

Exploratory Analysis of Brentuximab Vedotin plus CHP (A+CHP) in Frontline Treatment of Patients with CD30+ PTCL (ECHELON-2): Impact of Consolidative SCT

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Background: A+CHP Treatment in CD30+ PTCLs

- Brentuximab vedotin plus cyclophosphamide, doxorubicin, and prednisone (A+CHP) was approved for adults:
 - In 2018 by FDA for previously untreated patients with sALCL or CD30-expressing PTCL, including AITL and PTCL-NOS
 - In 2019 by Health Canada for previously untreated patients with sALCL, AITL, or PTCL-NOS whose tumors express CD30
- The approvals were based on superior PFS, the primary endpoint, compared to CHOP in the ECHELON-2 study¹ (NCT01777152):
 - PFS (HR=0.71 [95% CI: 0.54, 0.93], p=0.0110)
 - OS (HR=0.66 [95% CI: 0.46, 0.95], p=0.0244)
- Given the historically high relapse rate in PTCLs, consolidative stem cell transplant (SCT) is often used in the frontline setting:
 - Phase 2 study suggests improved PFS compared to historical expectations²
 - Most studies support use of SCT in first complete remission (CR)
 - No randomized studies, thus practices worldwide vary

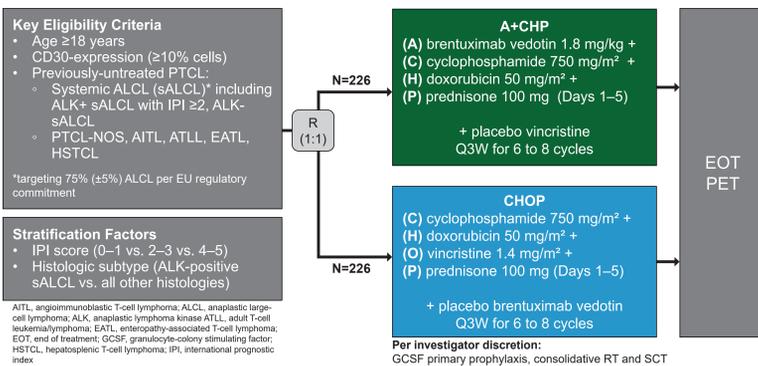
Background: Consolidative SCT in ECHELON-2

- Per protocol, patients in ECHELON-2 were permitted to receive a consolidative SCT at the discretion of the investigator.
 - Primary endpoint PFS: time from randomization to earliest of progressive disease, death, or receipt of subsequent systemic chemotherapy to treat residual or progressive disease
 - Consolidative autologous or allogeneic SCT was not considered a PFS event
 - Consolidative RT was also not considered a PFS event
 - 22% (50/226) in A+CHP arm received a consolidative SCT versus 17% (39/226) in CHOP arm

Purpose of current analysis:

- To explore the impact of consolidative SCT in ECHELON-2, a post-hoc analysis was performed of patients in a CR at end of treatment (EOT) after frontline A+CHP to compare the outcome of those who received an SCT and those who did not

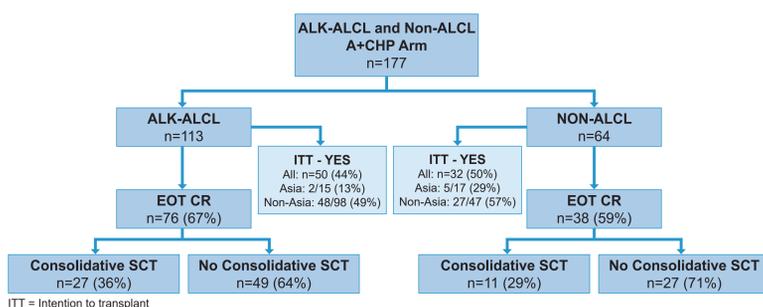
ECHELON-2 Study Design (NCT01777152)



Methods

- CR rate at EOT by blinded independent central review as defined per the Revised Response Criteria for Malignant Lymphoma.³
- Patients who discontinued treatment due to an adverse event were included in the analysis if they were in a CR at EOT.
- Patients with ALK+ sALCL histological subtype tend to have more favorable outcomes and therefore were excluded from this analysis.
- Both a univariate analysis of SCT versus no SCT and multivariate analyses adjusting for region and age were performed.

