

# Supplementary Materials: Viral load Reduction in SHIV-Positive Nonhuman Primates via Long-Acting Subcutaneous Tenofovir Alafenamide Fumarate Release from a Nanofluidic Implant

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**Table 1.** Histological characteristics scoring system to evaluate inflammation near the implants.

Histological characteristics	Score					Reactive Inflammation Multiplier
	0	1	2	3	4	$(m_{i,r})$
Cell characteristic						
Polymorphonuclear cells	0/HPF	Rare, 1-5/HPF	5-10/HPF	Heavy infiltrate	Packed	2
Lymphocytes	0/HPF	Rare, 1-5/HPF	5-10/HPF	Heavy infiltrate	Packed	2
Plasma cells	0/HPF	Rare, 1-5/HPF	5-10/HPF	Heavy infiltrate	Packed	2
Macrophages	0/HPF	Rare, 1-5/HPF	5-10/HPF	Heavy infiltrate	Packed	2
Giant cells	0/HPF	Rare, 1-5/HPF	5-10/HPF	Heavy infiltrate	Packed	2
Tissue characteristic						
Necrosis	0	Minimal	Mild	Moderate	Severe	2
Capsule thickness	0	Narrow band (<5 cells)	Moderate (5-10 cells)	Thick band (10-20 cells)	Extensive thick band	1
Tissue infiltrate	0	Minimal focal invasion of local tissue	Mild to multifocal inflammation in adjacent tissues	Moderate inflammation in adjacent tissues	Marked inflammation in adjacent tissues	1

Note: Reproduces from [1], ASM Journals, 2020.

**Table 2.** nTAF<sub>1</sub> histopathological scoring.

<b>Animal 15-162 (Treatment 1)</b>	<b>Score</b>		
	<b>Pathologist 1</b>	<b>Pathologist 2</b>	<b>Average</b>
Polymorphonuclear cells	3	2	2.5
Lymphocytes	3	1	2.0
Plasma cells	1	1	1.0
Macrophages	3	3	3.0
Giant cells	1	2	1.5
Necrosis	0	1	0.5
Capsule thickness	3	3	3.0
Tissue infiltrate	1	2	1.5
<b>Overall total</b>	<b>15</b>	<b>15</b>	<b>15.0</b>
<b>Animal 17-048 (Treatment 2)</b>	<b>Score</b>		
	<b>Pathologist 1</b>	<b>Pathologist 2</b>	<b>Average</b>
Polymorphonuclear cells	3	0	1.5
Lymphocytes	3	1	2.0
Plasma cells	0	1	0.5
Macrophages	3	3	3.0
Giant cells	0	1	0.5
Necrosis	1	0	0.5
Capsule thickness	3	3	3.0
Tissue infiltrate	2	3	2.5
<b>Overall total</b>	<b>15</b>	<b>12</b>	<b>13.5</b>
<b>Animal 17-071 (Treatment 3)</b>	<b>Score</b>		
	<b>Pathologist 1</b>	<b>Pathologist 2</b>	<b>Average</b>
Polymorphonuclear cells	1	1	1.0
Lymphocytes	3	2	2.5
Plasma cells	1	2	1.5
Macrophages	2	3	2.5
Giant cells	0	2	1.0
Necrosis	2	2	2.0
Capsule thickness	3	3	3.0
Tissue infiltrate	1	3	2.0
<b>Overall total</b>	<b>13</b>	<b>18</b>	<b>15.5</b>
<b>Animal 16-131 (Treatment 4)</b>	<b>Score</b>		
	<b>Pathologist 1</b>	<b>Pathologist 2 (Note increase in eosinophils)</b>	<b>Average</b>
Polymorphonuclear cells	3	2.5	2.8
Lymphocytes	3	3	3.0
Plasma cells	1	1	1.0
Macrophages	3	3	3.0
Giant cells	0	1	0.5
Necrosis	3	2	2.5

Capsule thickness	3	3	3.0
Tissue infiltrate	1	3	2.0
<b>Overall total</b>	<b>17</b>	<b>18.5</b>	<b>17.8</b>
<b>Animal 15-134 (Treatment 5)</b>			
	<b>Score</b>		
	<b>Pathologist 1</b>	<b>Pathologist 2 (Note increase in eosinophils)</b>	<b>Average</b>
Polymorphonuclear cells	3	2	2.5
Lymphocytes	3	3	3.0
Plasma cells	2	2	2.0
Macrophages	3	3	3.0
Giant cells	0	1	0.5
Necrosis	4	1	2.5
Capsule thickness	4	2	3.0
Tissue infiltrate	2	2	2.0
<b>Overall total</b>	<b>21</b>	<b>16</b>	<b>18.5</b>
<b>Animal 17-004 (Treatment 6)</b>			
	<b>Score</b>		
	<b>Pathologist 1</b>	<b>Pathologist 2</b>	<b>Average</b>
Polymorphonuclear cells	NA	0	NA
Lymphocytes		1	
Plasma cells		1	
Macrophages		1	
Giant cells		0	
Necrosis		0	
Capsule thickness	NA	1	
Tissue infiltrate	1	1	NA
<b>Overall total</b>	<b>1</b>	<b>5</b>	<b>0</b>

All pathologists are board-certified. Pathologist 1 and 2 are from Weill Cornell Medicine and Houston Methodist Hospital, respectively. Animal Treatment 6 was not used to calculate total histological score because the implant site was not easily identifiable.

## References

1. Su, J.T.; Simpson, S.M.; Sung, S.; Tfaily, E.B.; Veazey, R.; Marzinke, M.; Qiu, J.; Watrous, D.; Widanapathirana, L.; Pearson, E.; et al. A Subcutaneous Implant of Tenofovir Alafenamide Fumarate Causes Local Inflammation and Tissue Necrosis in Rabbits and Macaques. *Antimicrob. Agents Chemother.* **2019**, *64*, 775452, doi:10.1128/aac.01893-19.



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