

**ORAL ABSTRACT: OL-06**  
Tuesday, March 10, 2020

**DELAY IN VIRAL REBOUND  
WITH TLR7 AGONIST,  
N6-LS, AND PGT121 IN  
SHIV-INFECTED MACAQUES**

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Disclosures:  
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# Delay in Viral Rebound with TLR7 Agonist, N6-LS and PGT121 in SHIV-infected Macaques

Dr. Denise Hsu

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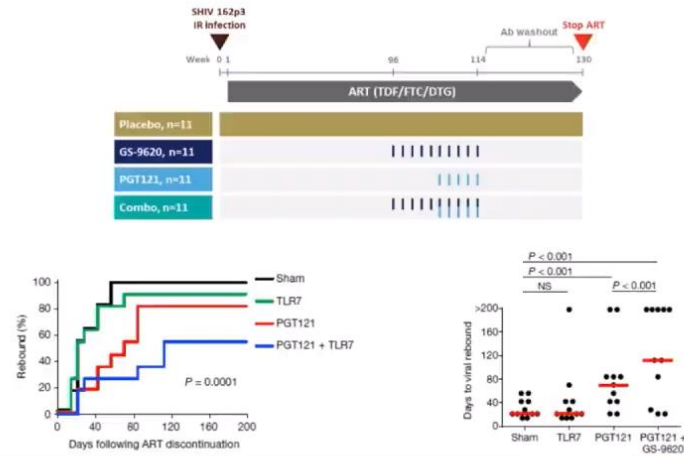
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## Background

- The administration of TLR7 agonist GS-9620 and PGT121 to rhesus macaques treated with ART 7 days post SHIV-SF162P3 infection was associated with delay in viral rebound



Borducchi et al., *Nature* 2018

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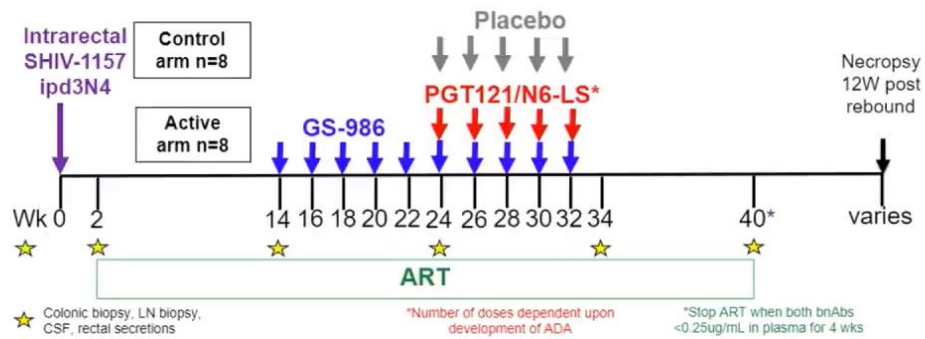
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### Aim: To evaluate the effects of TLR7 agonist and dual bnAbs on viral rebound

- 16 Male Indian-origin rhesus macaques
  - Animals with protective MHC allele (Mamu A-01, B-08, B-17) were excluded



★ Colonic biopsy, LN biopsy, CSF, rectal secretions

ART

\*Number of doses dependent upon development of ADA

\*Stop ART when both bnAbs <math>< 0.25\text{ug/mL}</math> in plasma for 4 wks

Conducted in collaboration with BIDMC, VRC, Gilead

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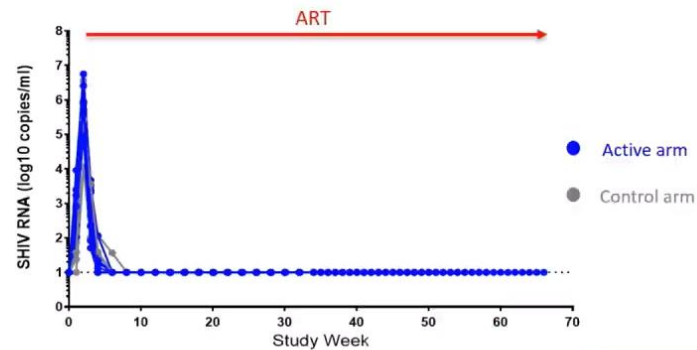
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### Plasma viral RNA dynamics

- Median viral RNA at wk 2 was 5.7 (range 4.1-6.8) log<sub>10</sub> copies/mL
- All animals achieved viral suppression on ART
- No detectable blips 24hrs post GS-986 administration



