25TH NATIONAL & 11TH INTERNATIONAL ANNUAL CONGRESS | ON RESEARCH AND TECHNOLOGY OF IRANIAN MEDICAL SCIENCES STUDENTS
URMIA UNIVERSITY OF MEDICAL SCIENCES, URMIA, IRAN

Emerging Therapeutic Roles of Natural Killer Cells in Patients with Multiple Myeloma: A Systematic Review

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Citation:
Farokhi M, Dashti M R, Khani-Eshratabadi M. Emerging Therapeutic Roles of Natural Killer Cells in Patients with Multiple Myeloma: A Systematic Review. *Iranian biomedical journal* 2024; 28(7): 157.

ABSTRACT

Introduction: Multiple myeloma (MM) is a proliferation of tumoral plasma B cells, which is still incurable. MM is a disease with known immune dysregulation; thus, a novel medical approach is needed. Natural killer (NK) cells are very potent effector lymphocytes that play an important role in immune surveillance for cancer, limiting neoplastic progression and effectors of anti-tumor therapies. NK cells can recognize and kill/limit MM cells growth in vitro; therefore, the present study aimed to investigate NK cell therapy in patients with MM.

Search Study: This systematic review included studies from WOS, PubMed, and Scopus databases (up to 2024). Two researchers independently and systematically searched in the mentioned databases using MeSH term keywords "Killer Cells" and "Natural" AND "Therapeutics" AND "Multiple Myeloma". Combining keywords was used to broaden the search results. Inclusion criteria entailed English language, MM disease, NK cell intervention. Exclusion criteria comprised non-English language studies, cell culture methods, other leukemias, other forms of cell therapy, and studies with uncertain results. Clinical trial studies were included, while animal models, cell lines, case reports, expert opinions, letters to editor, and reviews were excluded. Two researchers were selected to gather the data individually. The collected information from the studies included the primary author's name, publication year, trial phase, patient characteristics, number of patients, age, sex, intervention route, and dose, response, and adverse events.

Results: A total of 313 studies were identified. After excluding duplicate and unrelated articles, 169 were screened. Of 169 articles, 24 were selected for the screening of titles and abstracts eligibility assessment. After a comprehensive evaluation of the full texts, only four studies were included in the analysis. These four studies assessed the therapeutic roles of haploidentical NK cells, off-the-shelf NK cell products, and allogeneic NK cell that were culture-expanded and differentiated from human placental $CD34^+$ stem cells (PNK-007), as well as umbilical cord blood-derived NK cells, in a total of 37 patients across phases I and I/II. Among these patients, 10 exhibited increased degranulation and cytokine production activities, although there was a decrease in perforin expression in their NK cells. In 20 patients, the treatment was found to be safe and well-tolerated, with no cases of graft-versus-host disease and no infusion-related toxicities. Additionally, 15 patients were observed to be minimal residual disease negative. Of the total, 10 patients achieved complete remission, while 18 showed partial response, and 2 patients died.

Conclusion and Discussion: The findings of our study demonstrate the feasibility of NK cell therapy in MM and highlight the need to inform the design of future clinical studies.

Keywords: Multiple myeloma, Natural killer cells, Therapy