Outcomes of Relapsed and Refractory Peripheral T-Cell Lymphoma (PTCL) with Intention for Curative Therapy Incorporating High Dose Chemotherapy and Hematopoietic Stem Cell Transplant (HDC/SCT)

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Introduction

- Despite recent advances in therapy, a large proportion of patients with peripheral T-cell lymphoma (PTCL) relapse or have primary refractory disease following frontline therapy.
- The outcomes remain suboptimal in relapsed/refractory PTCL.[1]
- Treatment incorporating hematopoietic stem cell transplantation (SCT) is the only curative option and is recommended for transplant-eligible patients with relapsed and refractory PTCL.[2-3]
- Limited data available in those where there is an 'intention to transplant' (ITT).
- We evaluated the outcomes of relapsed/refractory PTCL from the time of first relapse/progression in patients intended for SCT.

Method

Patient Population:
- BC Cancer Centre for Lymphoid Cancer Database.
- Adult patients (≥ 18 years) with "nodal" PTCLs treated with curative-intent frontline regimen diagnosed between 1981-2020.
- Documented relapsed/refractory disease treated with second-line therapy and intention to stem cell transplant.

PTCL Subtypes:
- Systemic anaplastic large cell lymphoma (ALCL)
  - ALK-negative
  - ALK-positive
- Angioimmunoblastic T-cell lymphoma (AITL)
- PTCL-not otherwise specified (PTCL-NOS)

- Progression free survival (PFS) and overall survival (OS) were calculated from time of documented first relapsed or progressive disease and from the time of SCT.

Results

- 114 patients with relapsed/refractory PTCL and intention to transplant were identified with a median age of 53 years (range 18-69) at relapse/progression.
- The baseline characteristics are outlined in **Table 1**.
- Median follow-up time from time of documented relapsed/progression was 6.8 years (range 0.3-30.7).
- Most patients received anthracycline-based frontline chemotherapy and 3 patients received consolidative autologous SCT.
- 46 (40%) with refractory disease defined as progressive disease or progression within 3 months from frontline therapy and 68 (60%) with relapsed disease.
- Patients with refractory disease were more likely to have advanced-stage disease, poor performance status, and high sIPI (**Table 2**).

Table 1: Baseline Characteristics

Baseline Characteristics at Time of Relapse/Progression (n = 114)		
Median Age, years (range)		53 (18-69)
Male sex, n (%)		73 (64)
Stage, n (%)	I-II III-IV	18 (16) 96 (84)
Secondary IPI, n (%)	0-1 2 3 4-5 Not Available	41 (36) 39 (34) 25 (22) 4 (4) 5 (4)
Performance Status, n (%)	0-1 ≥2 Not available	73 (64) 30 (26) 11 (10)
Elevated LDH, n (%)	No Yes Not available	57 (50) 45 (40) 11 (10)
PTCL Subtypes, n (%)	ALK- ALCL ALK+ ALCL AITL PTCL-NOS	29 (25) 12 (10) 17 (15) 56 (60)
Relapsed/Refractory	Relapsed Refractory	68 (60) 46 (40)
Second-line therapy, n (%)	High dose cyclophosphamide Multiagent chemotherapy • GDP • Other Novel agents • Brentuximab vedotin • Romidepsin • Pralatrexate No second-line therapy	10 (9) 83 (73) 59 (52) 24 (21) 15 (13) 12 (11) 2 (2) 1 (1) 6 (5)

Table 2: Refractory vs. Relapsed PTCL

Clinical Factors	Refractory (n=46)	Relapsed (n=68)	P-value
Male sex	28 (61%)	45 (66%)	0.6
Elevated LDH	21 (50%)	24 (40%)	0.3
Stage III-IV	43 (94%)	53 (78%)	0.02
PS ≥ 2	18 (46%)	12 (19%)	<0.01
sIPI ≥ 2	33 (79%)	35 (52%)	0.01

Second-line therapy

- The majority received multi-agent chemotherapy with GDP (gemcitabine, dexamethasone, cisplatin) the most used regimen (n = 59, 52%).
- 15 patients (13%) received novel agents:
  - Brentuximab vedotin (BV) = 12: ALK-negative ALCL (8), ALK-positive ALCL (3), AITL (1)
  - Romidepsin = 2: AITL and PTCL-NOS
  - Pralatrexate = 1: PTCL-NOS.

Overall Response Rate (ORR)

- ORR to second-line therapy was 61% (24% CR; 37% PR).
  - GDP: 61% (17% CR; 44% PR) - higher responses observed in relapsed versus refractory pts (81% vs. 41%, p=0.002).
  - BV: 75% (25% CR; 50% PR).

