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A PROSPECTIVE STUDY OF TCR MEASURABLE RESIDUAL DISEASE IN PERIPHERAL T-CELL LYMPHOMA

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Background

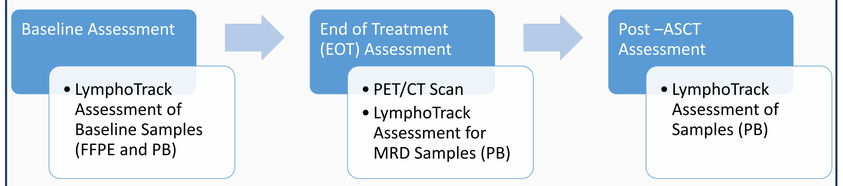
Peripheral T-Cell Lymphoma (PTCL) is an aggressive rare subset (~10-15%) of non-Hodgkin lymphomas. PTCL treatment often starts with anthracycline based chemotherapy and then autologous stem cell transplantation (ASCT) for applicable subjects. PET/CT scans are typically used to monitor disease recurrence after chemotherapy; however, its ability to predict relapse for PTCL is not ideal.

In this Washington University sponsored prospective study, we explored the use a next-generation-sequencing (NGS) based TCR measurable residual disease (MRD) assay as a potential prognostic indicator for PTCL (NCT03297697).

Methods

In this study 43 eligible subjects with previous untreated PTCL (PTCL-NOS, AITL, ALK-ALCL, ALK+ALCL, PTCL-NOS-TFH, and MEITL) were enrolled in this study. LymphoTrack® TCR (*TRG/TRB*) assays, which provide 10^{-5} sensitivity, were used to test both baseline samples (either tissue or PB), PB samples from end of chemotherapy (End of Treatment/Pre-ASCT), stem cells from eligible ASCT subjects, and PB samples from post-ASCT subjects. The stem cells were collected according to institutional protocols by apheresis after granulocyte colony stimulating factor (G-CSF) to stimulate the bone marrow production of stem cells for extraction.

NGS assessments were performed at each of the following timepoints:

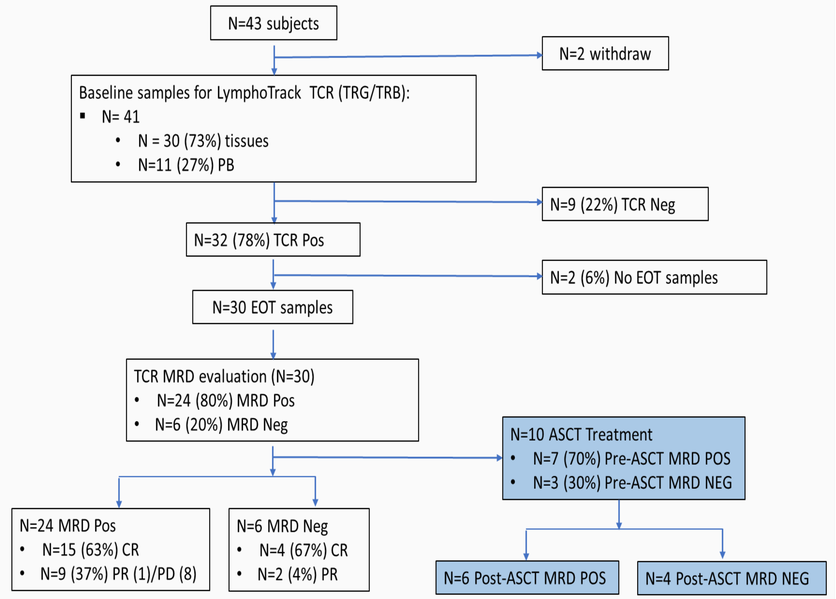


Schematic depiction of the TRB gene locus:

Schematic depiction of the TRG gene locus:

These PCR amplicons were then purified, quantified, and an equimolar library pool was created for sequencing on the MiSeq™ sequencer. Clonality from baseline and stem cell samples was determined when the top % reads from this assay were ≥2.5% and ≥2x the background. The identified clonal sequences from the baseline samples were then tracked for MRD assessment in both EOT and post-ASCT samples from the same subjects.

