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S218 A PHASE I/II STUDY OF GOLIDOCITINIB, A SELECTIVE JAK1 INHIBITOR, IN REFRACTORY OR RELAPSED PERIPHERAL T CELL LYMPHOMA

Topic: 19. Aggressive Non-Hodgkin lymphoma - Clinical

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Background:

Peripheral T cell lymphoma (PTCL) is a group of heterogeneous T cell lymphomas. Patients who relapse from or are refractory to 1st line therapy face dismal prognosis. The response rates to commonly used 2nd line agents such as histone deacetylase inhibitors are below 30%. Immunotherapies, such as anti-PD1 antibodies, may induce hyperprogression in certain PTCL subtypes. Hence, r/r PTCL patients urgently need better therapies.

Aims:

Preclinical data shows JAK/STAT pathway may mediate the pathogenesis of PTCL, making it a promising target. Golidocitinib (DZD4205) is an orally available, potent, JAK1 specific inhibitor, demonstrating profound anti-tumor activities in T lymphoma cells *in vitro* and tumor xenograft *in vivo*. Here we report the preliminary data from an ongoing phase I/II study (NCT04105010) of Golidocitinib in r/r PTCL.

Methods: The study included two parts: Part A (dose escalation) and Part B (dose expansion). In Part A, patients with r/r PTCL were enrolled and received Golidocitinib at different doses (150 mg or 250 mg, QD) to determine the recommended phase II dose (RP2D). Evaluation of safety and efficacy were performed by investigators per CTCAE and Lugano criteria, respectively. Part B is a single-arm, pivotal study, where patients with r/r PTCL will receive Golidocitinib at the RP2D till disease progression or intolerance.

Results:

As of May 31, 2021, a total of 51 patients enrolled in Part A and received Golidocitinib at 150 mg (n = 35) or 250 mg (n = 16). Patient characteristics: median age (range): 61.0 years (29-79); median prior systemic therapies (range): 2 lines (1-8). Ten patients (19.6%) had undergone hematopoietic stem cell transplantation. Fifteen patients (29.4%) had bone marrow involvement at baseline. Histological subtypes included PTCL-NOS (41.2%), AITL (39.2%), ALCL ALK- (7.8%), NKTCL (7.8%), and MEITL (3.9%).

At the data cut-off (DCO), 49 patients completed at least one post-treatment Lugano assessment, of whom 21

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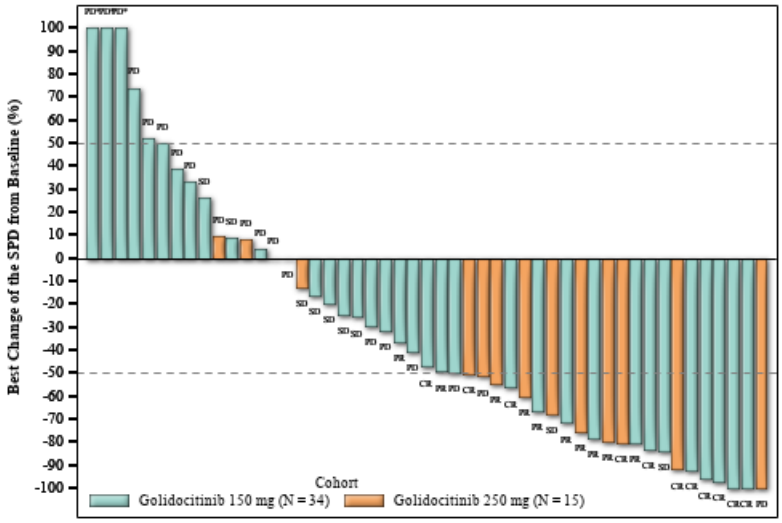
(42.9%) achieved tumor response, including 11 complete responses (CRs, 22.4%) and 10 partial responses (20.4%). Tumor response was observed in various subtypes, including AITL (13/20), PTCL-NOS (5/19), ALCL ALK- (2/4) and NKTCL (1/4). At the DCO, the median duration of response (DoR) was not reached, and the longest DoR was > 14 months.

Forty-eight patients (94.1%) experienced treatment emergent adverse events (TEAEs), of whom 30 (58.8%) experienced ≥ grade 3 TEAEs. Per investigators' assessment, 20 patients (39.2%) experienced ≥ grade 3 TEAEs possibly related to the drug. The most common (≥ 10%) ≥ grade 3 TEAEs were neutropenia (29.4%), thrombocytopenia (15.7%) and pneumonia (11.8%). The majority of TEAEs were reversible or clinically manageable with dose modifications.

Image:



Summary/Conclusion:

Golidocitinib shows good safety and promising anti-tumor efficacy in r/r PTCL, indicating its potential as a therapeutic option for this unmet medical need.

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