Use of Consolidative SCT in A+CHP Arm

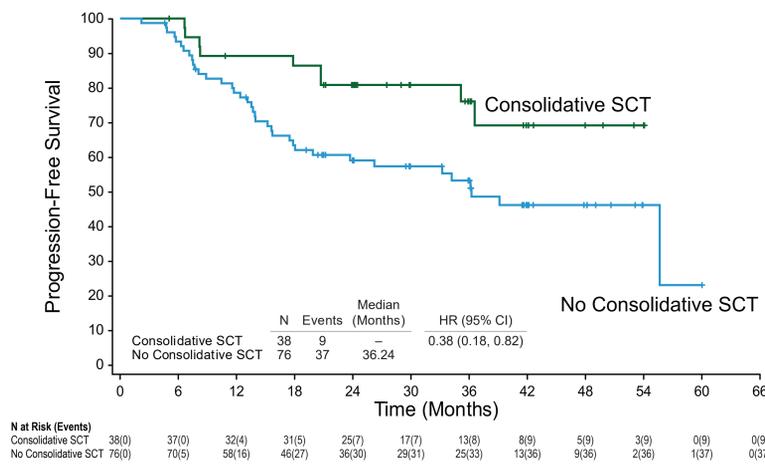


Study Population by Consolidative SCT in A+CHP Arm in Patients with CR at EOT

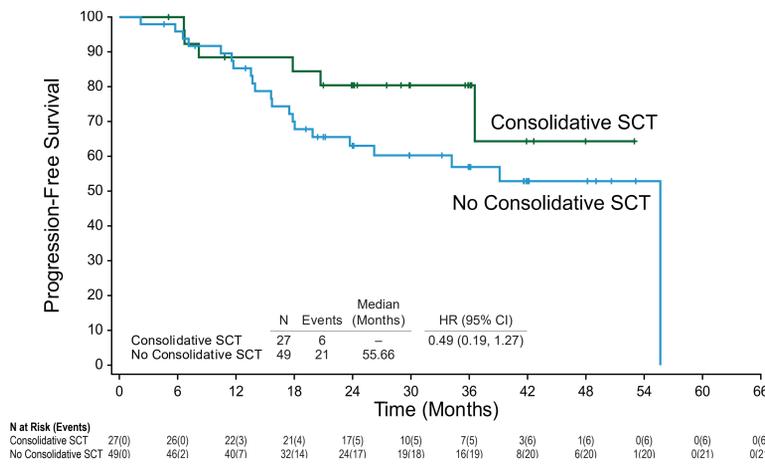
ALK- sALCL and Non-sALCL

	ALK- sALCL N=76		Non-sALCL N=38	
	SCT (n=27)	No SCT (n=49)	SCT (n=11)	No SCT (n=27)
Male, n (%)	16 (59)	24 (49)	6 (55)	15 (56)
Age in years, median (range)	50 (18, 68)	59 (20, 85)	57 (35, 73)	66 (49, 77)
IPI score, n (%)				
0-1	11 (41)	21 (43)	2 (18)	4 (15)
2-3	12 (44)	25 (51)	7 (64)	21 (78)
4-5	4 (15)	3 (6)	2 (18)	2 (7)
Stage III/IV, n (%)	22 (82)	31 (63)	11 (100)	23 (85)