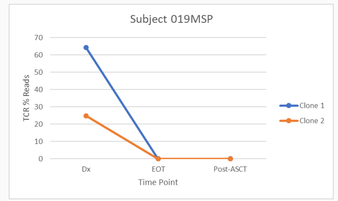
Study Flow Chart

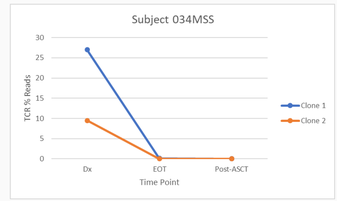


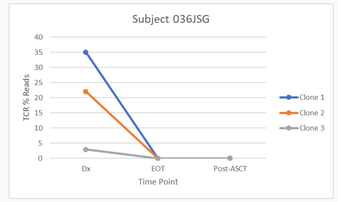
Result Summary for ASCT Subjects

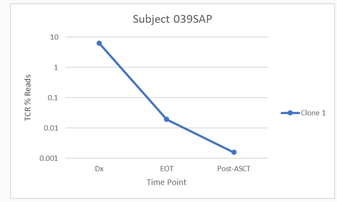
Sample	Age	Dx	Baseline Status	Induction Type	EOT (+ / -)	Pre-ASCT PET/CT	Stem Cell	Post-ASCT MRD (+ / -)	Relapse Post-ASCT
019MSP	52	ALK- ALCL	*TRG+/TRB+*	CHOEP	-	PR	*TRG-/TRB-*	-	No
034MSS	39	AITL	*TRG+/TRB+*	BV+CHP	-	CR	*TRG-/TRB-*	-	No
036JSG	69	PTCL NOS	*TRG+/TRB+*	BV+CHP	-	CR	*TRG-/TRB+*	-	No
039SAP	71	AITL	*TRG+/TRB+*	Aza + CHOP	+	CR	n/a	-	No
0111DRK	68	AITL	*TRG+/TRB+*	CHOEP	+	CR	*TRG-/TRB-*	+	No
0117NPP	77	AITL	*TRG+/TRB+*	Aza + CHOP	+	CR	*TRG-/TRB-*	+	Yes (3 mo)
0118TLL	70	MEITL	*TRG+/TRB+*	CHOEP	+	CR	*TRG-/TRB+*	+	Yes (9 mo)
0124PDR	68	PTCL NOS	*TRG+/TRB+*	CHOP	+	CR	*TRG+/TRB+*	+	No
0310JMC	38	AITL	*TRG+/TRB+*	Aza + CHOP	+	CR	n/a	+	No
0311MZK	67	TFH PTCL	*TRB+*	Aza + CHOP	+	CR	n/a	+	Yes (29 mo)

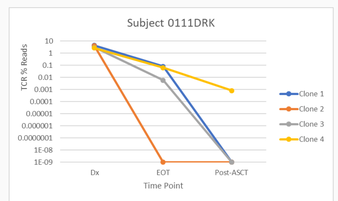
Results: Study Analysis for TCR

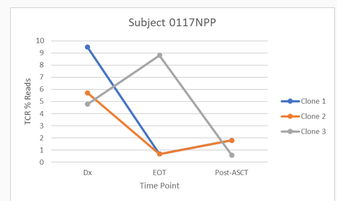


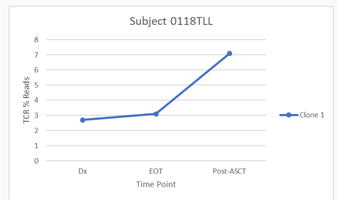


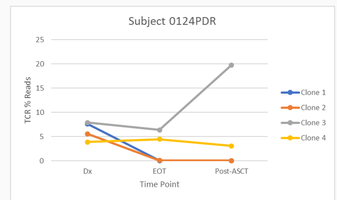


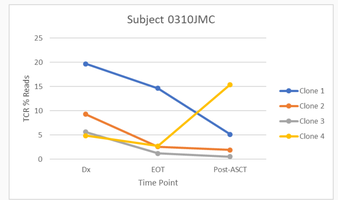


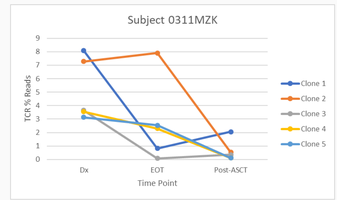












Conclusions

- This study demonstrated that RUO LymphoTrack® NGS assays were able to identify clonality from baseline and stem cell samples, and detect MRD in post-treatment (EOT and post ASCT) samples from PTCL subjects in a prospective study.
- Clonality analyses of stem cells confirmed absence of the matched baseline clonal sequences.
- All 4 subjects who tested TRG/*TRB* MRD negative post-ASCT remain in remission at median 32.5 months after ASCT treatment.
- While the negative predictive value of TCR MRD negative in post-ASCT subjects is promising, further evaluation with a larger sample size is needed.
- Development of in-house and/or IVD assays using NGS technology for PTCL MRD is supported by this research study.

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