Treatment of higher-risk MDS is still based on hypomethylating agents (HMA) as the standard 1st line treatment, but attempts are ongoing to overcome the barrier of 50% response rate and less than 2 years response duration. Younger patients may respond to antileukemic treatment with or without transplant. Ways to improve the HMA effect include treating the HMA-related complications; modified HMA formulation; combinations of HMA with other agents (venetoclax appears to be the frontrunner), novel agents and targeted molecules.

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Sp08

Blastic Plasmacytoid Dendritic Cell Neoplasm BPDCN

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Blastic plasmacytoid dendritic cell neoplasm (BPDCN) is a rare hematologic malignancy with an aggressive clinical course and poor prognosis. BPDCN is most often characterized by its presentation with cutaneous lesions which are often asymptomatic, can be solitary or multiple lesions, can be distributed widely, and may range from bruise-like lesions to plaques or nodules. Bone marrow involvement, central nervous system (CNS) infiltration, lymphadenopathy, splenomegaly, and/or cytopenias are also seen to varying degrees.

The nomenclature has changed many times over the years, making descriptions of the epidemiology more challenging. It was first described in 1995 as acute agranular CD41 natural killer (NK) cell leukemia. In the most recent WHO 2022 classification, BPDCN is classified under dendritic cell and histiocytic neoplasms along with plasmacytoid dendritic cell proliferation associated with myeloid BPDCN is more common in older men, with a sex ratio of 3:1 to 5:1 and a median age of diagnosis between 60 and 70 years. A bimodal age distribution was recently described, with higher incidence in patients aged ,20 and .60 years.

BPDCN cells characteristically express CD123, CD4, CD56, CD303, TCF4, and TCL-1, whereas certain specific lineage markers such as CD14, cCD3, CD19, and MPO are not expressed.

Genetic mutations implicated in the pathogenesis of BPDCN include inactivating tumor suppressors (ie, TP53, RB1, CDKN1B, and CDKN2A), activating oncogenes (ie, NRAS, KRAS, FLT3, RUNX2, and HES6), activated NF-κB pathway, mutated RNA spliceosomes (ie, ZRSR2 and others), immune response gene dysregulation (IFNGR, TGFB, CLEC4C, and IFNA cluster), and epigenetic dysregulation (ie, IDH1, IDH2, TET1, TET2, and ASXL1).

Historically, BPDCN treatments have been based on multiagent chemotherapy regimens for lymphoma, acute lymphoblastic leukemia, and AML. In addition, acute leukemia regimens achieve high complete response (CR) rates ranging from 40–90% and allogeneic hematopoietic cell transplantation (allo-HCT) can result in durable remission in some patients. However, their rarity and heterogeneity make it difficult to determine the most effective therapeutic strategies.

Owing to recent advances in molecular biology and genetics, targeted treatment strategies have been developed. In 2018, the FDA approved tagraxofusp, a firstin-class CD123-targeting therapy for treatment- naïve or relapsed/refractory BPDCN.However, unfit, relapsed, or refractory patients continue to require effective therapeutic strategies.

Besides CD123 Targeted therapy; many other modalities are considered e.g. Venetoclax-based therapy, Transplantation and many new potential therapeutic targets under investigation.

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Sp09

Sustained Remission and Decreased Severity of CAR T-Cell Related Adverse Events: A Pivotal Study Report of CNCT19 (inaticabtagene autoleucel) Treatment in Adult Patients with Relapsed/Refractory B-Cell Acute Lymphoblastic Leukemia (R/R B-Cell ALL) in China

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A B S T R A C T

CNCT19 (inaticabtagene autoleucel) is an autologous CD19-specific chimeric antigen receptor (CAR) T-cell product. The patent protected CAR structure of CNCT19 contains a unique CD19 scFv, HI19a, which is different from commonly used FMC63. Together with using 4-1BB co-stimulatory domain in the CAR structure, CNCT19 is expected to reduce the severity of treatment-associated cytokine release syndrome (CRS) and neurologic toxicities (NT) while maintaining a stronger and longer durable anti-tumor effect.

CNCT19 has been granted Breakthrough Therapy Designation by China National Medical Products Administration and Orphan Drug Designation by the U.S. FDA for the treatment of ALL.

The trial of CNCT19 in adult Chinese patients with R/R B-cell ALL (NCT04684147) is a single-arm, open-label pivotal study conducted at 10 centers in China. The primary endpoint was the overall complete response rate (OCR) of complete response (CR) and CR with incomplete hematological recovery (CRi) within 3 months and at the end of Month 3 after CNCT19 infusion by central assessment.

