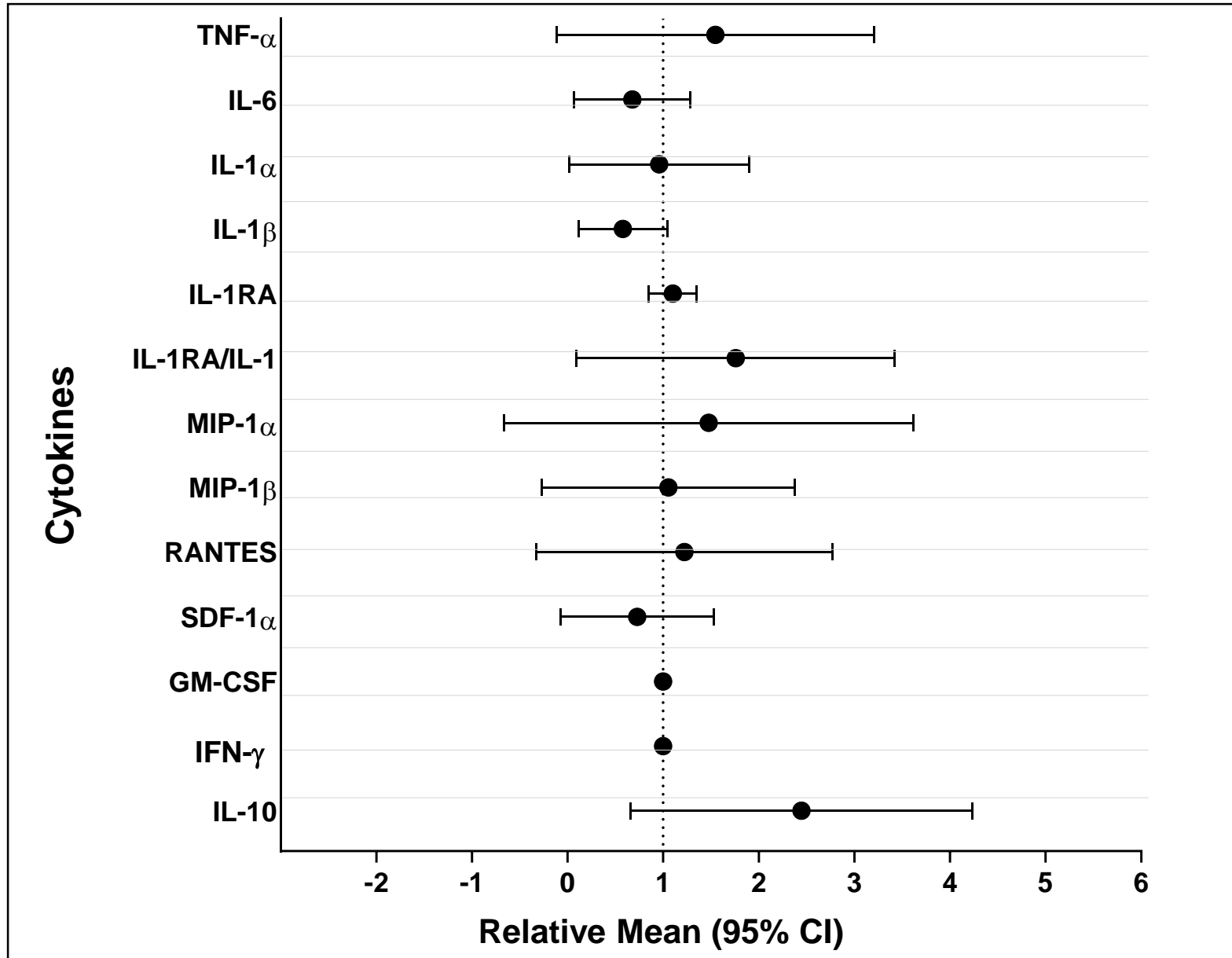


# Nugent Scores



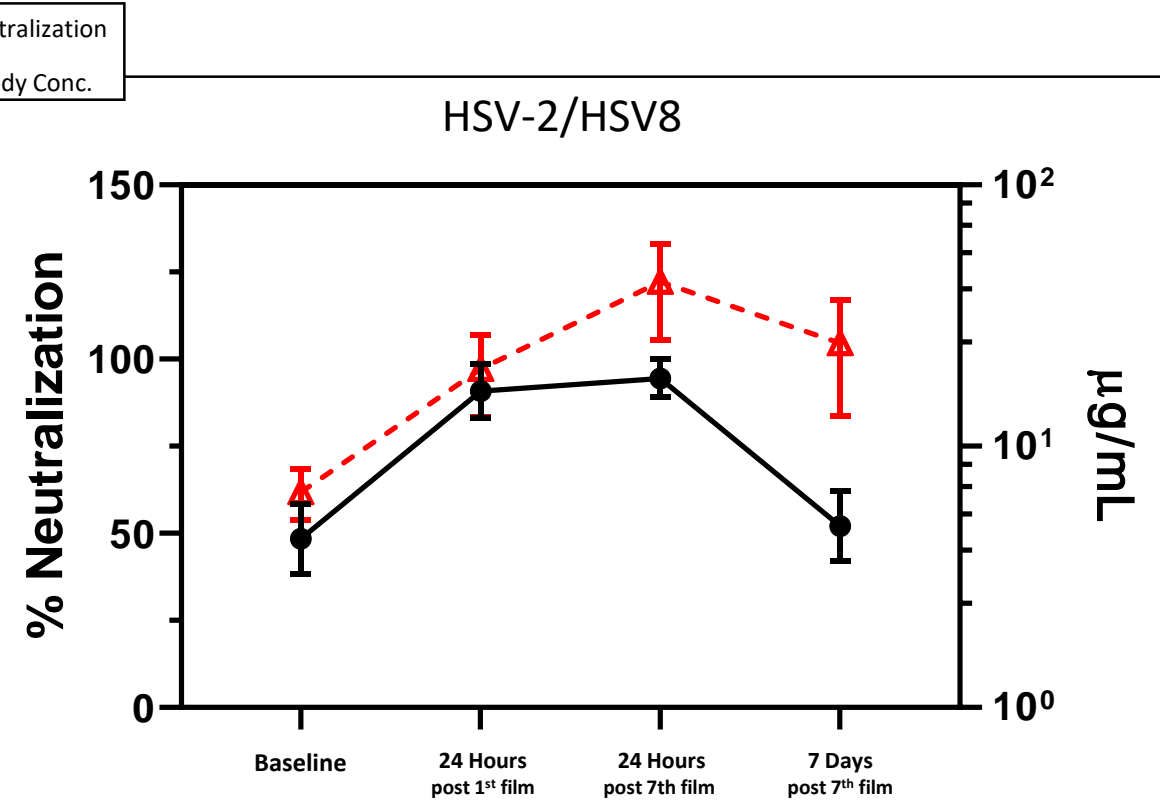
