New Long-Acting Agents for HIV Prevention

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DIVISION OF CLINICAL PHARMACOLOGY

leap

HPTN Annual Meeting

Disclosures

- Dr. Flexner has disclosed that during the past 24 months he has served as a paid consultant for American Gene Technologies, Gilead Sciences, Merck, Theratechnologies, and ViiV Healthcare, and served on the Scientific Advisory Board for Navigen.
- He is a co-inventor on five issued patents related to the development of long-acting formulations for delivery of antiretroviral drugs.

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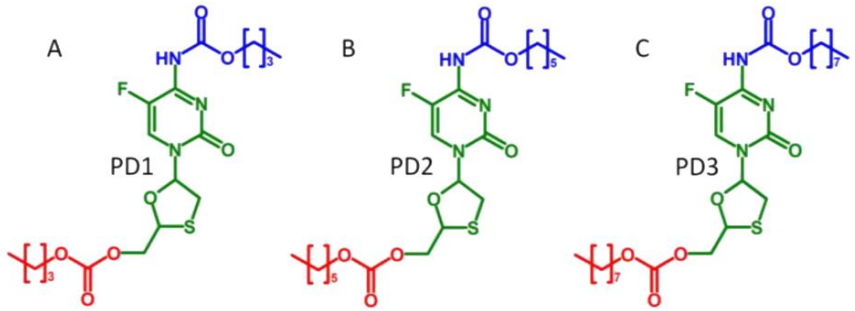


Advances in formulation science: Pro-drugging strategies to allow long-acting delivery of oral drugs

