(PB3874) MINE REGIMEN COMBINED WITH TARGETED AGENTS IN RELAPSED/REFRACTORY ANGIOIMMUNOBLASTIC T-CELL LYMPHOMA: A PRELIMINARY EXPLORATORY RETROSPECTIVE STUDY INTEGRATED WITH NEXT-GENERATION SEQUENCING

Topic: 20. Other aggressive lymphomas

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Background

Angioimmunoblastic T-cell lymphoma (AITL) is an aggressive peripheral T-cell lymphoma subtype with extremely poor prognosis in relapsed/refractory (rr) setting, requiring novel therapeutic strategies. The MINE regimen (ifosfamide, mitoxantrone, etoposide) is a salvage option, but data on its combination with targeted agents (azacitidine, chidamide, golidocitinib, tazemetostat, enasidenib, ruxolitinib) in rrAITL remain limited.

Aims

This study aimed to explore the clinical value of MINE plus targeted therapy in rrAITL and identify predictive biomarkers via next-generation sequencing (NGS).

Methods

This single-center retrospective study enrolled 9 rrAITL patients treated with MINE plus targeted agents between February 2024 and January 2026. Baseline NGS (119 genes: RHOA, CD28, TET2, DNMT3A, IDH2, TET1/TET3, STAT3, KMT2D, TP53, etc.) was performed on tumor or peripheral blood samples. Targeted agents were selected per molecular profiles: epigenetic drugs (azacitidine, chidamide) for TET2/DNMT3A mutations; JAK/STAT inhibitors (golidocitinib, ruxolitinib) for RHOA-driven JAK-STAT activation; enasidenib for IDH2 mutations. Efficacy was assessed by Lugano 2014 criteria (primary endpoints: ORR, CRR; secondary endpoints: PFS, DOR, OS). Safety was evaluated for ≥ grade 3 treatment-related adverse events (TRAEs).

Results

Median age was 56 (32–71) years; 7 (77.8%) had stage IV, 2 (22.2%) stage III disease. 77.8% (7/9) were male.High/intermediate-high IPI was noted in 8 (88.9%) patients, high PIT in 6 (66.7%). Coinfection rates: CMV 55.6% (5/9), EBV 77.8% (7/9), HHV6 22.2% (2/9), HHV8 11.1% (1/9). Median prior therapy lines: 3 (2–6). With median follow-up of 134 (23–292) days, ORR was 77.8% (7/9), CRR 55.6% (5/9), median DOR 86 days. Median PFS and OS were both 134 days (data immature due to short follow-up and early events). NGS showed frequent mutations: TET2 77.8% (7/9), RHOA 66.7% (6/9), DNMT3A 55.6% (5/9), IDH2 33.3% (3/9), STAT3/PLCG1/TP53 11.1% (1/9 each). Two non-responders (disease progression/death) had 5 and 7 mutations, respectively; 7 responders (≥PR) had median 2 mutations (0–3). Mean mutations: 6 in non-responders vs 1.2 in responders. Grade 3–4 TRAEs: neutropenia 55.6% (5/9), thrombocytopenia 33.3% (3/9), anemia 44.4% (4/9). Death causes: infection 44.4% (4/9), gastrointestinal bleeding 11.1% (1/9).

	Age	Gender	Ann-anbor	Group	bone marrow infiltration	IPI score	PIT score	gene mutation(NGS)	viral infection
Pt.01	71	male	III	A	No	2	3	RHOA,TET2,DNMT3A,IDH2	
Pt.02	65	female	IV	B	No	3	3	RHOA,TET2,DNMT3A	EBV
Pt.03	58	male	IV	A	No	3	2	TET2,DNMT3A,IDH2,TP53,	CMV,EBV
Pt.04	57	male	IV	B	Yes	3	3	RHOA,TET2	CMV,HHV6,HHV8,EBV
Pt.05	56	male	IV	A	No	3	3	RHOA,TET2	CMV,EBV
Pt.06	52	female	IV	B	No	3	2		EBV
Pt.07	47	male	IV	B	Yes	3	3	RHOA,TET2,DNMT3A,IDH2	CMV,HHV6,EBV
Pt.08	43	male	IV	B	Yes	3	3	TET2,DNMT3A	CMV,EBV
Pt.09	32	male	III	B	No	3	2		

Summary/Conclusion

To our knowledge, this is the first study showing MINE plus personalized targeted therapy yields promising efficacy (ORR 77.8%) and manageable toxicity in rrAITL. High tumor mutational burden was associated with early progression and poor outcome, suggesting a potential predictive biomarker for treatment selection. These preliminary findings warrant validation in larger prospective studies.