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Cell therapy of cancer with alloreactive intentionally mismatched IL-2 activated donor lymphocytes targeting anti-cancer killer NK & T cells using monoclonal and bispecific antibodies

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Graft vs. leukemia or solid tumors effects following allogeneic stem cell transplantation (SCT) are well established, however, use of SCT may be hazardous and associated with unavoidable graft-vs-host disease (GVHD). It was investigated whether short-term immunotherapy could be induced by intentionally mismatched alloreactive killer NK and T cells (IMAK), maximally activated with interleukin 2 with no SCT. Monoclonal and trifunctional bispecific antibodies (BSA) were used for targeting IMAK against antigens over-expressed on malignant cells confirmed efficacy of eradication of otherwise lethal inoculum of B16 melanoma while avoiding GVHD in mice. Successfully treated mice could also resist fresh tumor challenge, suggesting development of anti-cancer immunity by Fc binding of malignant cells to host dendritic cells and presentation to T cells cells. Commercially available monoclonal and BSA against target antigens (EGFR, VEGF, Her-2/neu, CD20, EpCAM) using Erbitux, Avastin, Herceptin, MabThera & Catumaxomab, respectively were used in a pilot clinical trial. We have confirmed that treatment of patients with hematologic malignancies and solid tumors with IMAK with (n=16) or without (n=40) targeting antibody is safe and potentially effective with no GVHD in patients with hematological malignancies and metastatic solid tumors. We are now investigating whether targeting of IMAK may be further improved using low energy acoustic shockwave therapy (AST) that may increase the perfusion of malignant tissue as well as increase binding of killer lymphocytes to cancer cells. Based on the cumulative experience we conclude that treatment with short-lived targeted IMAK may represent an effective future approach for personalized targeted cancer immunotherapy.

Biography

Shimon Slavin, MD, is Professor of Medicine, currently serving as the Medical & Scientific Director of the International Center for Cell Therapy & Cancer Immunotherapy (CTCI), Tel Aviv, and Israel. He pioneered the use of immunotherapy mediated by donor lymphocytes and innovative methods for stem cell transplantation for cure of hematological malignancies and solid tumors, and more recently, the use of multi-potent stem cells for regenerative medicine. He authors 4 books and >650 scientific publications and serves on many editorial boards and received many international awards in recognition of his excellence in basic science and clinical medicine based on his contributions towards large-scale clinical application of targeted, personalized medicine for treatment of malignant and a long list of life threatening non-malignant disorders.

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