

## TREATMENT OF METASTATIC HEAD AND NECK CANCER WITH MESENCHYMAL STEM CELLS COMBINED WITH PRODRUG GENE THERAPY

J. Lakota<sup>1,2,\*</sup>, K. Gocarova<sup>3</sup>, S. Spanik<sup>3</sup>

<sup>1</sup>Laboratory of Molecular Oncology, Cancer Research Institute, Slovak Academy of Sciences, Bratislava 83391, Slovakia

<sup>2</sup>Center for Cell Therapy and Regenerative Medicine, St. Elizabeth Cancer Institute, Bratislava 81250, Slovakia

<sup>3</sup>Department of Medical Oncology, St. Elizabeth Cancer Institute, Bratislava 81250, Slovakia

This is a clinical observation of a patient treated for metastatic head and neck cancer with mesenchymal stem cells mediated prodrug gene therapy. The cells were applied intravenously. We did not observe any therapeutic effect. However, a temporal bicytopenia was observed.

**Key Words:** metastatic head and neck cancer, therapeutic stem cells, blood counts.

A 41 years old male patient with squamous carcinoma of the tongue (T2N0M0) refused any adjuvant chemotherapy after the surgery. He developed lung metastases 9 months after the second surgery for local relapse. After an approval of the Ministry of Health of the Slovak Republic, on day -2 he was admitted to the hospital. Infusion of Ancotil (2.5 g flucytosine/250 ml solution) started on day -1 bid 24 hours before the administration of therapeutic stem cells (TSC), and continued for 7 days. On day 0 the patient received  $60 \times 10^6$  allogenic TSC intravenously. The therapeutic adipose tissue-derived mesenchymal stem cells were prepared as described previously [1]. There were no adverse effects during and 6 h after the administration. 18 hours after the intravenous administration of the TSC, the patient developed fever (39.0 °C) with no signs of circulation instability. The fever resolved after antipyretics. There were no signs of any microbial infection. The following days the patient remained afebrile. Due to a sudden drop of white blood cells he received an oral antibacterial and antimycotic prophylaxis. On the day +6 he was discharged from the hospital with almost normalized blood counts. On day +18 during the outpatient control he was doing well. His blood counts (except mild anemia) were normal (Table). The CT scan performed on day +6 showed no difference in the size or density of his pulmonary metastases compared to the CT scan on day -1. On the day +40 there were signs of a progression of the metastases on the CT scan.

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\*Correspondence: E-mail: jan.lakota@savba.sk

Abbreviation used: TSC – therapeutic stem cells.

**Table.** Blood counts of the patient during and after the therapy

Day	Leukocytes ( $\times 10^{12}/l$ )	Neutrophils ( $\times 10^{12}/l$ )	Erythrocytes ( $\times 10^{15}/l$ )	Hb (g/l)	Pit ( $\times 10^{14}/l$ )
-2	6.88	4.86	4.41	134	179
0	5.82	3.98	3.71	119	150
+1	4.06	3.41	3.80	119	119
+2	<b>1.99</b>	<b>1.00</b>	3.41	112	<b>100</b>
+3	2.89	1.58	3.72	117	115
+4	3.50	2.16	3.72	115	122
+5	4.50	2.98	3.79	118	129
+6	4.29	2.63	3.89	121	132
+18	6.57	4.66	4.06	125	191

The treatment with TSC of this patient highlighted two points: 1) There was no sign of any therapeutic effect after intravenous (not local, i.e. intratumoral) administration of the TSC. 6 days after the administration the metastatic process did not show any signs of regression. Moreover, after 40 days after the treatment there was a progression of the metastases. 2) After the intravenous administration the TSC are probably "homing" in the bone marrow despite the adipose tissue origin. Even a rather low cell count ( $60 \times 10^6$ ) was able to cause grade 2 (3) thrombopenia (neutropenia). It should be noted that this patient did not receive any systemic chemotherapy in the past. The observed bicytopenia with a nadir occurred 48 h after the administration of TSC (with concomitant prodrug administration). Therefore it should be carefully considered when a medical team decides to use the intravenous route.

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### REFERENCE

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