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