

**Table 3: Lymphocytes analysis in the organs of Artemis mice treated by gene therapy**

**Bone marrow Sca1+ cells from Artemis-deficient mice (Art-/-) were transduced by PGK-Art lentiviral vector and transplanted in Artemis-deficient mice after 3Gy irradiation**

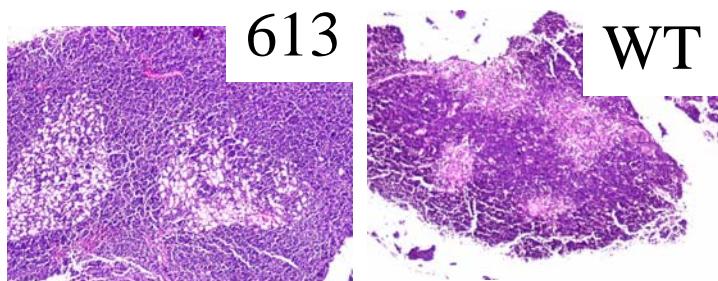
**Mouse 613 was analysed 6 months after transplantation.**

|                                    | <b>5 Weeks PT</b> | <b>15 Weeks PT</b> | <b>25 Weeks PT</b> |
|------------------------------------|-------------------|--------------------|--------------------|
| <b>PBL ( cells/mm<sup>3</sup>)</b> | 720               | 1400               | 1200               |
| <b>T lymphocytes</b>               |                   |                    |                    |
| CD3+/CD4+ (%)                      | 10.4              | 16.2               | 6.3                |
| total CD3+/CD4+                    | 75.2              | 227.4              | 75.6               |
| CD3+/CD8+ (%)                      | 6.5               | 9.4                | 6.6                |
| total CD3+/CD8+                    | 46.6              | 131.6              | 79.2               |
| CD4+/CD8+ (%)                      | ND                | ND                 | 0.3                |
| total CD4+/CD8+                    | ND                | ND                 | 0.2                |
| CD3+/TCRb+ (%)                     | 17.4              | 27.4               | 14.6               |
| total CD3+/TCRb+                   | 125.5             | 383.6              | 11.6               |
| <b>B lymphocytes</b>               |                   |                    |                    |
| B220+ /IgM+ (%)                    | 1.7               | 2.6                | 1.9                |
| total B220+ /IgM+                  | 12                | 36.4               | 22.8               |
| B220+ /IgD+ (%)                    | 0.8               | 2.6                | 1.9                |
| total B220+ /IgD+                  | 5.6               | 36.4               | 22.8               |
| <b>Myeloid cells</b>               |                   |                    |                    |
| Gr1+ /Mac1+ (%)                    | ND                | <b>40</b>          | <b>41</b>          |
| total Gr1+ /Mac1+                  | ND                | 560                | 491.6              |
| Gr1- /Mac1+ (%)                    | ND                | 9                  | ND                 |
| total Gr1- /Mac1+                  | ND                | 126                | ND                 |
| NK1.1+ (%)                         | ND                | 12.7               | ND                 |
| total NK1.1+                       | ND                | 177.8              | ND                 |

**25 Weeks PT**

|                      | <b>Spleen</b>       | <b>Lymph nodes</b>  | <b>Thymus</b>             | <b>BM</b>            |
|----------------------|---------------------|---------------------|---------------------------|----------------------|
|                      | 15.10 <sup>6</sup>  | 4.3.10 <sup>6</sup> | <b>312.10<sup>6</sup></b> | 31.5.10 <sup>6</sup> |
| <b>T lymphocytes</b> |                     |                     |                           |                      |
| CD3+/CD4+ (%)        | 18.7                | 42.3                | 4                         | 1                    |
| total CD3+/CD4+      | 2.8.10 <sup>6</sup> | 1.8.10 <sup>6</sup> | 12.5.10 <sup>6</sup>      | 3.1.10 <sup>5</sup>  |
| CD3+/CD8+ (%)        | 11.6                | 41.7                | 3.9                       | 1.4                  |
| total CD3+/CD8+      | 1.7.10 <sup>6</sup> | 1.8.10 <sup>6</sup> | 12.3.10 <sup>6</sup>      | 4.2.10 <sup>5</sup>  |
| CD4+/CD8+ (%)        | 0.5                 | 0.9                 | <b>96.8</b>               | 0.3                  |
| total CD4+/CD8+      | 7.5.10 <sup>4</sup> | 3.9.10 <sup>4</sup> | 302.10 <sup>6</sup>       | 7.9.10 <sup>4</sup>  |
| CD3+/TCRb+ (%)       |                     | 83                  | 4.2                       |                      |
| total CD3+/TCRb+     |                     | 3.6.10 <sup>6</sup> | 13.10 <sup>6</sup>        |                      |
| <b>B lymphocytes</b> |                     |                     |                           |                      |

|                      |                  |                  |     |                  |
|----------------------|------------------|------------------|-----|------------------|
| B220+ /IgM+ (%)      | 23.2             | 8.2              |     | 0.5              |
| total B220+ /IgM+    | $3.5 \cdot 10^6$ | $3.5 \cdot 10^5$ |     | $1.6 \cdot 10^5$ |
| B220+ /IgD+ (%)      | 19.2             | 7.4              |     | 0.5              |
| total B220+ /IgD+    | $2.9 \cdot 10^6$ | $3.2 \cdot 10^5$ |     | $1.6 \cdot 10^5$ |
| <b>Myeloid cells</b> |                  |                  |     |                  |
| Gr1+ /Mac1+ (%)      | 1.5              |                  |     | 45.2             |
| total Gr1+ /Mac1+    | $2.2 \cdot 10^5$ |                  |     | $1.4 \cdot 10^7$ |
| Chimerism (%)        |                  | 58               | 56  | 7                |
| PGK-Art (copy/cell)  |                  | 0.3              | 0.9 | 0.05             |



