(PB3985) MECHANISM-GUIDED HDAC INHIBITION INDUCES COMPLETE RESPONSE IN PRIMARY REFRACTORY GATA3-POSITIVE PTCL-NOS: A BIOLOGICALLY INFORMED THERAPEUTIC STRATEGY

Topic: 21. Lymphoma biology & translational research

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Background

Peripheral T-cell lymphoma, not otherwise specified (PTCL-NOS), particularly the GATA3 subtype, represents a critical unmet medical need. PTCL-GATA3 is characterized by high genomic instability and a Th2-like signature, leading to a dismal 5-year overall survival of only 19%. Literature indicates that GATA3+ patients frequently exhibit primary refractoriness to anthracycline-based induction (CHOP/CHOEP), with no significant survival benefit compared to supportive care. While allogeneic stem cell transplantation (allo-SCT) is the only reliable curative strategy in the relapsed/refractory (R/R) setting, patient-specific factors often preclude this option, highlighting the need for biologically informed therapeutic approaches.

Aims

To report a rare case of primary refractory Stage IVA GATA3 PTCL-NOS in a young patient in whom mechanism-based precision therapy with the HDAC inhibitor Belinostat achieved a Complete Response (CR) after the failure of multiple standard salvage lines and formal exclusion from allo-SCT.

Methods

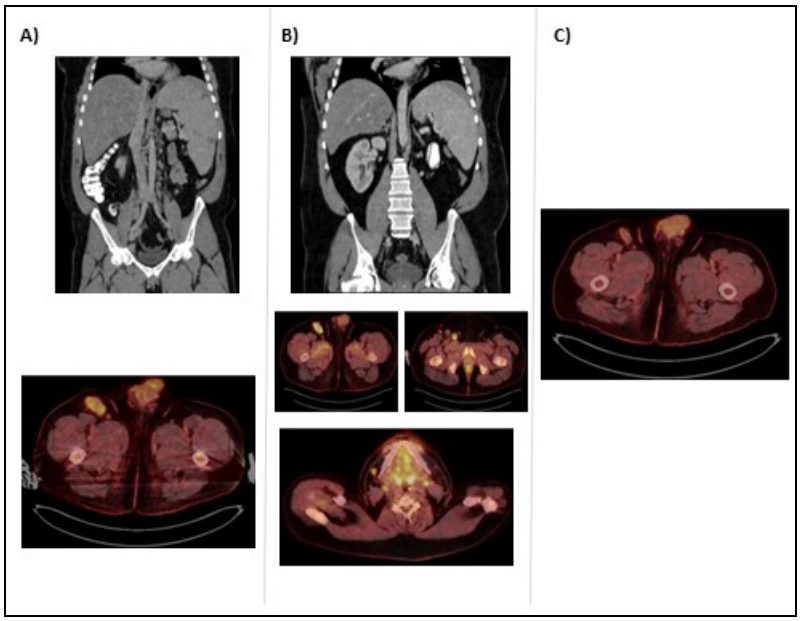
A 34-year-old male with morbid obesity was diagnosed in June 2024 with Stage IVA GATA3-PTCL-NOS, presenting with massive splenomegaly (26 cm), splenic infarcts, and a high proliferative index (Ki67 60%). The patient demonstrated marked chemo-refractoriness to consecutive lines of treatment. First-line CHOEP-TIT resulted in primary progression after 6 cycles. Subsequent second-line DHAP was refractory and complicated by septic shock (Serratia marcescens) and acute renal failure. Third-line Pralatrexate had to be truncated before completing the first cycle due to intolerable Grade IV mucositis, severe cytopenias, and recurrent bacteremia. Despite his young age, the patient was formally rejected for allo-SCT by the referral center due to social characteristics and a high-risk clinical profile. Given the absence of curative options, fourth-line therapy with the HDAC inhibitor Belinostat was initiated in June 2025. Additional molecular studies are ongoing to explore potential predictive biomarkers of response to HDAC inhibition.

Results

The patient achieved a Complete Response (CR) with a Deauville Score of 2 and a reduction of splenomegaly to 17 cm after 4 cycles of Belinostat. Following the 6th cycle, he underwent consolidation with Autologous Stem Cell Transplantation (ASCT) in November 2025. The post-transplant course was severe, involving abdominal septic shock and suspected intestinal ischemia, but the patient achieved full recovery. As of February 2026, he remains in morphometabolic stability (SUV max 2.2), is clinically asymptomatic, and has successfully returned to work.

Summary/Conclusion

This case underscores the limited efficacy of conventional cytotoxic chemotherapy in biologically defined high-risk GATA3-positive PTCL-NOS. It further supports the integration of molecular subtype information into therapeutic decision-making, suggesting that HDAC inhibition may provide a bridge to consolidation when allo-SCT is not an option. Although limited to a single case, this observation supports further investigation of HDAC inhibition in biologically defined GATA3-PTCL subsets. Our ongoing management strategy, in the event of relapse, includes reassessment of transplant eligibility and consideration of HDAC inhibition re-challenge based on prior response. Molecular studies are also in progress to explore potential biomarkers predicting response to HDAC inhibition in high-risk GATA3-positive PTCL-NOS.



Sequential 18F-FDG PET/CT imaging illustrating clinical evolution. (A) Baseline (July 2024): Initial staging of Stage IVA GATA3 PTCL-NOS showing 21-cm splenomegaly and hypermetabolic right iliac and inguinal lymphadenopathy (SUV max 4.38). (B) Progression (November 2024): Disease progression after first-line CHOEP-TIT, demonstrating increased metabolic activity in right iliac (SUV max 5.83) and inguinal nodes (SUV max 7.0), alongside new bilateral laterocervical involvement (SUV max 5.12). (C) Complete Response (September 2025): Metabolic complete response after 4 cycles of 4th-line Belinostat, with reduction of splenomegaly to 17 cm and minimal residual right inguinal uptake (SUV max 1.87; Deauville Score 2).