pharmaceutics

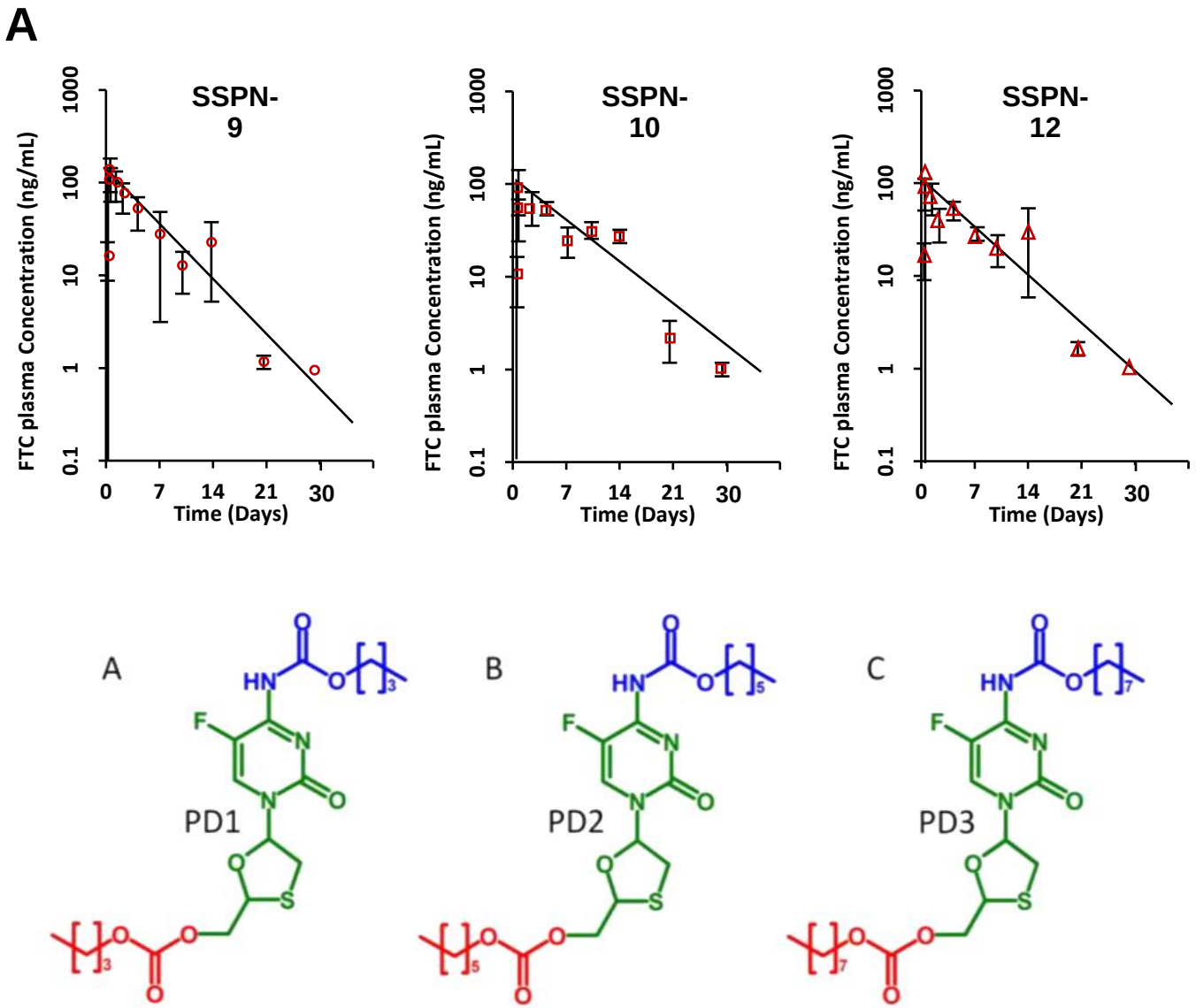
MDPI

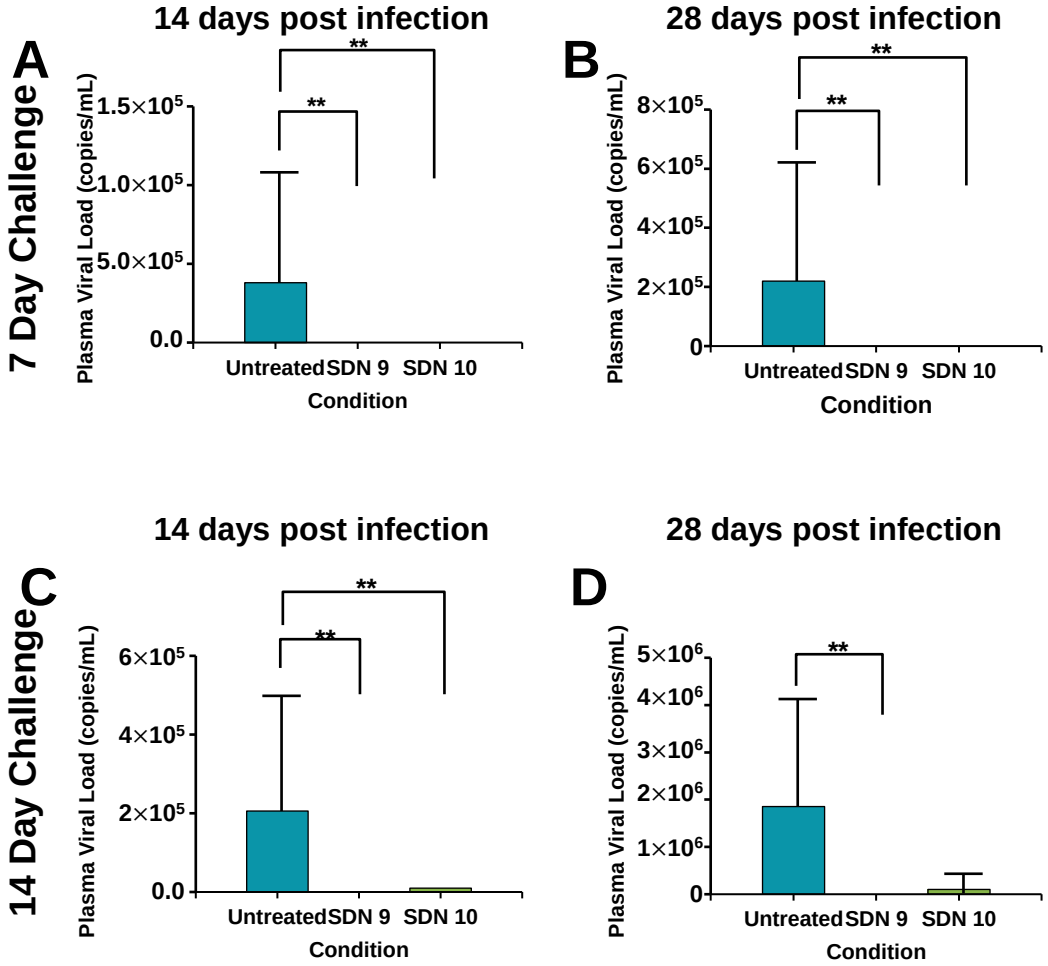
Article

Preclinical Evaluation of Long-Acting Emtricitabine Semi-Solid Prodrug Nanoparticle Formulations

Paul Curley [1], James J. Hobson [1], Neill J. Liptrott [1], Edward Makarov [2], Amer Al-khouja [3], Lee Tatham [1], Christopher A. W. David [1], Helen Box [1], Megan Neary [1], Joanne Sharp [1], Henry Pertinez [1], David Meyers [3], Charles Flexner [3], Caren L. Freel Meyers [3], Larisa Poluektova [2], Steve Rannard [1] and Andrew Owen [1,*]

Pharmaceutics **2023**, *15*, 1835. https://doi.org/10.3390/pharmaceutics15071835 https://www.mdpi.com/journal/pharmaceutics



