Better conversations about HIV cure research

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Doherty Institute
HIV Cure Community Partnership

AUSTRALIAN HIV Cure Community Partnership
BRIDGING HIV CURE SCIENCE AND THE HIV COMMUNITY

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AUSTRALIAN ENGAGEMENT IN HIV CURE

AUSTRALIAN HIV Cure Community Partnership
BRIDGING HIV CURE SCIENCE AND THE HIV COMMUNITY

napwha national association of people with HIV australia · Doherty Institute · Kirby Institute · theAlfred
living positive victoria · PositiveWomen · ??

MELBOURNE HIV CURE CONSORTIUM

Community Advisory Board

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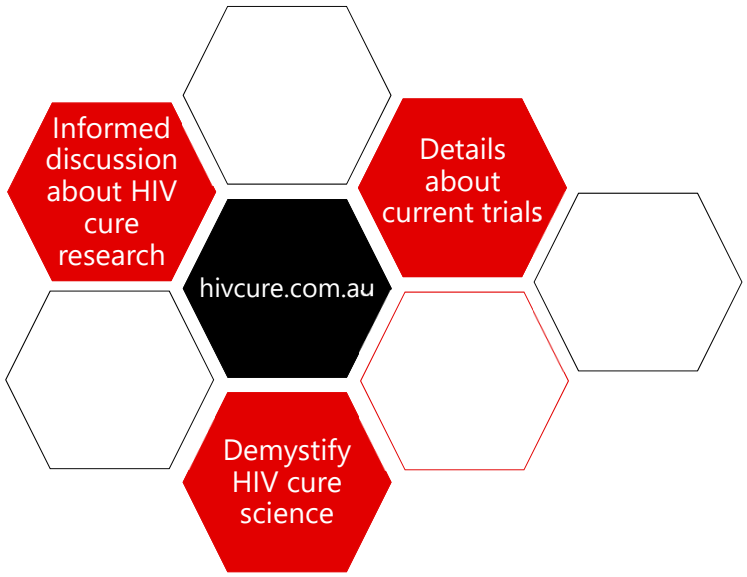
WHY DO WE NEED HIVCURE.COM.AU?



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Which HIV cure channels do you engage with?

Website
hivcure.com.au

Twitter
@HIVcureAU

Facebook
@HIVcureAU

Start the presentation to see live content. Still no live content? Install the app or get help at PollEv.com/app

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Why is HIVcure.com.au important for you?

Top

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Cure conversation

Transplantation and gene therapy

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Have you heard about the London patient?

Yes

No

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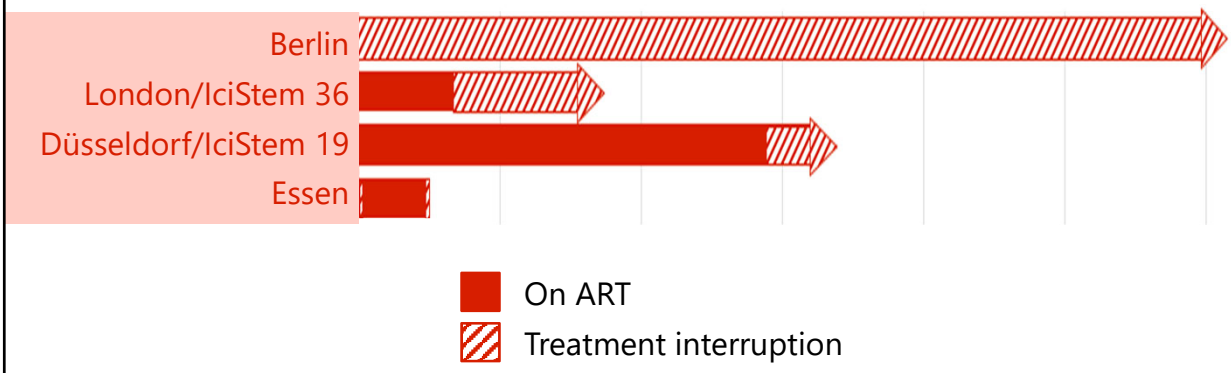
CCR5Δ32 STEM CELL TRANSPLANTS



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KEY FEATURES OF TRANSPLANT CASES

- All have underlying cancer
- Each is a case study (n=1)
- Procedure is risky
- Replace the entire blood stem cell population

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WHAT'S UP WITH CCR5Δ32?

- CCR5 is a key co-receptor for HIV
- CCR5Δ32 does not make functional CCR5
- Recent study suggesting Δ32/Δ32 results in increased risk of death

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GENE EDITING CCR5

- CRISPR babies
- CRISPR stem cells in adult male

ORIGINAL ARTICLE BRIEF REPORT FREE PREVIEW

CRISPR-Edited Stem Cells in a Patient with HIV and Acute Lymphocytic Leukemia

Lei Xu, M.D., Ph.D., Jun Wang, M.D., Ph.D., Yulin Liu, B.S., Liangfu Xie, B.S., Bin Su, Ph.D., Danlei Mou, M.D., Ph.D., Longteng Wang, B.S., Tingting Liu, M.D., Xiaobao Wang, B.S., Bin Zhang, M.D., Ph.D., Long Zhao, Ph.D., Liangding Hu, M.D., et al.

