therapy directed against CD19, such as blinatumomab and Inotuzumab. Clinical response was evaluated 1 to 2 months after CAR-T cell administration. One ALL patient died of sepsis before evaluation and one NHL patient is still awaiting his evaluation. Of 36 evaluated ALL patients, 24 (67%) achieved measurable residual disease (MRD) negative CR, 6 (17%) MRD positive CR and 5 patients (14%) progressed. One ALL patient with an initial response was treated a second time with CAR-T, but did not respond. Of 52 evaluated NHL patients, 32 (62%) achieved an objective response, including 16 complete remissions and 16 partial responses. Twenty (38%) patients had disease progression.[1,2] Notably, we recently show that CD19 CAR T-cells were able to induce remission in a patient with CD19+ AML with t (8; 21)(q22;q22.1) that relapsed 6 months post allogeneic transplant and failed re-induction. On day 28 post CAR-T CD19 infusion BM aspiration disclosed normal hematopoiesis with no excess blasts, full donor chimerism and lack of t (8; 21) by FISH confirming clinical and molecular remission.[3] We also assessed kinetic of cell phenotype on PBMCs of the CAR-T treated patients using multiparametric flow cytometry. The manufactured CAR-T products ($n = 9$) were also subjected to immunophenotypic analysis in order to elucidate the mechanisms of CAR-T cell trafficking and activity. We observed increased immunosuppressive phenotype as well as induction of T cell senescence/exhaustion in non-responding compare to responding patients.[4]

REFERENCES

1. Itzhaki O, Jacoby E, Nissani A, Levi M, Nagler A, Kubi A, et al. Head-to-head comparison of in-house produced CD19 CAR-T cell in ALL and NHL patients. J Immunother Cancer. 2020;8(1):e000148, http://dx.doi.org/10.1136/jitc-2019-000148.
2. Danylesko I, Chowers G, Shouval R, Besser MJ, Jacoby E, Shimoni A, et al. Treatment with anti CD19 chimeric antigen receptor T cells after antibody-based immunotherapy in adults with acute lymphoblastic leukemia. Curr Res Transl Med. 2020;68(January (1)):17–22, http://dx.doi.org/10.1016/j.retram.2019.12.001. Epub 2019 Dec 25.
3. Danylesko I, Jacoby E, Yerushalmi R, Shem-Tov N, Besser MJ, Vernitsky H, et al. Remission of acute myeloid leukemia with t(8;21) following CD19 CAR T-cells. Immunotherapy. 2020;34(7):1939–42, http://dx.doi.org/10.1038/s41375-020-0719-y.
4. Beider K, Besser MJ, Schachter J, Grushchenko-Polaq AH, Voevoda-Dimenshtein V, Wolf I, et al. Upregulation of senescent/exhausted phenotype of CAR-T cells and induction of both Treg and myeloid suppressive cells correlate with reduced response to CAR T cell therapy in relapsed/refractory B cell malignancies. ASH. 2019.

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SP 14

Treatment of sickle cell crises

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Sickle cell disease (SCD) is an inherited disorder prevalent in Sub-Saharan Africa, Middle East and parts of India. Its characterized by repetitive episodes of vaso-occlusive (VOC) process leading to recurrent painful episodes, hemolytic anemia and predisposition to infection. Sickle cell crises varies and this what brings patients to hospital including VOC leading to recurrent painful episodes, or organ specific complications such as acute chest syndrome, stroke, splenic sequestration, and many skeletal complications. Although the prognosis of patients with SCD has improved, however still these events contributes to decrease quality of life and increased risk of death. Also unfortunately, progress on the management of these acute complications is slow, and tended to be supportive including vaccination, use of antibiotics prophylaxis and blood transfusions. Better understanding of pathophysiology of the disease has allowed more accelerated progress on preventing these complications and development of more focused pharmacological therapies. Hemoglobin polymerization is a primary triggering event in the pathophysiology of the disease, leading to the sickling process, this usually ignite an inflammatory process/tissue ischemia and increased adhesions. This understanding of the pathophysiology has allowed scientist to develop drugs that interfere with these processes such as Voxeletor & Hydroxyurea (interfere with polymerization-both approved by FDA), L-glutamine and Omega 3 (interfere with inflammatory process and oxidative stress) and crizanlizumab and Tinzaparin (works by inhibiting adhesion molecules). This will allow patients and physicians the freedom for a number of therapeutic interventions including development of combinations protocols. SCD is very complex and require a drug with multi-faceted action such as Hydroxyurea and this is of the limiting factors in the new recently approved drugs, limiting the patients who can benefit from each of them. Further progress is also seen in the area of bone marrow transplant (including alternative donor pool) and gene therapy/gene editing.

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SP 15

Secondary acute leukemia evolving from myeloproliferative neoplasm (MPN)

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The natural history of myeloproliferative neoplasms (MPNs), both Philadelphia-chromosome positive – [chronic myeloid leukemia(CML)] and negative – [essential thrombocythemia (ET), polycythemia vera (PV), and primary myelofibrosis (PMF)] has been well documented but the mechanism underlying the apparently inexorable progression from an initial, rather indolent or chronic phase (CP) to advance phase, a term including accelerated phase (AP) and blast crisis (BC) remains obscure. Most patients with MPNs present in the indolent phase, during which myeloid progenitor numbers are greatly increased in the bone marrow and blood. This phase may continue for as little as one year or as long as 20 years or more, but eventually it transforms into acute leukaemia (BC), in which an increasing proportion of blast cells are found in the marrow and peripheral blood. The risk associated with the development of advanced-phase disease differs depending on the MPN subtype and is influenced by a number of factors such as duration of disease, clinical factors, the presence of