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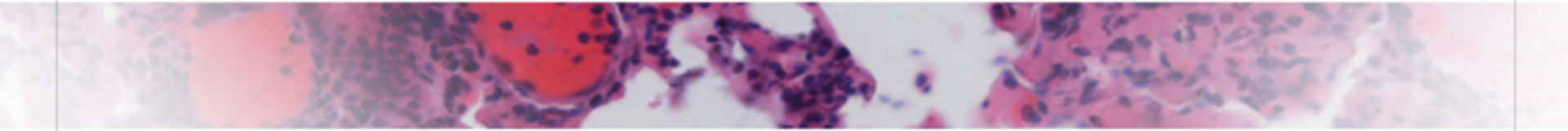

End of Treatment Peripheral Blood TCR Evaluation for Minimal Residual Disease Evaluation in Peripheral T-cell Lymphomas

Neha Mehta-Shah, MD, MSCI[1], Todd A Fehniger, MD, PhD[1], Eric D Jacobsen, MD[2], Katrina Peterson[1], Brad S. Kahl, MD[1], Nancy L. Bartlett, MD[1], Amanda F Cashen, MD[1], Armin Ghobadi, MD[1], Anne Fischer, BS[1], Beth Reagan[1], Alison J. Moskowitz, MD[3], Fei Wan[1], Natalie Hill[4], Ying Huang, PhD[4], Kasey Hutt, PhD[4], Edgar Vigil[4], Meredith Olson[4], Austin Jacobsen[4] and Steven M. Horwitz, MD[3]

[1]Washington University in St. Louis, St. Louis, MO; [2]Dana Farber Cancer Institute, Boston, MA; [3]Memorial Sloan Kettering Cancer Center, New York, NY; [4]Invivoscribe, San Diego, CA

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Background

- Peripheral T-cell lymphomas are a rare subtype of non-Hodgkin lymphoma
- High rate of relapse to standard therapy:
  - 80% overall response rate to anthracyline based chemotherapy
  - 5 year PFS approximately 20% for most subtypes
- Autologous transplant is considered in first remission
  - Benefits approximately 20% of patients
- Allogeneic transplant can be curative
  - Median survival from relapsed/refractory disease is 6-10 months
- Biomarkers would be critical:
  - To evaluate who is at highest risk of relapse
  - Who most benefits from a consolidative autologous transplant

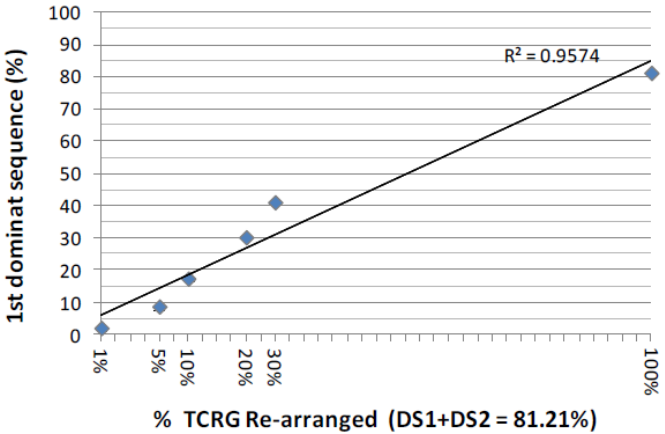
Outcomes By Intent to Consolidated with Auto-HSCT in Swedish Registry

	Auto-SCT (n = 128)	No Auto-SCT (n = 124)
5 yr OS	48%	26%
5 yr PFS	41%	20%

Ellin et al Blood 2014

Background

- Minimal residual disease markers are being studied to:
  - Predict relapse
  - Determine who benefits from maintenance or consolidative therapy
  - Promote early discontinuation of therapy
- T-cell receptor gene rearrangement (TCR) by next generation sequencing is able to detect a known TCR clonotype at 10^{-5}
  - Highly specific and sensitive
  - Lends itself towards MRD evaluation in T-cell lymphomas



Courtesy of Maria Arcila (MSKCC)