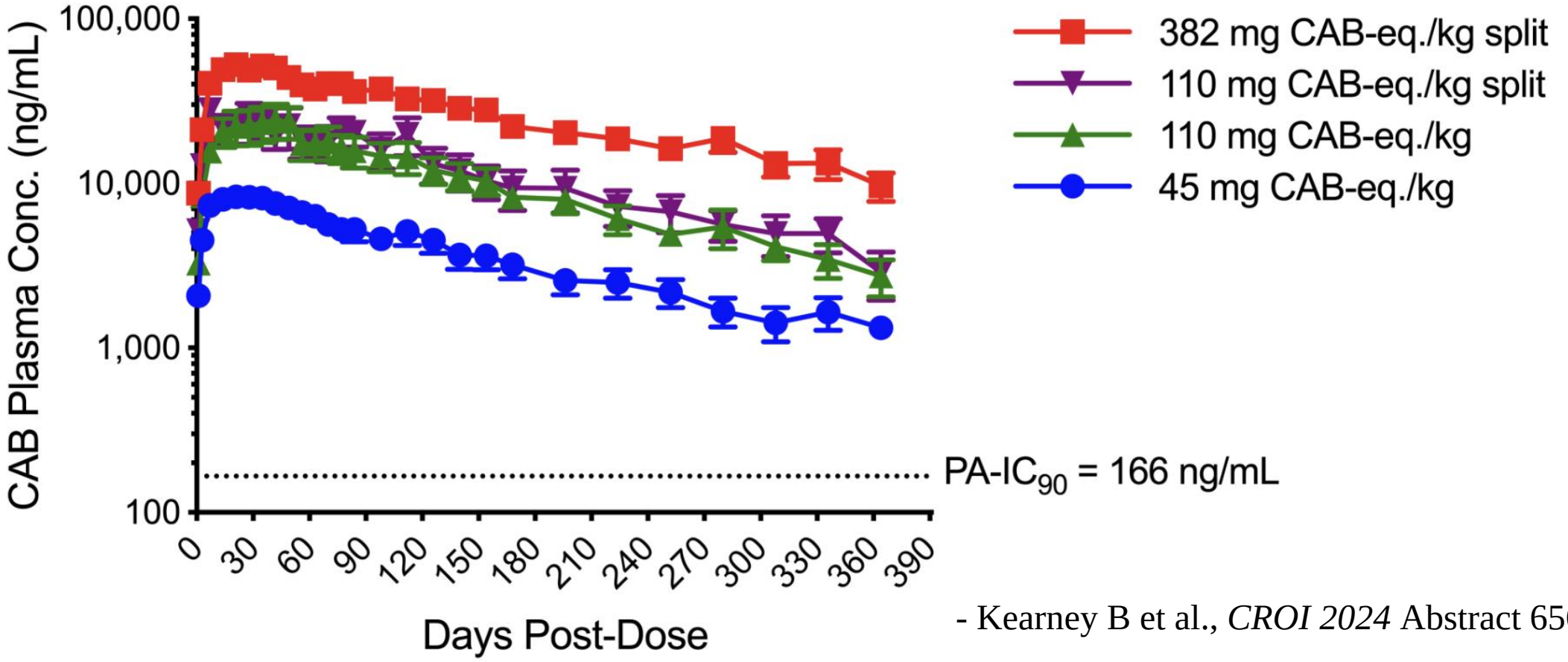


- Curley P et al., *Pharmaceutics* 2023; 15: 1835

Cabotegravir Stearate (XVIR-110) Provides Ultra-Long-Acting CAB Exposure and was Well-Tolerated in GLP Toxicology Studies

HPTN HIV Prevention Trials Network

SD Rats Administered XVIR-110 IM x 1



- Kearney B et al., *CROI 2024* Abstract 656

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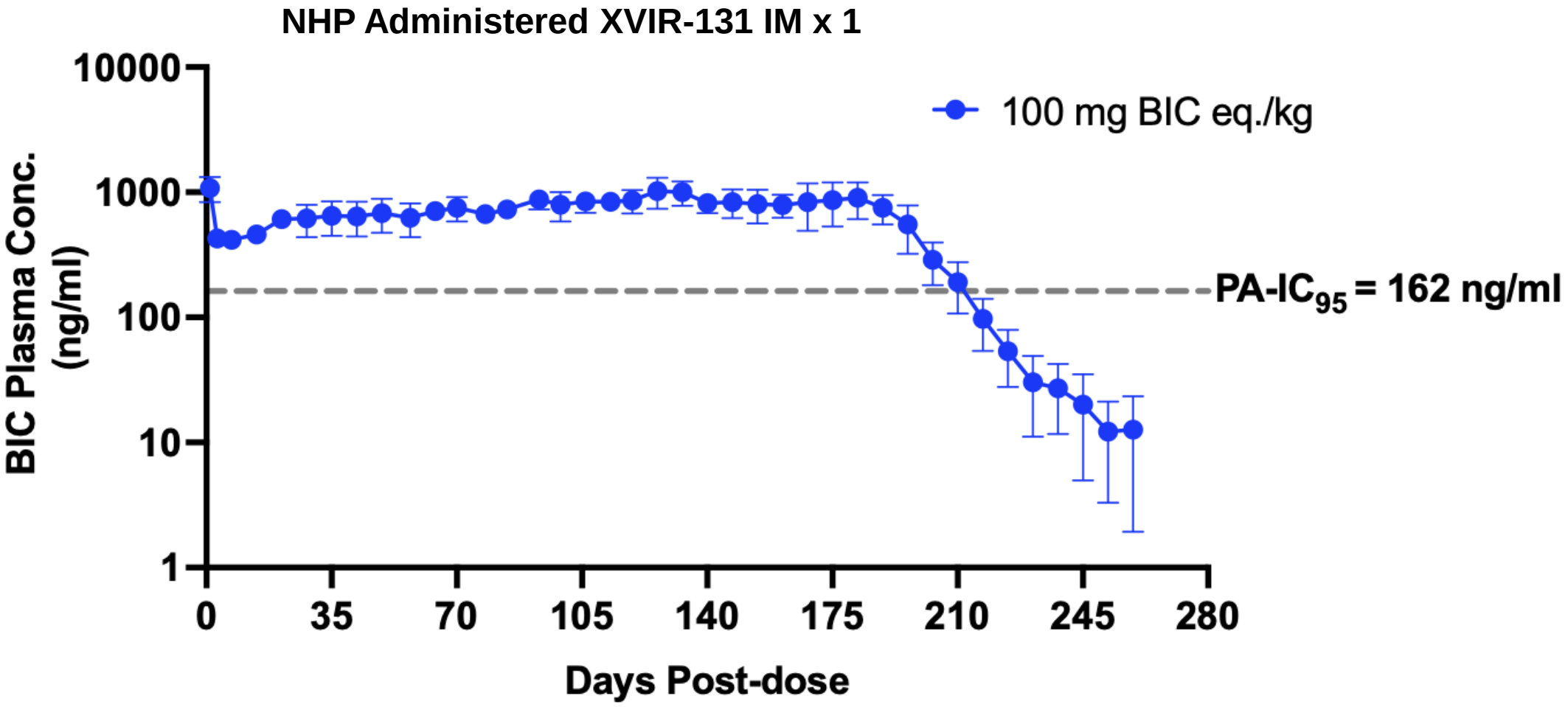
Bictegravir Dimer (XVIR-131) Could Potentially Enable Q6M Dosing of BIC with a Shorter Terminal PK Tail Phase