Immunohistochemical staining performed on thymus section demonstrated the disturbed architecture of this organ

**Bone marrow Sca1+ cells from Artemis-deficient mice (Art-/-) were transduced by EF1 $\alpha$ -Art lentiviral vector and transplanted in Artemis-deficient mice after 5Gy irradiation**

**Mouse 8 was analysed 9 months after transplantation.**

|                                    | <b>5 Weeks PT</b> | <b>15 Weeks PT</b> | <b>25 Weeks PT</b> |
|------------------------------------|-------------------|--------------------|--------------------|
| <b>PBL ( cells/mm<sup>3</sup>)</b> | 1440              | 1260               | 1000               |
| <b>T lymphocytes</b>               |                   |                    |                    |
| CD3+/CD4+ (%)                      | 6.9               | 19.3               | 2.6                |
| total CD3+/CD4+                    | 99.5              | 243.2              | 25.5               |
| CD3+/CD8+ (%)                      | 5.1               | 13.3               | 1.9                |
| total CD3+/CD8+                    | 72.7              | 167.6              | 18.8               |
| CD4+/CD8+ (%)                      | ND                | ND                 | ND                 |
| total CD4+/CD8+                    | ND                | ND                 | ND                 |
| CD3+/TCRb+ (%)                     | 11.9              | 30.9               | 6.4                |
| total CD3+/TCRb+                   | 171.9             | 388.7              | 64.1               |
| <b>B lymphocytes</b>               |                   |                    |                    |
| B220+ /IgM+ (%)                    | 3                 | 8.6                | 0.7                |
| total B220+ /IgM+                  | 42.5              | 108.4              | 6.9                |
| B220+ /IgD+ (%)                    | 2.8               | 8.6                | 0.7                |
| total B220+ /IgD+                  | 40.3              | 108.4              | 6.6                |
| <b>Myeloid cells</b>               |                   |                    |                    |
| Gr1+ /Mac1+ (%)                    | ND                | <b>38</b>          | 4.4                |
| total Gr1+ /Mac1+                  | ND                | 478.8              | 44.2               |
| Gr1- /Mac1+ (%)                    | ND                | 34.8               | 6.4                |
| total Gr1- /Mac1+                  | ND                | 438.5              | 64.4               |
| NK1.1+ (%)                         | ND                | 0.2                | 0.9                |
| total NK1.1+                       | ND                | 1.9                | 8.7                |

|                        | <b>Spleen</b> | <b>liver</b> | <b>Lymph nodes</b> | <b>Thymus</b> | <b>Ascite</b> |
|------------------------|---------------|--------------|--------------------|---------------|---------------|
| Chimerism (%)          | 71            | 64           | 100                | 97            | 95            |
| PGK-Art<br>(copy/cell) | 3             | 3            | 1.9                | 2.1           | 2             |

**Mouse 31 was analysed 4 months after transplantation.**

|                                    | <b>5 Weeks PT</b> | <b>15 Weeks PT</b> |
|------------------------------------|-------------------|--------------------|
| <b>PBL ( cells/mm<sup>3</sup>)</b> | 2880              | 1240               |
| <b>T lymphocytes</b>               |                   |                    |
| CD3+/CD4+ (%)                      | 15.5              | 19.8               |
| total CD3+/CD4+                    | 446.4             | 245.5              |
| CD3+/CD8+ (%)                      | 5.7               | 13.8               |
| total CD3+/CD8+                    | 162.7             | 171.1              |
| CD4+/CD8+ (%)                      | ND                | ND                 |
| total CD4+/CD8+                    | ND                | ND                 |
| CD3+/TCRb+ (%)                     | 21.5              | 31.2               |
| total CD3+/TCRb+                   | 619.2             | 386.9              |
| <b>B lymphocytes</b>               |                   |                    |
| B220+ /IgM+ (%)                    | 1.9               | 6.9                |
| total B220+ /IgM+                  | 54.7              | 85.6               |
| B220+ /IgD+ (%)                    | 2.4               | 6.6                |
| total B220+ /IgD+                  | 69.1              | 81.8               |
| <b>Myéloid cells</b>               |                   |                    |
| Gr1+ /Mac1+ (%)                    | ND                | <b>33.4</b>        |
| total Gr1+ /Mac1+                  | ND                | 413.5              |
| Gr1- /Mac1+ (%)                    | ND                | <b>23.4</b>        |
| total Gr1- /Mac1+                  | ND                | 290.2              |
| NK1.1+ (%)                         | ND                | <b>35</b>          |
| total NK1.1+                       | ND                | 434                |

|                        | <b>Spleen</b> | <b>Lymph nodes</b> |
|------------------------|---------------|--------------------|
| Chimerism (%)          | 47            | 44                 |
| PGK-Art<br>(copy/cell) | 1.4           | 3.5                |

PT = post-transplantation

PBL = peripheral blood cells

ND = Not done

The chimerism is calculated as followed: % donor cells / %recipient cells