Shah et al AMP 2017

Methods

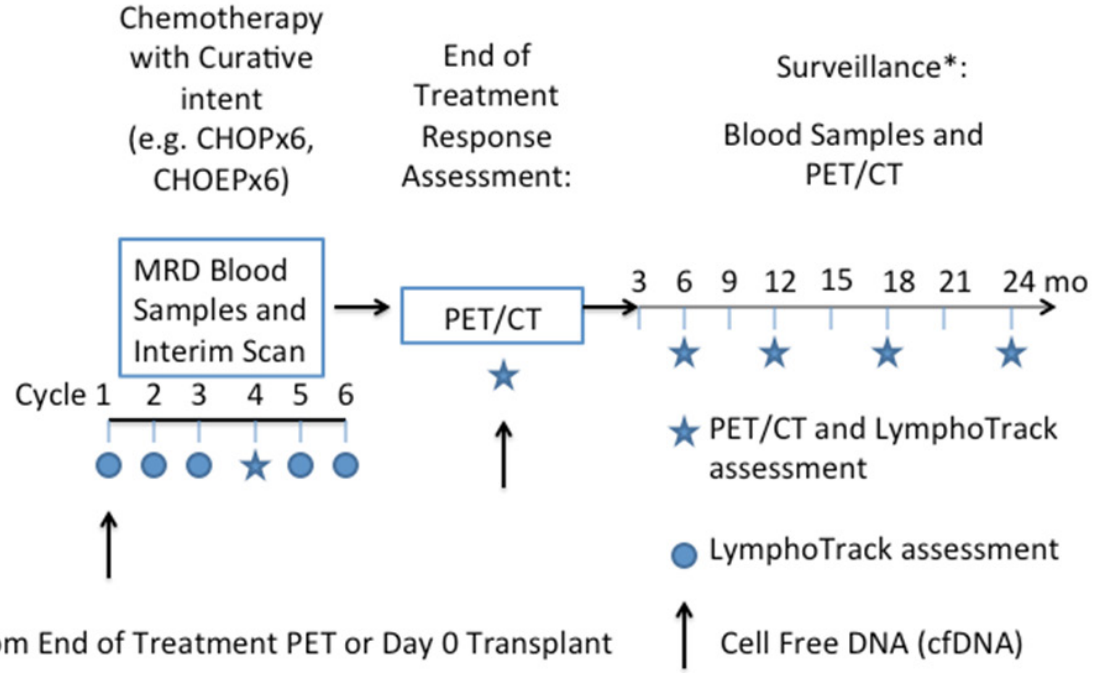
- **Hypothesis**:
  - Next generation sequencing based TCR clonality assays is a feasible method of evaluating minimal residual disease
- **Primary Objective:**
  - To estimate the percentage of patients with a dominant tumor sequence identified from the pre-treatment tumor specimen.
- **Secondary Objectives**
  - To study whether a novel NGS-based TCR clonality assay to evaluate MRD (LymphoTrack) can prognosticate risk of relapse in PTCL, predict response to treatment
  - To evaluate whether the rate of decline of the tumor specific sequence or sequences predict duration of response.
  - To characterize the lead time from MRD positivity to subsequent clinical relapse.
- **Exploratory Objective**
  - To explore the ability of cfDNA sequencing analysis to assess MRD in PTCL.

Study Design

A prospective, multi-institutional, non-therapeutic cohort study

Eligibility:
- Untreated PTCL-NOS, AITL, ALK- ALCL, ALK+ ALCL, MEITL, EATL
- Pretreatment sample to evaluate tumor TCR sequence