September 26, 2019

- Only 5-8% cells retained edited CCR5 in 19 months of follow-up post transplant

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CURRENT CCR5 GENE EDITING TRIALS

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Currently recruiting

- **CRISPR** (China, n=5) NCT03164135
- **ZFN (SB-728T)** (USA, n=30) NCT03666871
- **CAR/ZFN** (USA, n=12) NCT03617198

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Completed

- **ZFN x 5** (total n=78)
- **Cal1 (shRNA + fusion inhibitor)** (n=12)

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Active, not recruiting

- **ZFN** (n=12)
- **Lentivirus (shRNA)** (n=3)

clinicaltrials.gov 15.10.19

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Cure conversation

Combination trials

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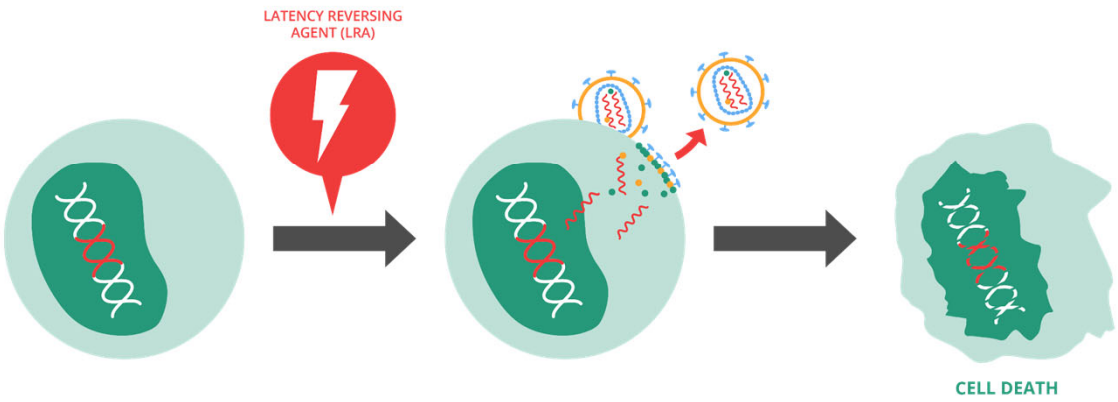
LATENCY REVERSING AGENTS



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LATENCY REVERSING AGENTS

Examples

- Histone deacetylase inhibitors (HDACi) e.g. vorinostat, romidepsin
- Anti-alcohol drug, disulfiram
- TLR agonists e.g. vesatolimod (GS-9620), lefitolimod (MGN1703)

Pros

- Many agents already licenced for human use
- Can 'switch on' viral production from latent cells

Cons

- Trials so far have not shown a reduction in the HIV reservoir
- Effects are not HIV-specific
- Safety concerns with effects on gene expression (HDACi)

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WHY COMBINATION?

- Single agents not effective
- Some evidence of activation (e.g. RNA production)
- No evidence of reservoir depletion (e.g. drop in DNA levels)

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THE TITAN TRIAL

- Combining a **T**LR9 agon**I**st with broadly neu**T**ralizing **AN**tibodies for reservoir reduction and immunological control of HIV infection

TLR agonist
Lefitolimod

bNAbs
3BNC117
+
10-1074

- Denmark (Australia, USA)
- Blinded, placebo-controlled study
- Includes analytical treatment interruption

clinicaltrials.gov NCT03837756

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THE TITAN TRIAL

Inclusion
- HIV+ adults (18-65 yrs)
- ART >18 mths (VL <50 copies/mL 15 mths)
- CD4 >500 cells/mL
- Sensitivity to 3BNC117 and 10-1074

Exclusion
- Acute medical illness or evidence of AIDS-defining opportunistic infection
- Hepatitis B or C co-infection
- History of cancer or organ transplantation
- People unwilling to use barrier contraception during ATI

- **Primary endpoint:** time to viral load rebound >10,000 copies/mL
- **Secondary endpoints:** safety and tolerability, plasma RNA doubling time

clinicaltrials.gov NCT03837756

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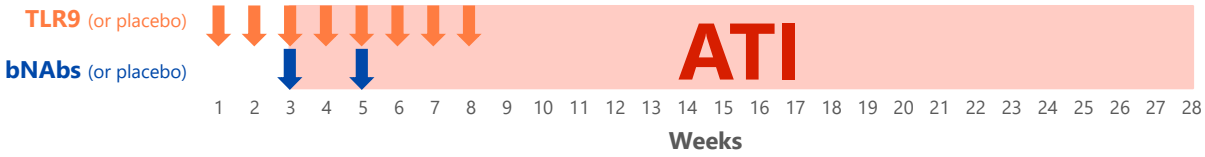
THE TITAN TRIAL

- 4 groups:

1	Placebo	Placebo
2	**Lefitolimod**	Placebo
3	Placebo	**3BNC117/10-1074**
4	**Lefitolimod**	**3BNC117/10-1074**



clinicaltrials.gov NCT03837756

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What else would you like to know to feel more confident talking about HIV cure?

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