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Peptide-based polymers for long-acting drug delivery

JACS
JOURNAL OF THE AMERICAN CHEMICAL SOCIETY

pubs.acs.org/JACS

Article

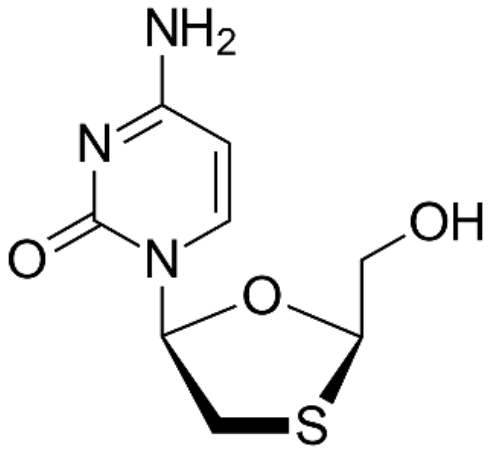
Constructing Antiretroviral Supramolecular Polymers as Long-Acting Injectables through Rational Design of Drug Amphiphiles with Alternating Antiretroviral-Based and Hydrophobic Residues

Han Wang, Maya K. Monroe, Feihu Wang, Mingjiao Sun, Charles Flexner, and Honggang Cui*

Cite This: *J. Am. Chem. Soc.* 2023, 145, 21293–21302

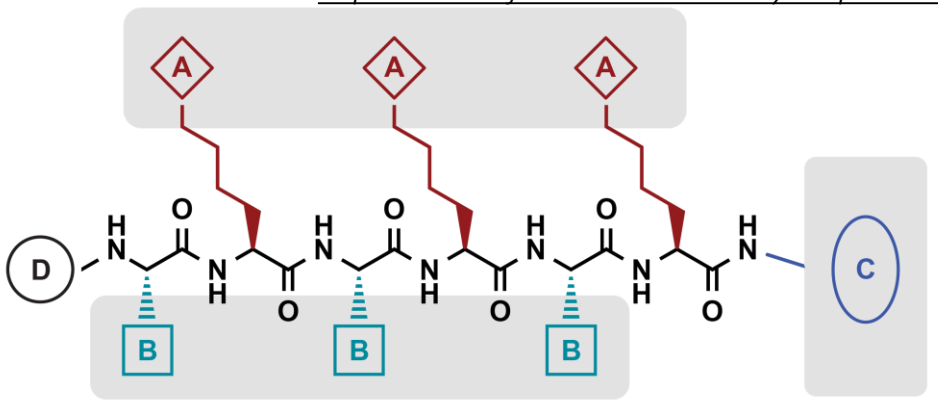
Read Online

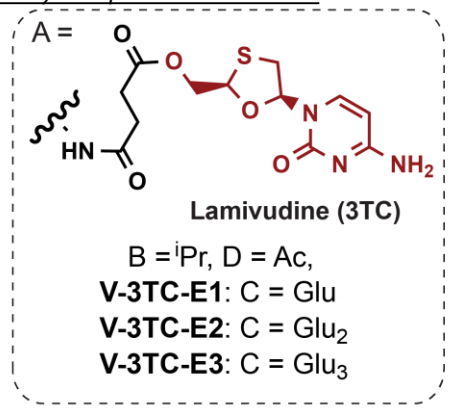
Lamivudine Long-Acting Injectable Peptide Polymers: Molecular Design and Synthesis



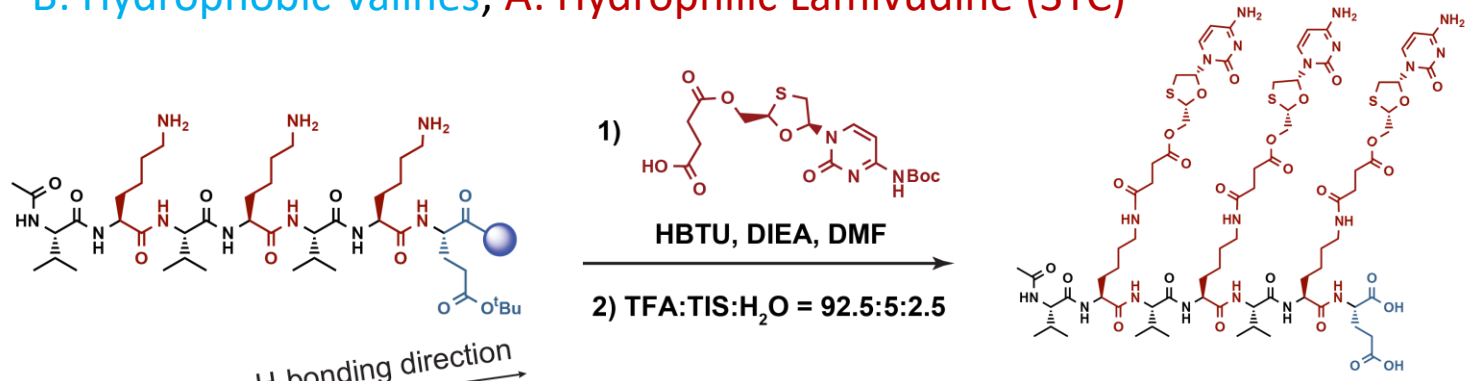
Lamivudine (3TC)