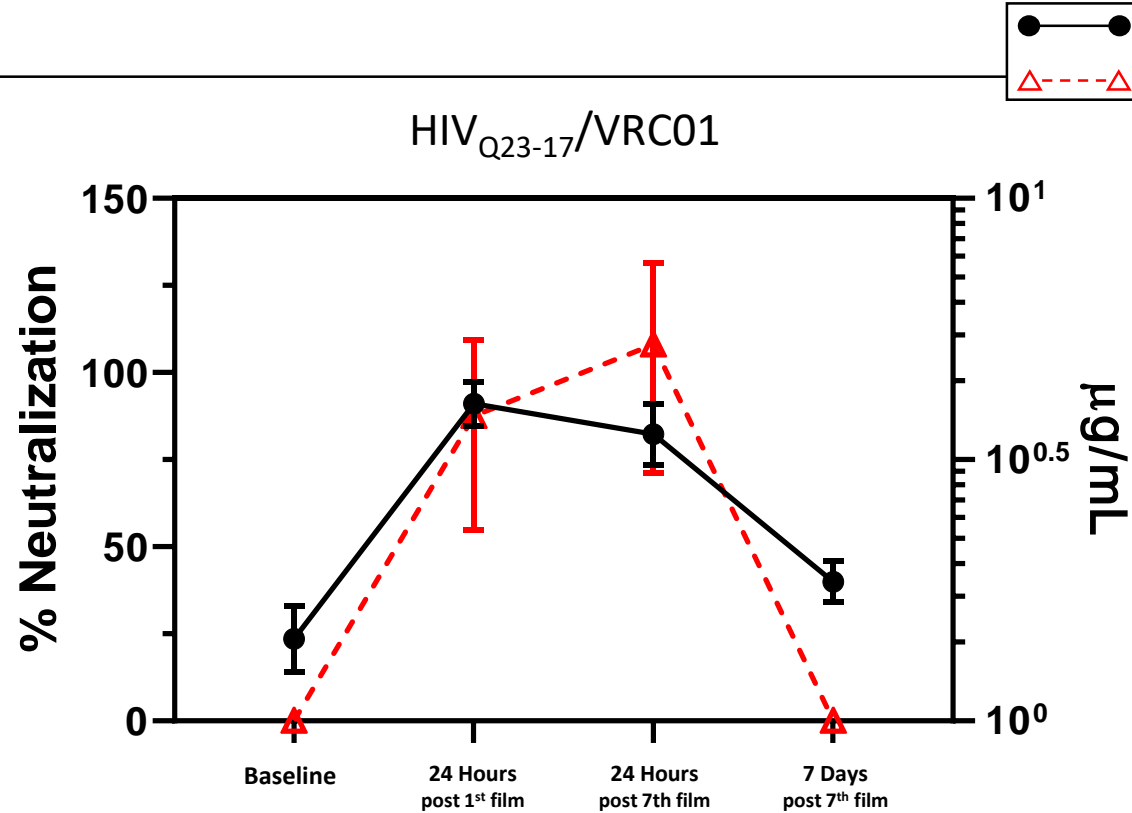
# Forest Plot of CVL Cytokines