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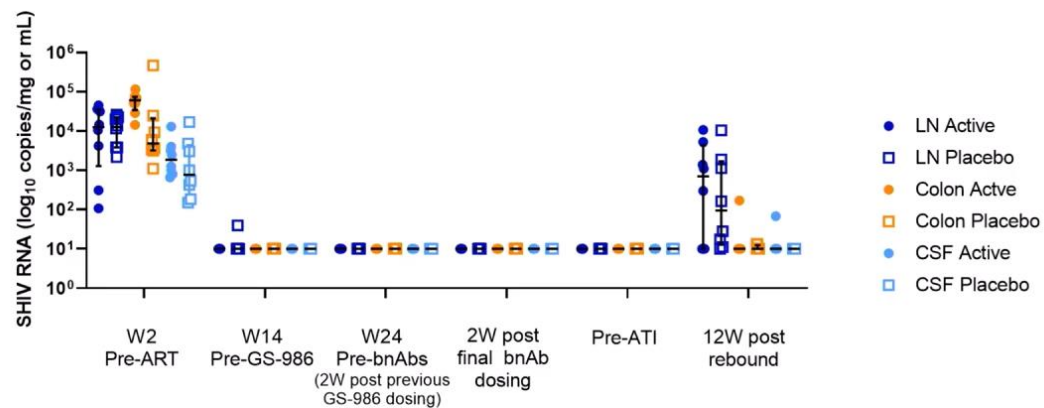
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### No detectable persistent viral expression in tissues



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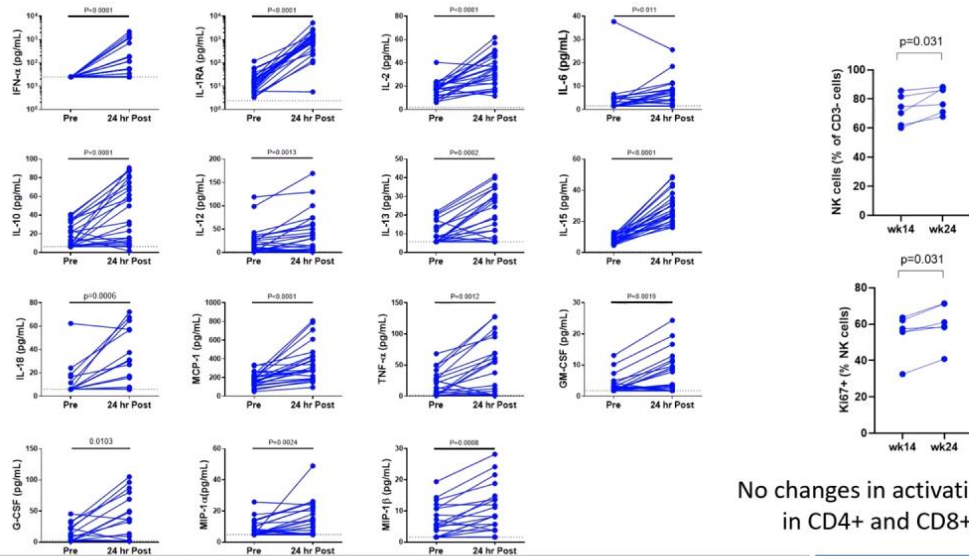
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### GS-986 induced immune activation



No changes in activation markers in CD4+ and CD8+ T cells

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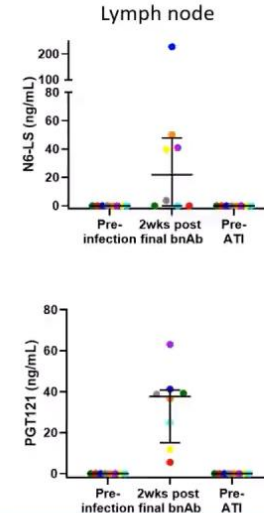
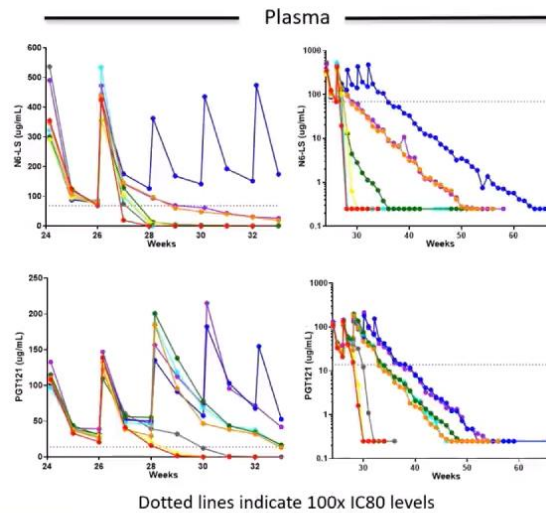


## BnAbs levels in plasma and LN

### Doses administered\*

	GS-968 (0.1mg/kg)	N6-LS (30mg/kg)	PGT121 (10mg/kg)
R1104	7	2	2
R1159	7	2	2
R1330	7	2	2
R1118	8	2	3
R1248	8	2	3
R1154	8	2	3
R1316	9	2	4
R1261	10	5	5

