

## Special Article - Hematopoietic Stem Cell Transplantation

# The Use of Donor Mesenchymal Stem Cells in the Treatment of Steroid Refractory Graft Versus Host Disease. Ten Years of Single Center Experience

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## Short Communication

During the years 2003-2012 there were 94 sibling allogeneic stem cell transplants (alloTx) performed at the National Cancer Institute, Bratislava, Slovakia. From them 43 (46%) patients were treated with reduced intensity conditioning (RI) and 10 (11%) patients received a HLA haploidentical graft. Eight patients (8.5%) developed steroid refractory graft versus host disease (GVHD). After obtaining a general approval from Ethics Committee, all 8 patients had been eligible for the infusion of freshly prepared *ex vivo* expanded mesenchymal stem cells (MSC). The MSC for *ex vivo* expansion were isolated from the bone marrow of the sibling donor and expanded according to Koç, et

al. [1]. The patients' characteristics are shown in the Table 1. The mean number of the MSC infused was  $0.4 \times 10^6$  cells per kg of body weight. (Range  $0.3-0.5 \times 10^6$  cells/kg). Two patients (No 5 and 7) received the MSC twice. Four patients died because of refractory GVHD. From the other 4 patients, two died because of the disease progression, one because of the fungal infection and one is alive up to 10 years after alloTx in complete remission without any signs of cGVHD. It should be noted that all patients were heavily pretreated but the last one who is alive, with more than 5 lines of chemotherapy including autologous stem cell transplantation. Nevertheless, the steroid refractory GVHD resolved in half (4) of them. Moreover it seems to be plausible to have the MSC "in stock" for rapid *ex vivo* expansion in order to use the cells freshly prepared (not frozen, thawed and immediately applied) [2].

## References

- Koç O, Gerson S, Cooper B, Dyhouse SM, Haynesworth SE, Caplan AI, et al. Rapid hematopoietic recovery after co-infusion of autologous culture-expanded human mesenchymal stem cells (hMSCs) and PBPCs in breast cancer patients receiving high dose chemotherapy. *J Clin Oncol*. 2000; 18: 307-316.
- Lakota J. Unpublished observation.

**Table 1:** Patients' characteristics, date of transplantation, MSC infusion, date of the patients' death and the reason of death (Haplo Tx: HLA Haploidentical Transplantation; RI Tx: Reduced Intensity Conditioning Transplantation).

| Patient No | Gender | Born | Diagnosis | Transplantation | MSC infusion | Death    | Reason of death     | Comment  |
|------------|--------|------|-----------|-----------------|--------------|----------|---------------------|----------|
| 1          | M      | 1971 | AML       | 16.03.04        | d +206       | 09.11.04 | cGvHD               |          |
| 2          | M      | 1976 | HD        | 30.01.05        | d +1         | 14.02.05 | aGvHD               | Haplo Tx |
| 3          | M      | 1971 | ALL       | 13.12.05        | d +9         | 05.04.06 | disease progression |          |
| 4          | F      | 1970 | Ph- CML   | 26.04.07        | d +33        | -        | alive (31.12.16)    |          |
| 5          | F      | 1978 | HD        | 13.10.09        | d +60, d+80  | 23.02.10 | aGvHD               | RI Tx    |
| 6          | M      | 1969 | ALL       | 23.02.10        | d +168       | 16.08.10 | cGvHD               |          |
| 7          | F      | 1973 | HD        | 21.10.10        | d +92, d+178 | 22.09.11 | infection           | Haplo Tx |
| 8          | M      | 1987 | HD        | 18.10.11        | d +43        | 09.04.13 | disease progression | RI Tx    |