Ratio of Visit 4 Active to Placebo Film

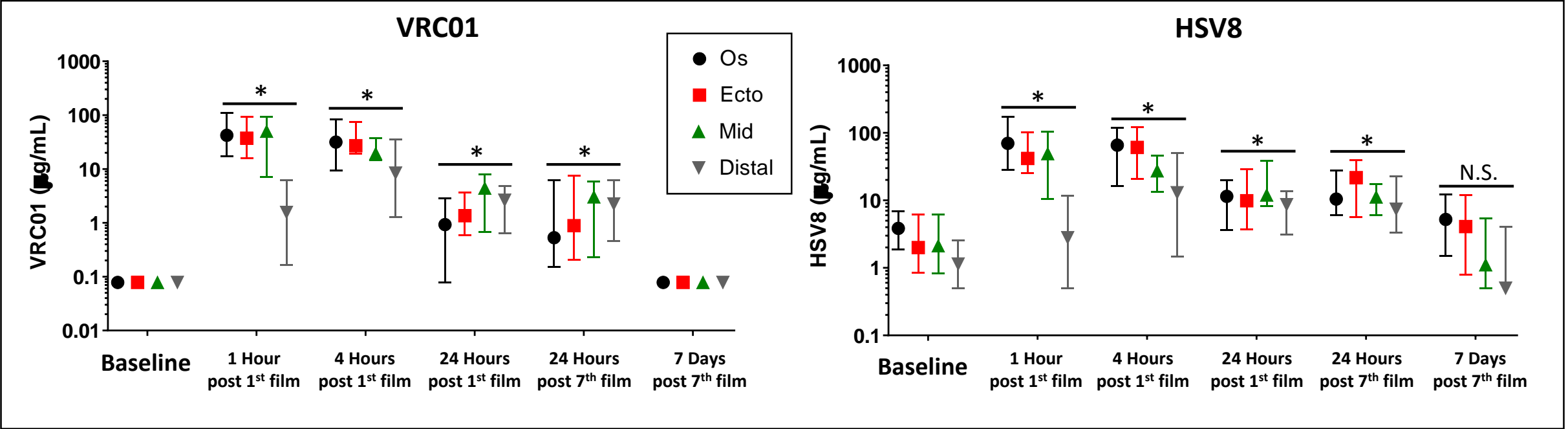




# Viral Neutralization and Antibody PK Data (CVLs)



# VRC01 and HSV8 Concentrations in Vaginal TearFlo Samples



# Conclusions:

- Repeated dose vaginal application of MB66 film was safe and well tolerated
- Significant film dissolution after one hour
- Vaginal pH and Nugent scores did not significantly change
- No significant increases in proinflammatory cytokine concentrations following film insertion
- Concentrations of VRCO1 and HSV8 mAbs increased significantly in vaginal secretions following insertion of active film, peaking at one hour and remaining elevated at 24 hours post film insertion
- *Ex vivo* efficacy: Significant neutralization of all 3 HIV strains and HSV-2 24 hours after multiple film insertion
- These data indicate that MB66 is a safe and promising MPT product to protect women against HIV-1 and HSV

# Acknowledgements:

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