\* Number of doses administered were dependent on the development of ADA



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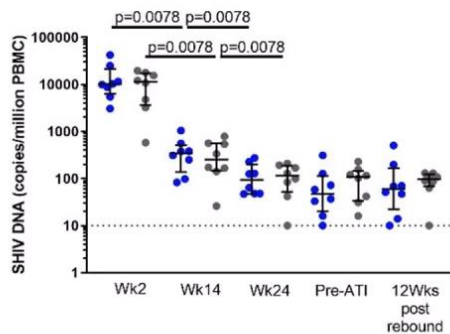
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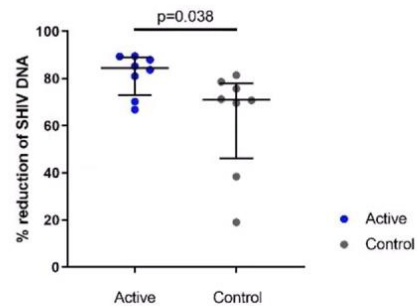
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### SHIV DNA levels



No difference in SHIV DNA levels pre-ATI



Greater % of reduction in SHIV DNA levels from wk14 to pre-ATI in active arm

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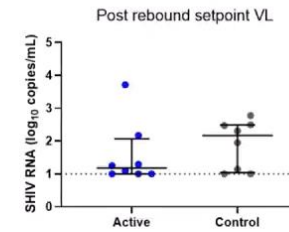
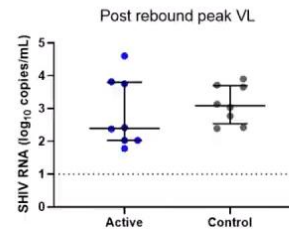
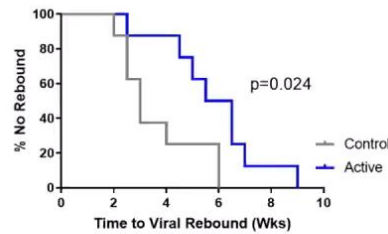
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## Viral Rebound

- All animals experienced plasma viral rebound
- Median time to rebound
  - Placebo arm: 3 weeks vs Active arm: 6 weeks ( $p=0.024$ )
- No difference in post rebound peak or set-point viremia between arms



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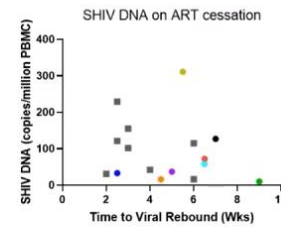
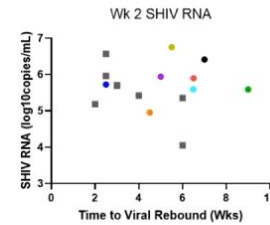
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## No clear predictors of time to rebound

Doses of interventions administered

	GS-968	N6-LS	PGT12 1	Time to rebound
R1104	7	2	2	6.5
R1159	7	2	2	5.5
R1330	7	2	2	7.0
R1116	8	2	3	4.5
R1248	8	2	3	9.0
R1254	8	2	3	6.5
R1316	9	2	4	5.0
R1261	10	5	5	2.5



Each dot corresponds to an individual animal. Color key displayed in table. Gray squares depict values from control animals

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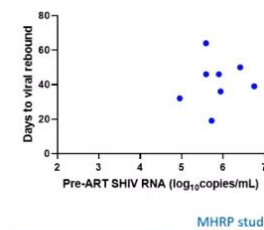
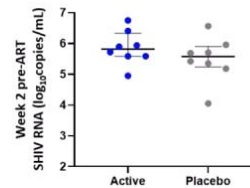
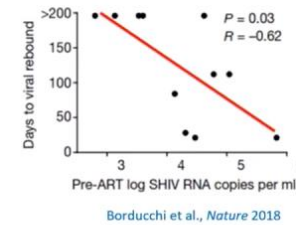
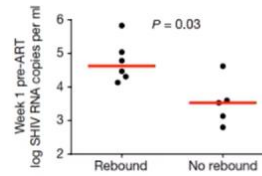
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## Key differences between Borducchi et al and MHRP study

- Timing of ART initiation
  - 1wk vs 2 wks
- Duration of ART prior to interventions
  - 96 wks vs 14 wks
- Number of doses of bNAbs
  - 5 vs 2-5
- Different SHIV
  - SF162P3 vs 1157ipd3N4



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## Summary

- GS-986 administration was associated with
  - Upregulation of cytokines consistent with human data
  - No detectable plasma viral blips 24 hr post dosing
- The combinational use of N6-LS and PGT121 was associated with
  - More rapid development of ADA than PGT121 alone
- GS-986/PGT121/N6-LS kick and kill strategy was associated with
  - Greater reduction in SHIV DNA
  - A modest delay in rebound

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# Acknowledgements

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- Viiv Healthcare:** James Demarest
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