ANALYTIC TREATMENT INTERRUPTION (ATI) AFTER ALLOGENEIC CCR5-D32 HSCT FOR AML IN 2013
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BACKGROUND

As reported before (CRCI 2016) a now 49y old HIV-infected male patient did receive unmodified HSCT from a female 10/10 CCR5-d32 DKMS-donor in February 2013 because of acute myeloid leukemia while being in 2nd complete remission (CR).

- By then proviral DNA load was 29400 cop/mL and all anticipated bands could be detected by western blot.
- At the time of HSCT coreceptor-usage was predicted as R5-tropic (Sanger: FPR 44.5%; NGS: 0.14% X4 at 3.5% FPR, geno2phen).

METHODS

PBMC and tissues were analysed by ddPCR, qPCR and in situ hybridization in several laboratories as well as humeral and T-cell responses. Infectious virus was analysed on CD4+ T cells (qVOA, MVOA). Patient was registered to icistem as patient #19.

POST-TRANSPLANTATION

- Concerning HIV, all PBMC samples were negative for proviral DNA by conventional and digital droplet PCR in different labs at multiple time points.
- Liquor (July 2014), rectum (April 2015, March 2016), ileum (March 2016) and bone marrow (August 2015) showed also negative test results.
- Further testing with 0.1 Mio cells from the ileum showed 1/4 replicates positive with LTR, but negative with gag-primers. There were also 2 positive signals in T-cell subsets (Tcm, 0.2 Mio cells: ddPCR 6.7 cop/10^6 cells, qPCR neg., Tcm 0.96 Mio cells: qPCR 5 cop/10^6 cells, ddPCR neg.) with all other subsets negative in ddPCR and qPCR.
- No HIV-DNA could be detected by PCR in lymph nodes collected 05/17, but via in situ hybridization assays (DNAscope, RNAscope) few positive signals were detected.
- Viral outgrowth assays (VOA) were negative February 2016, March 2016 and May 2016 (23 Mio CD4+ Tcells, IUPM <0.031/10^6 CD4 T cells).
- Mouse viral outgrowth assays (mVOA, April 2016 RAG2/-/-, April 2017 NOD SCID IL2Rg/-/-) also showed negative test results.
- CTL assays showed a strong response against HLA-A2-epitope Y9V (RT) and HLA-B7-epitope Y9 (Gag-P6), which was not present in cells from the stem-cell donor.
- The Western blot shows an incomplete pattern (gp160 slightly positive, others negative).

SUMMARY & CONCLUSION

- Despite low signals in ultrasensitive assays no virus could be detected in qVOA/mVOA in the Duesseldorf patient. Taking into account the homozygous CCR5-d32 status we consider a viral rebound to be unlikely.
- Since the functional relevance is unclear an ATI is the only way to find out whether HIV has been eradicated by allogeneic CCR5-d32 HSCT.
- Therefore ART was stopped in November 2018 after thorough discussion with the patient.
- Plasma viral load and proviral DNA is measured twice weekly since stopping cART, immunological follow-up is performed monthly.
- Despite all plasma samples being negative after ATI longer surveillance is essential.

We are grateful to the patient for his participation and commitment.