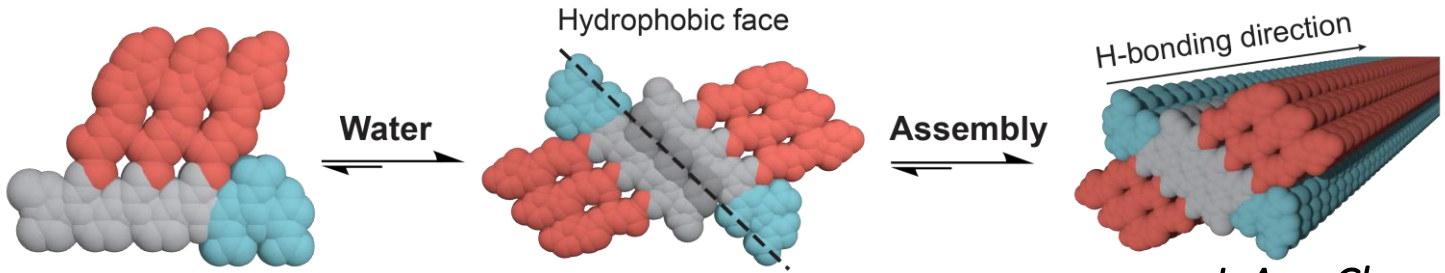
Peptide Motif with alterative hydrophobic and hydrophilic residues





B: Hydrophobic Valines; A: Hydrophilic Lamivudine (3TC)





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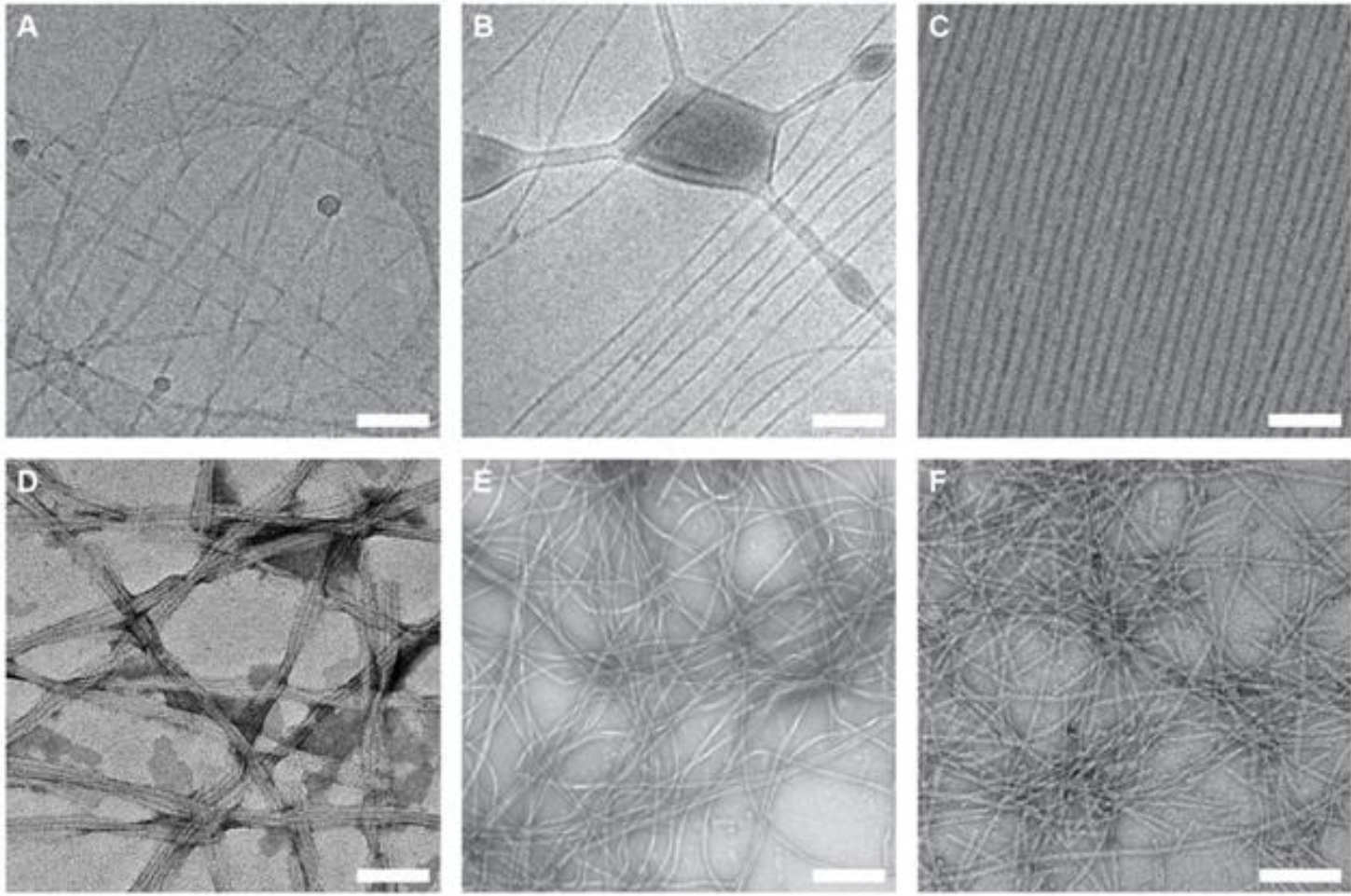
Lamivudine Long-Acting Injectable Peptide P sign and Synthesis



