Allogeneic Stem Cell Transplantation in HIV-1 infected individuals; the EpiStem Consortium

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Project to guide and investigate the potential for HIV cure in HIV-infected patients requiring allogeneic stem cell transplantation for hematological disorders

Supported by AmfAR Research Consortium on HIV eradication (ARCHE)

www.epistem-project.org
To guide clinicians involved in allogeneic SCT procedures in HIV infected individuals on

- Clinical procedures (access to expert panel of hematologists, ID specialists, virologists, immunologists and pharmacologist)
- Ethical issues/IRB procedures
- Donor Search and CCR5Δ32 screening
- Sampling Strategy
- Access to advanced ultra-sensitive virological and immunological assays to gain insight in HIV persistence
To systematically study samples from HIV infected patients receiving allogeneic SCT aiming at:

- quantification of the viral reservoirs
- molecular and functional characterization of infecting virus
- assessment of the dynamics of the innate and adaptive immune responses

to understand the biological bases of a potential new case of HIV-1 cure
Country Overview

24 patients included with hematological cancer
15 patients received an SCT

Patients included in EpiStem
Potential new patients
EpiStem Patient Overview post SCT

N = 15

Months post-transplantation

<table>
<thead>
<tr>
<th>Patient</th>
<th>Donor Type</th>
<th>CCR5</th>
<th>CCR5</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>WT/WT</td>
<td>Δ32/Δ32</td>
<td></td>
</tr>
<tr>
<td>Adult Donor</td>
<td>9*</td>
<td>3</td>
<td>12</td>
</tr>
<tr>
<td>Umbilical cord</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Total</td>
<td>10</td>
<td>5</td>
<td>15</td>
</tr>
</tbody>
</table>

*One CCR5 Δ32/WT

Donor Types:
- wt/wt donor
- wt/Δ32 donor
- Δ32/Δ32 donor

Living Status:
- Alive

Surveillance:
- Blood
- Apheresis
- Bone Marrow
- CSF
- Ileum biopsies
Viral Reservoir Analysis

Total HIV-1 DNA over time

Median (Q1,Q3)

Total HIV-1 DNA copies per 10^6 PBMC or CD4+ T-cells

Years on ART

TIME BEFORE/AFTER SCT (DAYS)

-100 0 100 200 300 400 500 600 700

Number
EpiStem Patient overview

Months post-transplantation

- **Pt 17**
- **Pt 1**
- **Pt 19**
- **Pt 3**

### CCR5 WT/WT vs. CCR5 Δ32/Δ32

<table>
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<tr>
<th>Donor Type</th>
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<th>Pt 19</th>
<th>Pt 3</th>
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<td>5</td>
<td></td>
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</tbody>
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*One CCR5 Δ32/WT

- **Blood**
- **Apheresis**
- **Bone Marrow**
- **CSF**
- **Ileum biopsies**

- **wt/wt donor**
- **wt/Δ32 donor**
- **Δ32/Δ32 donor**

- **Alive**
- **Cord blood donor**

msalgado
Patient 1

- Myeloblastic conditioning
- Cord Blood (5/6)
- HLA- Mismatched donor
- Burkitt NHL

Cord Blood (5/6) → CCR5 WT donors → Chimera. 0.2% BM/0.1% PB No GvHD → eART continued → +29 month post SCT

towards an HIV Cure
people focused science driven
Patient 1
- Myeloablative conditioning
- Cord Blood (5/6)
- Burkitt NHL
- HLA- Mismatched donor
- CCR5 WT donors

2012
- Chimera: 0.2% BM/0.1% PB
- No GvHD
- cART continued

+29 month post SCT

Patient 19
- Reduced intensity conditioning
- CCR5d32 homozygous donor
- AML
- HLA- Matched unrelated donor (10/10)

2013
- Chimera: Full GvHD
- cART continued

+37 month post SCT
Viral reservoir analysis

- Leucopheresis was performed or multiple 500 ml blood draws were taken for ddPCR and qVOA
- SCA was performed on 10 ml plasma
- Multiple biopsies were taken
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<th>Patient 3</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Single copy assay</strong> (HIV-RNA cp/mL)</td>
<td>5</td>
<td>-</td>
<td>Undetectable</td>
</tr>
<tr>
<td><strong>Total DNA</strong> (cp/10e6 CD4)</td>
<td>25</td>
<td>Undetectable</td>
<td>Undetectable</td>
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<tr>
<td><strong>qVOA (IUPM)</strong></td>
<td>0.034</td>
<td>Undetectable</td>
<td>Undetectable</td>
</tr>
<tr>
<td><strong>Ileum (CD4 cells)</strong></td>
<td>-</td>
<td>Trace</td>
<td>Undetectable</td>
</tr>
</tbody>
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<table>
<thead>
<tr>
<th></th>
<th>No GvHD</th>
<th>GvHD</th>
<th>GvHD</th>
</tr>
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<tbody>
<tr>
<td><strong>CCR5WT</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>CCR5d32</strong></td>
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Patient 1: CCR5WT
Patient 19: CCR5d32
Patient 3: CCR5WT
Preliminary Conclusions

- Preliminary analysis shows a systematic reduction of HIV-1 reservoirs to very low levels post SCT

- In two cases with long term follow up we were unable to detect infectious virus in blood independent of the CCR5 status of the donor

- In tissue only traces of HIV DNA could be detected

- We hypothesize that the “graft versus HIV-1 reservoir effect” contributes to the clearance of the viral reservoir.
Acknowledgements

The EpiStem consortium

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EpiStem researchers & project management

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