Exclusion:
- CTCL, NK/T-cell, ATLL, HSPTCL



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Statistical Design

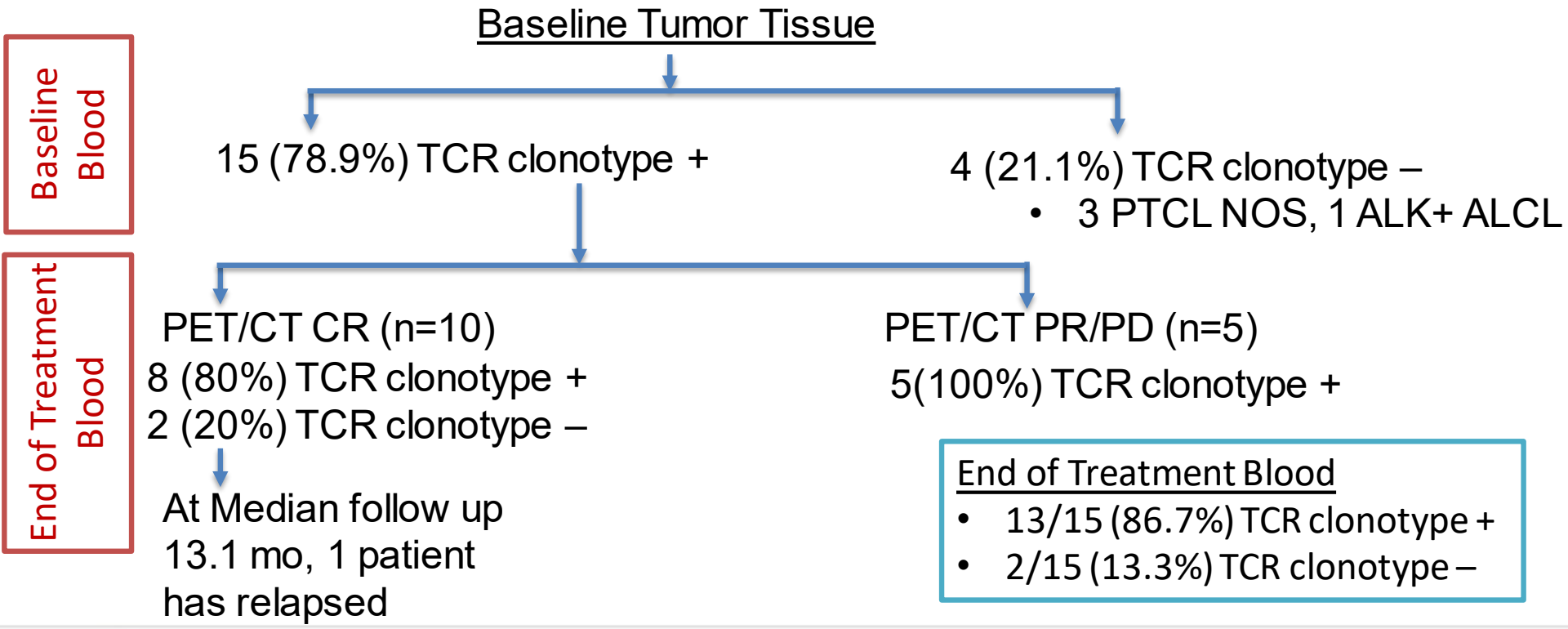
- Aim to demonstrate feasibility of evaluating for MRD by TCR clonotype (Lymphotrack) in peripheral blood at baseline
  - Feasibility: if TCR clonotype positive at baseline in >60% of cases
- Powered to detect 35% difference in 2 year PFS between those who have negative vs. positive peripheral blood MRD evaluation at end of treatment
  - 2 year PFS for End of Treatment PET
  - Negative: 60%, Positive 25%
- Sample size: 42 patients.
  - A one-sided log rank test with type I error of 0.1 will have power of 0.9 to detect a 35% difference in 2-year PFS

Patient Characteristics

Histology	N (%)	Therapy	N (%)
PTCL	16 (42%)	CHOP	3 (16%)
AITL	10 (26%)	CHOEP	10 (52%)
ALCL, ALK-	7 (18%)	BV-CHP	4 (21%)
ALCL, ALK+	5 (13%)	CEOP	1 (5%)
MEITL	1 (3%)	CHOP+ azacitidine	1 (5%)
		Autologous Transplant	7 (37%)
		Response to Therapy	
Age		CR	13 (68%)
Median (Range)	61 (22-80)	PR	1 (5%)
		PD	5 (26%)

- 38 patients enrolled
- 19 completed therapy and had end of treatment TCR available for analysis

Results


Baseline Blood
End of Treatment Blood
Baseline Tumor Tissue
15 (78.9%) TCR clonotype +
4 (21.1%) TCR clonotype –
• 3 PTCL NOS, 1 ALK+ ALCL
PET/CT CR (n=10)
8 (80%) TCR clonotype +
2 (20%) TCR clonotype –
At Median follow up 13.1 mo, 1 patient has relapsed
PET/CT PR/PD (n=5)
5(100%) TCR clonotype +
End of Treatment Blood
• 13/15 (86.7%) TCR clonotype +
• 2/15 (13.3%) TCR clonotype –

Conclusions

- Measurement of peripheral blood TCR at the end of treatment is feasible in PTCL using next generation sequencing with a known tumor clonotype.
- Lack of radiographic CR was highly correlated with detectable TCR,
- Detectable TCR was also frequently seen in complete remission by PET/CT.
- Longer follow up is required to:
  - Determine if peripheral blood TCR clonotype at the end of CHOP-based therapy predicts likelihood of relapse
  - Evaluate the dynamics of TCR clonotype during and after completion of treatment
  - Evaluate if ASCT changes presence of minimal residual disease

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