Table 1: Summary of results of clinical trials

Target cells	Vector	Transgene	Anti-HIV method	Results
$CD8^+$	Retrovirus	HyTk	Introduction of suicide gene	CTL response cleared modified cells [16].
$CD4^+$	Gold-particle-mediated	Rev M10	Transdominant negative protein	Detected Rev M10 until 2 months post infusion, preferential survival [36].
$CD4^+$	Retrovirus	Rev M10	Transdominant negative protein	Detected Rev M10 until 6 months post infusion, preferential survival [37].
$CD4^+$	Retrovirus	TdRev and/or anti-sense TAR	Transdominant negative proteins and anti-sense RNA	Anti-HIV genes consistently detected for >100 weeks in six of six patients. Preferential survival of transduced cells during a period of high viral load in one patient [47].
$CD34^+$	Retrovirus	TdRev	Transdominant negative protein	One patient died due to relapse to Hodgkin's disease. In second patient, detected vector in the progeny for >3 years, remission of leukemia and good viral load control achieved by administering HAART that cannot be attributed to gene therapy [38,39].
$CD34^+$	Retrovirus	huM10	Transdominant negative protein	huM10 could be detected in peripheral blood mononuclear cells (PBMC) for 1–3 months and then dropped to at or below the limit of detection over a two year follow-up period. Preferential survival of transduced cells during a period of high viral load in one patient [40].
$CD4^+$	Retrovirus	CD4ζ	Chimeric receptor	Decrease of greater than 0.5 log mean in rectal tissue-associated HIV RNA for at least 14 days, detected CD4ζ in 1–3% of PBMCs at 8 weeks [42]
$CD4^+$	Retrovirus	CD4ζ	Chimeric receptor	Good expression of CD4ζ for at least 24 weeks in all patients; no difference between control and study group [43].
$CD4^+$ and $CD8^+$	Retrovirus	CD4ζ	Chimeric receptor	In 11 of 12 patients who received higher doses of modified $CD8^+$ cells (10^9 or 10^{10}), CD4ζ could be detected post-infusion for at least 15–40 weeks when they received additional infusions of modified cells. The group receiving IL-2 along with modified $CD8^+$ cells showed a higher persistence of CD4ζ as compared to the group receiving no IL-2. In patients who received modified $CD8^+$ and $CD4^+$ cells, the cells were detected in the peripheral blood for at least 1 year post-infusion [41].
$CD34^+$	Retrovirus	(RRE) decoy	RNA decoy	RRE-decoy-containing leukocytes could be isolated from peripheral blood even 1 year post-infusion but the numbers were extremely low [44].
$CD4^+$	Retrovirus	RRz2	Ribozyme	Over a 4 year period, PBMCs containing both RRz2 and LNL6 were consistently detected [46].
$CD34^+$	Retrovirus	*tat*/*vpr* ribozyme	Ribozyme	Vector was detected in naïve T cells for >3 years; no correlation between changes in viremia or CD4+ T cell counts with vector expression or its detection in any cell type [45].

HIV-positive patients [40]. Two children were enrolled in this study, a nine-year-old and an eight-year-old who were both on HAART. $CD34^+$ bone marrow cells from the participants were transduced with two retroviral vectors, one encoding a "humanized" dominant negative REV protein (huM10) and one encoding an internal control for gene marking (FX) that is not translated. A humanized protein is one in which the codon usage has been optimized for mammalian expression. Following infusion of the modified cells, huM10 and FX could be detected in peripheral blood mononuclear cells (PBMC) for 1–3 months. During a two-year follow-up period, levels of huM10 and FX expression dropped to at or below the limit of detection. In one patient, during a period of non-compliance to HAART regimen, PBMCs containing huM10 reappeared suggesting a selective increase in survival for PBMCs containing huM10 during periods of high viral loads [40].

Using a chimeric receptor approach, Walker *et al.* (2000) investigated the effect of CD4ζ-modified syngeneic T-cells in HIV-positive patients [41]. The study was conducted using sets of twins, one of whom was HIV-positive and the other HIV-negative. The HIV-negative twin acted as the donor for syngeneic T-cells (either $CD8^+$ or $CD4^+$), while the HIV-positive twin was the recipient. T cells from the donor were genetically modified *ex vivo* to express CD4ζ and then transfused into the recipient twin. The study was performed in two phases.

In the first phase, 27 patients were enrolled and received one to six cell infusions every eight weeks. Three patients received 10^7 modified cells, while the remaining 24 patients were randomly assigned to four groups, receiving either 10^8, 10^9, or 10^{10} modified cells or 10^{10} unmodified cells. The researchers observed that one of three subjects receiving 10^7 cells and four of six subjects receiving 10^8 cells showed low levels of CD4ζ expression. In three of these five CD4ζ-positive patients, CD4ζ was no longer detected after one to three days, but in two of them, CD4ζ could be detected for up to 2 and 24 weeks, respectively. In 11 of 12 patients receiving higher doses and multiple infusions of modified $CD8^+$ cells, CD4ζ could be detected for up to 15 to 40 weeks post-infusion [41].

In the second phase of the Walker *et al*. trial, 33 patients were enrolled, 25 from the previous phase and 8 new par-