

unique molecular genetic features, and in some cases, the therapeutic interventions. ET probably carries the lowest rate of transformation to acute myeloid leukaemia (AML), whereas MF may carry a relatively high risk; lymphoid transformation has been reported in rare cases. The risk of transformation in CML to BC in the *ABL1*-tyrosine kinase inhibitors (TKI) era appears to be quite low, <2% per annum. Transformed disease in general tends to be difficult to be managed and is associated with a poor prognosis. The best treatment strategy, therefore, remains the prevention of transformation. Allogeneic stem cell transplantation is currently the only treatment that has been observed to confer long-term benefit to a small minority of patients who qualify for it. In this presentation, I will address the evolving genetic landscape, translational research efforts and investigational therapies for transformed MPNs.

<https://doi.org/10.1016/j.htct.2020.09.016>

SP 16

The new European leukemianet recommendations for treating CML



Rüdiger Hehlmann

Twenty-two years after the first patients with chronic myeloid leukemia (CML) were treated with the tyrosine kinase inhibitor (TKI) imatinib, outcome exceeds all expectations: the vast majority of CML patients have achieved normal life expectancy and some patients in sustained deep molecular remissions (DMR) may even be operationally cured in durable treatment-free remissions (TFR). However, some expectations remain unmet. Most patients are not yet cured and require life-long maintenance therapy. Also, progression to blast crisis still occurs in 5–7% of patients and remains a challenge. CML has not become the expected model disease for treating other leukemias or cancers, but the principle of elucidating the pathogenesis as a successful approach for cancer treatment has been impressively demonstrated in CML.

New insights have emerged from maturing long-term academic and commercial clinical trials regarding optimum management of CML. Velocity of response has unexpectedly proved less important than hitherto thought, does not predict survival, and is of unclear relevance for TFR. Serious and cumulative toxicity has been observed with TKI that had been expected to replace imatinib. Generic imatinib has become cost-effective first-line treatment in chronic phase despite chronic low-grade side-effects in many patients. Earlier recognition of CML end-phase by genetic assessment might improve prospects for blast crisis. Treatment discontinuation and TFR has become an important new treatment goal of CML. Duration of DMR (MR4, MR4.5) may be the best predictor of success. To reflect this new situation, the European LeukemiaNet has recently revised and updated its recommendations for treating CML. The presentation will focus on recent developments and on current evidence for treating CML in 2020.

<https://doi.org/10.1016/j.htct.2020.09.017>

SP 17

Ex vivo activation of pleural T cells in pleural malignancies



Vera S. Donnenberg, James D. Luketich,
Albert D. Donnenberg

Introduction: MPE are uniformly fatal. It is estimated that the incidence of MPE in the United States is more than 150,000 cases per year, making this a common terminal pathway for a variety of cancers and a dire problem without a solution. Currently available cellular therapeutics are costly and often lack polyclonality, polyfunctionality, and the ability to persist as central memory. The treatment of this deadly complication is potentially at a turning point if the rich immune infiltrates that characterize the majority of effusions can be redirected to an efficacious anti-tumor response. Despite this promise, pleural immune infiltrates have not been used to generate effector cells for adoptive cellular therapy.

Objectives: We have exploited the heterogeneous cellular composition of MPE by piloting the generation of therapeutic T-cell products, using conventional methods used for expanding tumor-infiltrating lymphocytes (TIL). The advantages of plural T cells are: (1) Fewer cycles of expansion owing to several orders of magnitude greater starting number of T cells; (2) Greater initial clonal and functional heterogeneity; (3) Likelihood of preserving polyclonality, polyfunctionality and central memory.

Results: MPE have abundant tumor infiltrating CD3+ T-cells, CD19+ B-cells, CD14+ macrophages, and EpCAM-/Cytokeratin+ mesothelial cells. Regulatory T-cells, which may be abundant in TIL, are low or absent in MPE. Our laboratory's average recovery of viable nucleated cells per MPE is $7.8 \pm 4.0 \times 10^8$ cells, with viability exceeding 95%. The cellular composition (tumor, lymphocytes, macrophages, neutrophils, mesothelial cells) varies from patient to patient, but T-cell recovery averages $2.0 \pm 1.6 \times 10^8$ (mean, SD). In pilot experiments we cultured whole breast cancer MPE in the presence of anti-CD3/anti-CD28 Dynal beads, IL-2 and IL-7 for 96 h. CD3+ T cells were FACS-sorted and added to autologous tumor monolayer cultures and expanded for an additional passage (2 weeks). Expanded passage 2 T cells were compared to freshly isolated T cells (2nd MPE drainage) for ability to kill autologous tumor and non-tumor targets (live cell imaging). Expanded T cells were potently cytotoxic, whereas freshly isolated MPE had no activity against autologous tumor. Expanded T cells did not kill the autologous non-tumor target (adherent cells isolated from peripheral blood). Additionally, we tested freshly isolated breast cancer MPE T cells for the ability to secrete cytokines associated with expansion and effector generation (IL-2, IFN γ and TNF α). We also measured the immunosuppressive cytokine IL-10. Freshly isolated plastic nonadherent cells from a breast cancer MPE were incubated with TPA+ ionomycin for 1 h, followed by brefeldin for 2 h. CD4+ T cells (85%) and CD8+ T cells (9%) were gated on cells co-expressing intracellular IL-2 and IFN γ . Polyfunctional T cells, defined as IL-2+/IFN γ +/TNF α +/IL-10-, comprised 0.38%, and 0.82% of CD4+ and CD8+ T cells. Unstimulated control cultures constitutively secreted IL-10 and IFN γ but not IL-2 or TNF α .