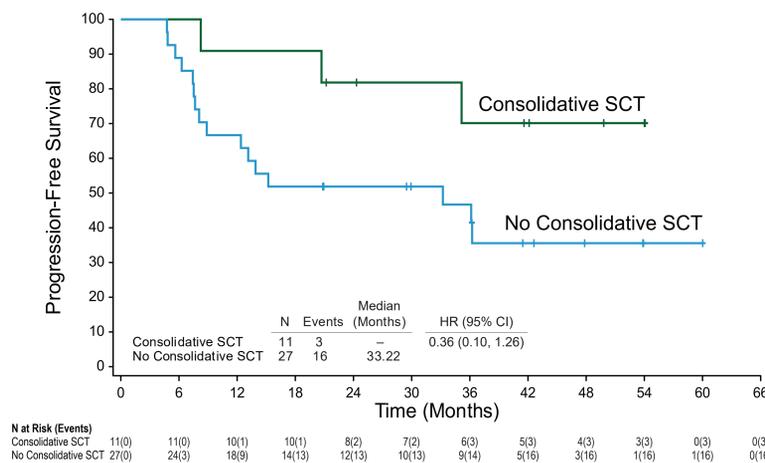
PFS by Consolidative SCT After A+CHP in Patients with CR at EOT: ALK- sALCL and Non-sALCL



PFS by Consolidative SCT After A+CHP in Patients with CR at EOT: ALK- sALCL



PFS by Consolidative SCT After A+CHP in Patients with CR at EOT: Non-sALCL



ALK- sALCL and Non-sALCL: Asia and Non-Asia Countries

	ALK- sALCL N=76		Non-sALCL N=38	
	Asia (n=10)	Non-Asian (n=66)	Asia (n=9)	Non-Asian (n=29) ^a
Intention to transplant at baseline, (%)				
Yes	1 (10)	37 (56)	1 (11)	18 (62)
No	9 (90)	29 (44)	8 (89)	10 (34)
Received consolidative SCT				
Yes	1 (10)	26 (39)	1 (11)	10 (34)
No	9 (90)	40 (61)	8 (89)	19 (66)

Asia = Taiwan, South Korea, Japan; Non-Asia = rest of world.
a One patient had no response recorded for intention to transplant at baseline.

Summary of PFS by Consolidative SCT After A+CHP in Patients with CR at EOT

	ALK- sALCL N=76		Non-sALCL N=38		Combined N=144	
	SCT (n=27)	No SCT (n=49)	SCT (n=11)	No SCT (n=27)	SCT (n=38) ^a	No SCT (n=76)
Estimated PFS at 3 years, % (95% CI)	80.4 (59.1, 91.4)	56.9 (40.6, 70.3)	70.1 (32.3, 89.5)	46.7 (26.7, 64.4)	76.1 (56.9, 87.6)	53.3 (40.7, 64.3)
Univariate, HR (95% CI)	0.49 (0.19, 1.27)		0.36 (0.10, 1.26)		0.38 (0.18, 0.82)	
Multivariate, HR (95% CI) adjusted for:						
Age (<65, ≥65)	0.54 (0.20, 1.45)		0.32 (0.09, 1.15)		0.39 (0.18, 0.86)	
Region (ROW, Asia)	0.47 (0.18, 1.22)		0.37 (0.10, 1.33)		0.38 (0.18, 0.82)	
Age + Region	0.52 (0.19, 1.41)		0.32 (0.09, 1.19)		0.39 (0.18, 0.86)	
Median follow-up, months (95% CI)	29.9 (24.2, 36.1)	41.6 (29.8, 42.0)	49.8 (21.2, 54.0)	42.6 (29.5, 53.9)	35.9 (24.5, 41.9)	41.6 (33.2, 42.1)

Table presents HR of PFS for patients who achieved CR on A+CHP, SCT vs no SCT; HR<1 favors SCT; all HRs were stratified for baseline IPI score (0-1, 2-3, 4-5).
a Includes 2 allogeneic SCTs.

Limitations

- This exploratory subgroup analysis was post-hoc, which may introduce unknown bias.
- Comparisons by SCT may be confounded, as SCT is a non-randomized, post-baseline outcome.
- The study was not powered to make a definitive assessment of the use of SCT in patients with PTCL.
- The sample sizes were small.

Conclusions

- Numerical PFS estimates favor the use of consolidative SCT in patients with PTCL in a CR at EOT after frontline A+CHP treatment.
- The use of consolidative SCT was infrequent in Asian countries, suggesting regional practice differences.
- The overall impact of consolidative SCT remains unconfirmed, including in patients treated with A+CHP.
- Additional studies are needed to establish the role of consolidative SCT in this setting.

Acknowledgments

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References

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