All 39 patients diagnosed with B-cell ALL were refractory and relapsed to multiple lines of prior therapy. Among the 39 patients 32 (82.1%) had reached MRD-negative OCR within 3 months after CNCT19 infusion, The median duration of response and OS have not been reached. 25 patients (64.1%) remained on CR (51.3%) or CRi (12.8%). at the end of Month 3 after CNCT19 infusion These patients had sustained long-term remission regardless of whether subsequent allo-HSCT treatment was done or not. The most common CNCT19-related adverse events (AEs) were CRS and NT and there were

4 cases of Grade ≥ 3 CRS (n=4, 10.3%) and 3 cases of Grade ≥ 3 NT (n=3, 7.7%). Following CNCT19 infusion, all the patients recovered. No death cases were reported due to CRS or NT.

CNCT19 CAR-T cell therapy achieved a high rate of MRD-negative complete remission in adult patients with R/R B-cell ALL. Thus, with its distinct CAR structure containing a unique CD19 scFv (HI19a), CNCT19 provides effective treatment with potential long-term clinical benefits for adult patients with R/R B-cell ALL.

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Sp10

Personalized Dendritic Cell Vaccines

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Due to their ability to cross-present antigens associated with tumor cells to naive T cells, DCS play an important role in generating specific T-cell-mediated antitumor effector responses in controlling tumor growth and tumor cell dissemination. Clinical trials in this area have demonstrated the possibility of immunotherapy based on dendritic cells. In the current study, we give a brief overview of the biology of DC, describe the sources of obtaining tumor-associated antigen, and also consider the current status of the field of application of DC as anti-cancer vaccines.

Methodology: Peripheral blood mononuclears were used in the work, as well as lung tumor cells, from which tumor lysate was obtained. Tumor lysate was obtained by freezing and thawing a cell suspension by placing an ampoule with cells in liquid nitrogen or warm water, respectively. Dendritic cells were obtained by culturing human peripheral blood monocytes. The key cytokines used in the cultivation of DC from monocytes are GM-CSF and interleukin-4 (IL-4). DC was loaded with antigens after replacing the culture medium with the addition of tumor lysate to the cells and incubation for 2 hours. The main way to assess the quality of the vaccine created on the basis of DC was the method of flow cytofluorimetry. The main characteristics by which DC is evaluated are the immunophenotype and the percentage of living cells.

Conclusion: The proven method of obtaining dendritic cells loaded with tumor lysate makes it possible to apply this approach more widely in oncological practice. The use of an antitumor vaccine based on autologous dendritic cells for the prevention of relapses may become a new way of adjuvant treatment.

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Sp11

CPi -Clalit Proactive and Preventative Intervention

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Clalit is the largest HMO in Israel that insures more than 4.7 million people and the second HMO worldwide after Kisser in USA. CPi - Clalit Proactive and Preventative Intervention, is the flag project innovation of clalit community division, in collaboration with clalit research institute and clalit digital division. This innovation combines big data, medical databases, artificial intelligence and a complex computer algorithm, which guides the doctor during the visit, to provide evidence-based personalized knowledge.

No more, surrogate outcomes but rather pure major events outcome. The vision - Patients will receive a proactive and preventive care suitable to their current condition based on the most updated clinical guidelines in an attempt to reduce the gaps in good clinical practice and combined them together to a pure handy knowledge for the primary care physician. The former name of the project Was POEMS -Patient oriented evidence that matters meaning we treat our patients in order to improve their morbidity and to reduce their mortality.

For example, Diabetes is a major issue at the primary care clinic. When I started to practice medicine there were 3-treatment option: Sulphonyls urea Metformin and Insulin. Unfortunately, nowadays there are more than 60 drugs on the shelf, each one of them with pros and cons, and as the one responsible for the evidence based care, it is hard and almost impossible to remember the names, the inclusion criteria and the adverse effect of each drug concerning the patient history.

We used the current guidelines from the American Diabetes Association and converted those guidelines to the Israeli basket aiming to give the right medication to the right patient considering the patient morbidity as; Atherosclerotic disease, Heart Failure, and Chronic Kidney Disease. Expert committees create an ideal "clinical pathway" for each clinical condition and so, patients “travel” through these pathways every single day and gather their personalized recommendations. CPI can advise to add another diabetic medication for the patient, while taking into account his cardiac, kidney and liver functions. Detailed Explanation is available for each recommendation from Dynamed (wwwdynamed.com)

This is already happening nowadays, more than 1500 physicians, half of the primary care physician at Clalit use this platform.

In 7 years the WHO is aiming to declare the world as free from hepatitis C. In march 2023 we added, hepatitis C as a major issue at CPi. We developed strict algorithm by Artificial Intelligence according to patient's risk factors. The patients are sent to Antibody Blood test (AB for Hepatitis C). People