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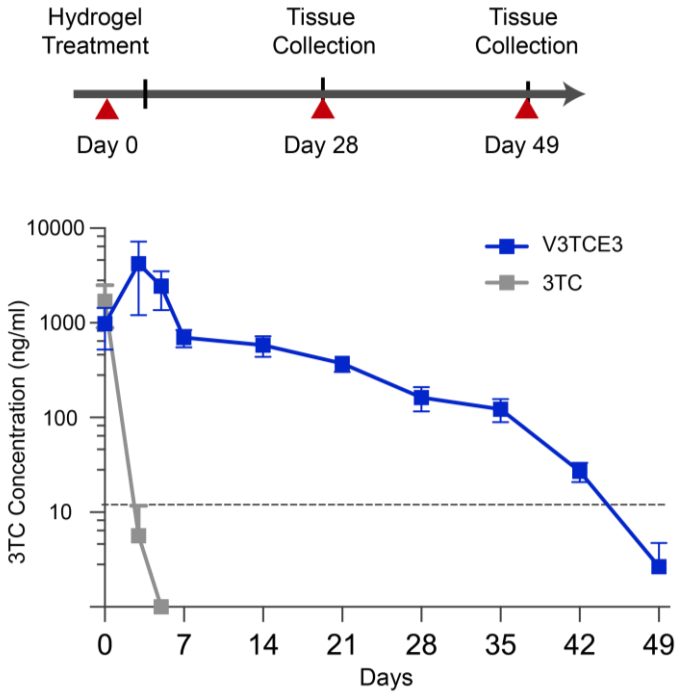
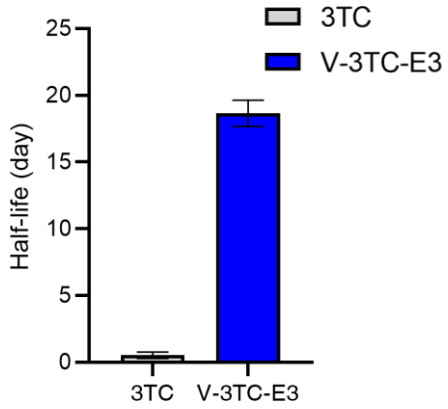
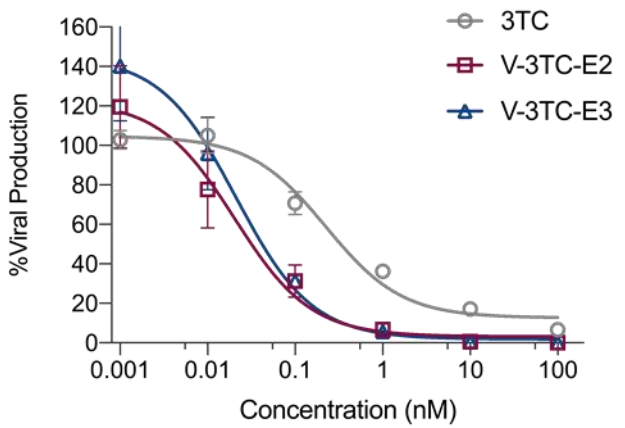
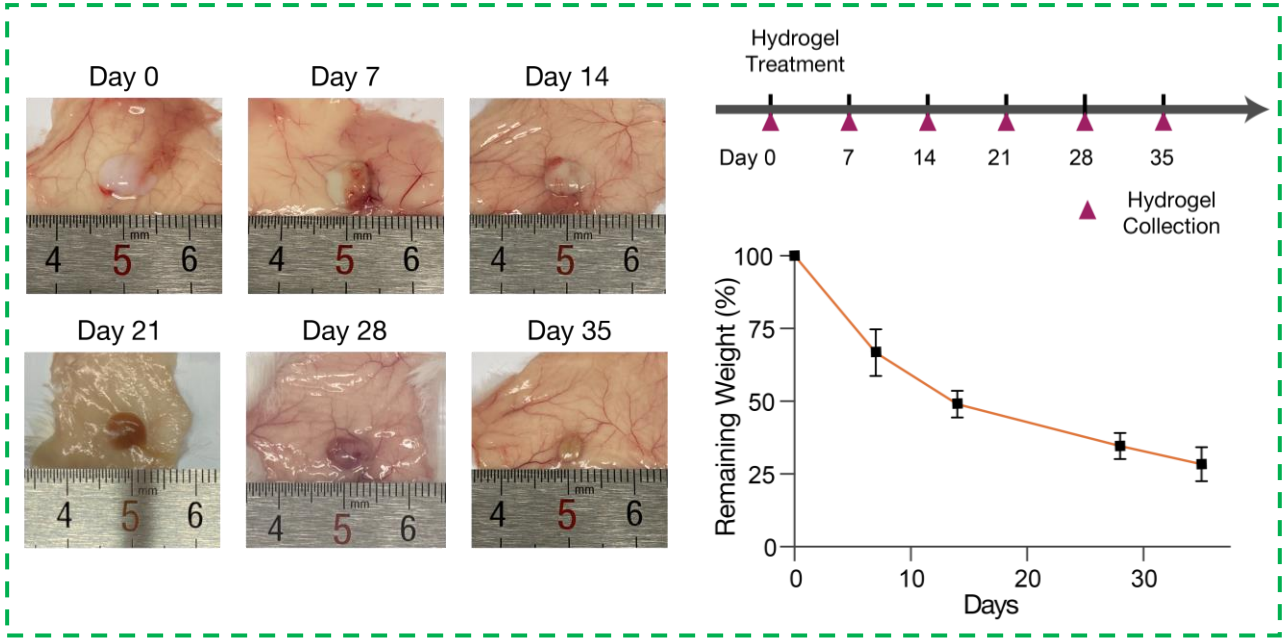
Lamivudine Long-Acting Injectables: In Vivo Pharmacokinetics and Anti-HBV Activity