High Dose Chemotherapy and Hematolopoietic Stem Cell Transplant (HDC/SCT)

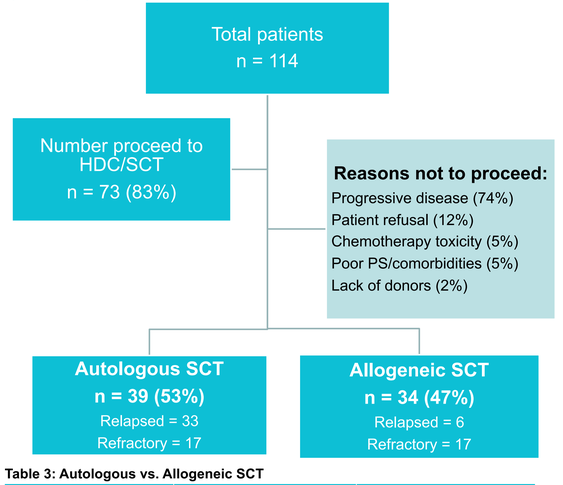


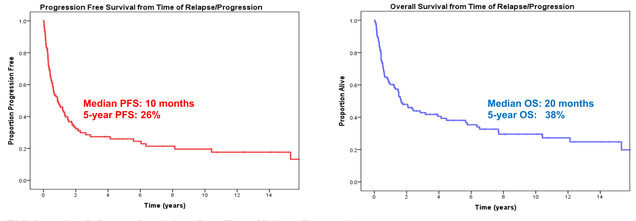
Table 3: Autologous vs. Allogeneic SCT

	Autologous SCT (n = 39)	Allogeneic SCT (n = 34)
Median age (range) (y)	58 (22-69)	47 (23-62)
Relapsed	33 (85%)	6 (15%)
Refractory	17 (50%)	17 (50%)
PTCL subtypes:		
ALK –ve ALCL	14 (67%)	7 (33%)
ALK +ve ALCL	6 (67%)	3 (33%)
AITL	4 (29%)	10 (71%)
PTCL-NOS	15 (52%)	14 (48%)

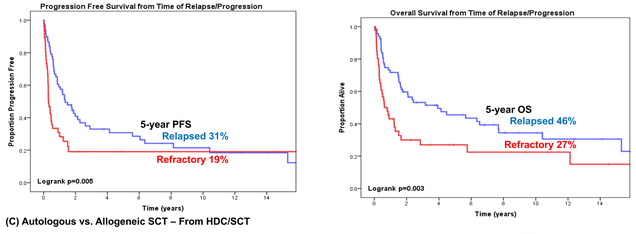
- 50/67 (75%) received only second-line therapy prior to SCT, most commonly GDP (23/50, 46%). 17/67(25%) required additional third-line therapy, including novel agents in 9 cases prior to SCT.
- 5-year progression free survival (PFS) and overall survival (OS) from the time of first relapse/progression for the ITT population was 26% and 38% respectively (**Figure 2A**)
  - Inferior outcomes in refractory vs relapsed disease (5-year PFS 19% vs 31%, p=0.005; 5-year OS 27% vs 46% p=0.003). (**Figure 2B**)
- 5-year PFS from autologous and allogeneic SCT were 34% and 52% (p = 0.4) and 5-year OS were 44% and 67% (p = 0.5) respectively. (**Figure 2C**)
- 5-year PFS and OS for patients who received GDP as second-line therapy were 21% and 35% from first relapse/progression, and 39% and 48% from SCT (auto n=21; allo n=14).
- Outcome was similar amongst the PTCL subtypes.

Figure 2: Progression Free Survival (PFS) and Overall Survival (OS)

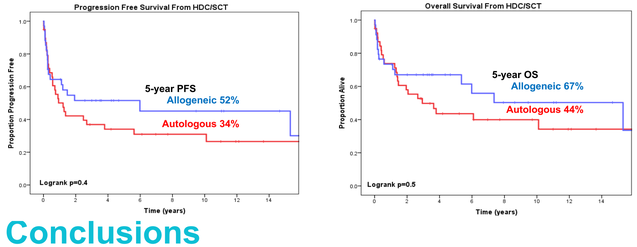
(A) From Time of Relapse/Progression



(B) Relapsed vs. Refractory Population - From Time of Relapse/Progression



(C) Autologous vs. Allogeneic SCT – From HDC/SCT



Conclusions

- Outcomes remain suboptimal in relapsed/refractory PTCL intended for transplant, with long term survival of ~30%
- Over 50% are alive at 5 years if they are able to receive HDC/SCT
- Refractory population has inferior outcomes from time of first relapse/progression but the results are encouraging with allogeneic SCT
- GDP chemotherapy is a viable salvage option for relapsed PTCL
- Novel agents should be considered as bridge to SCT particularly for those with chemo refractory disease

References

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3. El-Asmar J et al Efficacy of High-Dose Therapy and Autologous Hematopoietic Cell Transplantation in Peripheral T Cell Lymphomas as Front-Line Consolidation or in the Relapsed/Refractory Setting: A Systematic Review/Meta-Analysis. Biol Blood Marrow Transplant 2016