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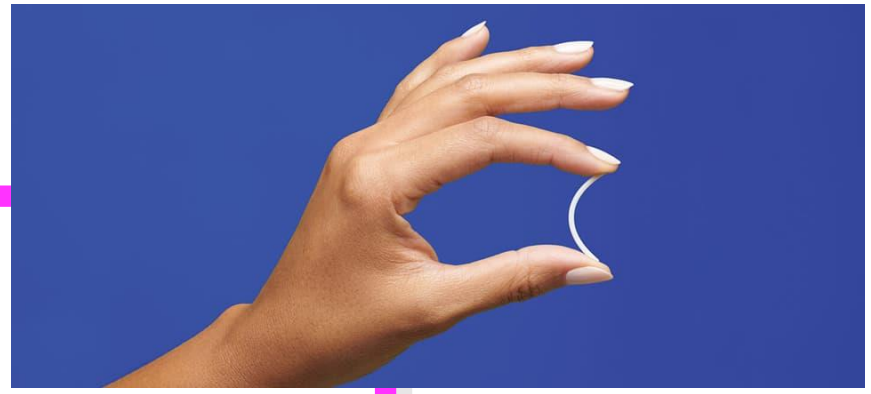
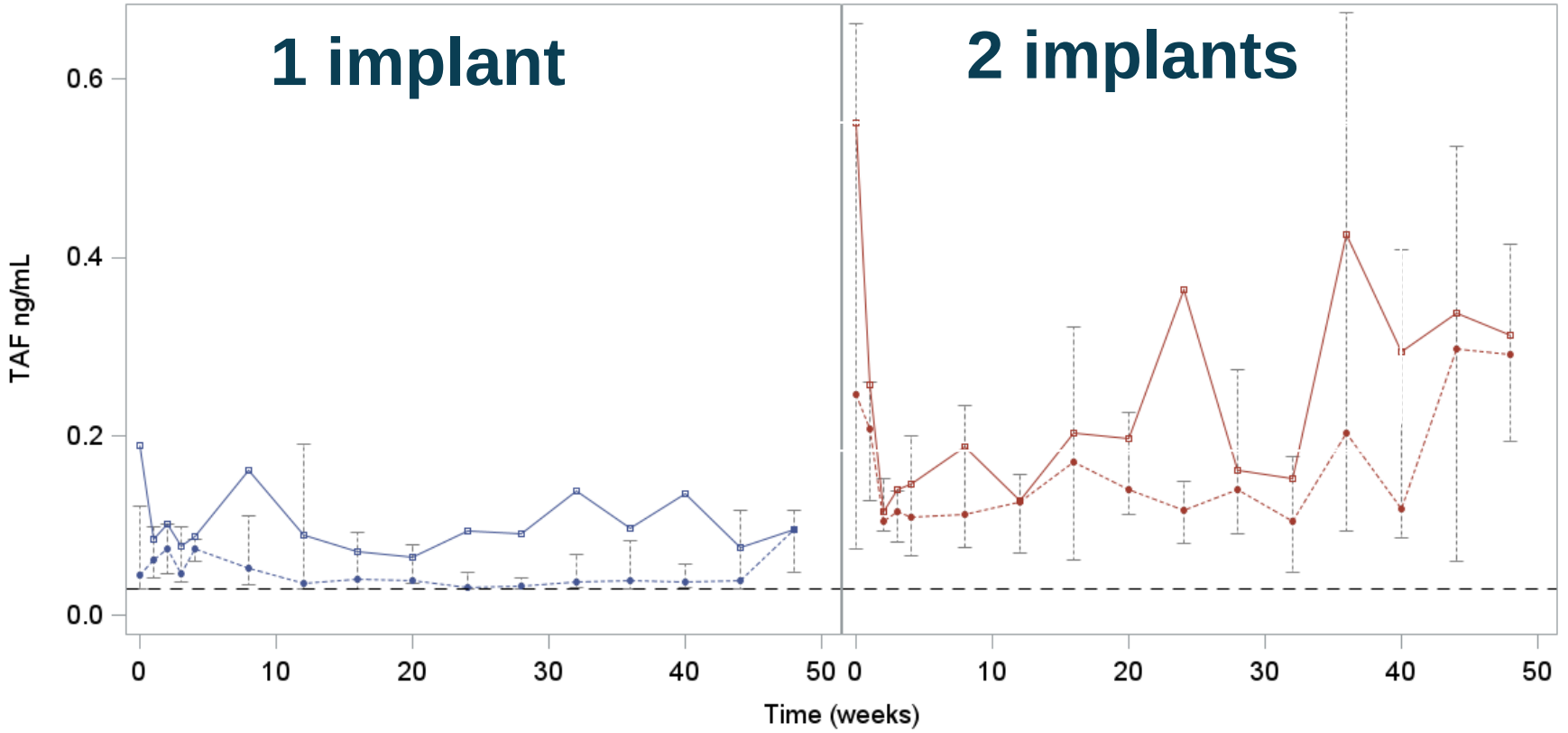


A one-year implant for HIV and HBV prevention?

48-week PK of a TAF Implant – CAPRISA 018

Detectable in **77%** of samples: 100% detection 0.5 hours post-insertion & 50% detection at 6 hours post-insertion



Means represented as solid lines, medians with dashed lines and IQR with grey dashed bars

N	12	12	12	10	10	9	10	10	8	8	8	8	8	12	11	11	11	9	10	9	7	7	7	6	6	6
N BLQ	5	0	2	3	4	2	5	3	2	4	2	3	2	2	1	0	0	0	0	1	0	0	0	0	0	0

- Gengiah TN et al., CROI 2024 Abstract 123

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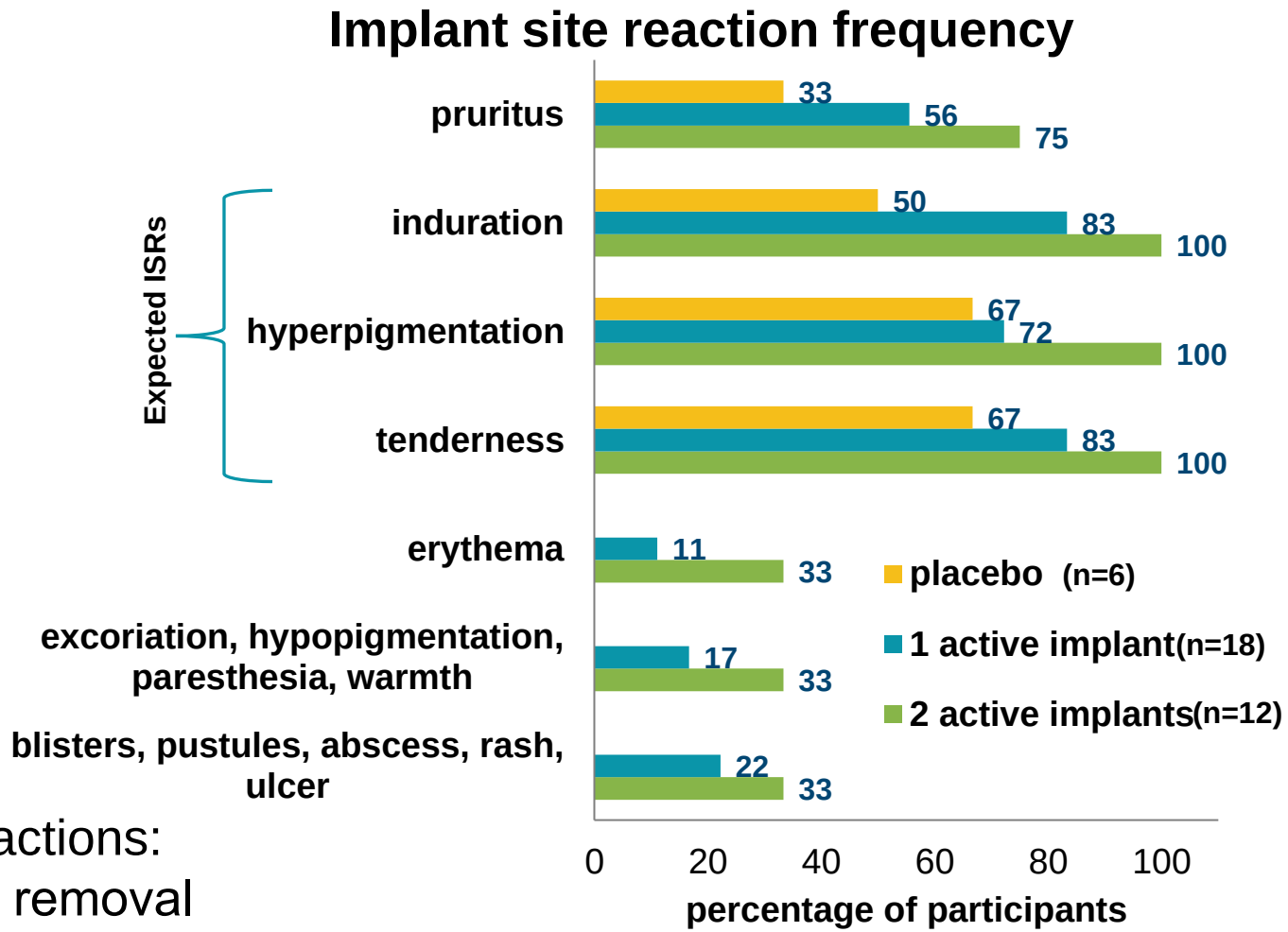
Systemic and Local Insertion Site Adverse Events

Systemic AE severity:

Grade 1: 55.3 %
Grade 2: 42.5%
Grade 3: 2.2%

Implant local site reaction severity:

Grade 1: 90.9%
Grade 2: 8.3%
Grade 3: 0.8%*



*2 of the 36 women had grade 3 local reactions: both had implant site abscesses → early removal

- Gengiah TN et al., CROI 2024 Abstract 123

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Presentation Highlights

1. A variety of long-acting drug delivery strategies can be employed for HIV prevention.
2. Pro-drugs or implants can deliver LA ARV NRTIs that also have anti-HBV activity.
3. Available technology has generated anti-HIV formulations that deliver effective drug concentrations for more than a year in laboratory animals.

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