THE ECHELON-2 TRIAL: 5-YEAR EXPLORATORY SUBGROUP ANALYSES OF A RANDOMIZED, DOUBLE-BLIND, PHASE 3 STUDY OF BRENTUXIMAB VEDOTIN AND CHP (A+CHP) VS CHOP IN FRONTLINE TREATMENT OF PTS WITH CD30-POSITIVE PERIPHERAL T-CELL LYMPHOMA

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Speaker Disclosures

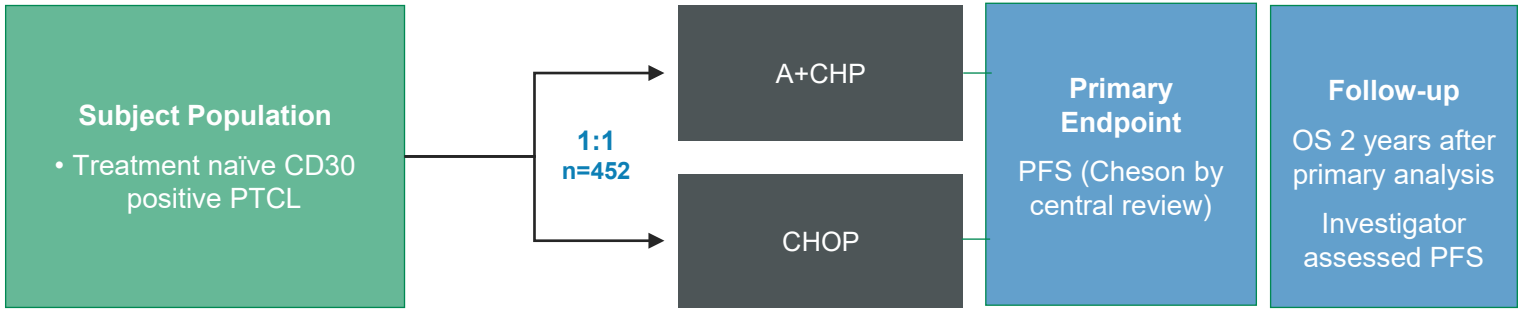
Dr. Steven Horwitz:

- Acrotech Biopharma
- Affimed
- ADC Therapeutics
- Astex
- Merck
- Portola Pharma
- C4 Therapeutics
- Celgene
- Janssen
- Kura Oncology
- Kyowa Hakko Kirin
- Myeloid Therapeutics
- ONO Pharmaceuticals
- Seagen Inc.
- Shoreline Biosciences, Inc
- Takeda
- Trillium Th
- Daiichi Sankyo
- Forty Seven, Inc.
- Millennium/Takeda
- Verastem/SecuraBio
- AstraZeneca Rare Disease
- Alexion

Background

- ECHELON-2 is the largest prospective study of patients with previously untreated PTCL with potential utility in informing future studies
  - It was a phase 3 randomized, double-blind, placebo-controlled multicenter study of brentuximab vedotin and CHP (A+CHP) versus CHOP in the frontline treatment of patients with CD30-positive mature T-cell lymphomas
  - A+CHP was the first regimen to show an OS benefit vs CHOP for patients with PTCL (peripheral T-cell lymphoma)
- At 5 years median follow up, A+CHP continues to provide clinically meaningful improvement in PFS and OS vs CHOP for patients with PTCL
  - Ongoing remission was observed in ~60% of patients with sALCL (anaplastic large cell lymphoma)
  - A+CHP showed a manageable safety profile, including continued resolution or improvement of peripheral neuropathy[1]
- Here we conducted additional hypothesis generating analyses of subgroups of interest (outcomes by subtype, risk factors, gender, age, etc.) that may provide additional context in the design of future studies

ECHELON-2 is a global, phase 3, randomized study



- The primary endpoint was PFS per blinded independent review facility (IRF). Secondary endpoints included OS, ORR and CR rate per IRF, safety, and PFS per IRF for patients with sALCL
- PFS per investigator (INV) was defined as time from randomization to the date of:
  - First documentation of progressive disease (PD)
  - Death due to any cause
  - Receipt of subsequent anticancer chemotherapy

- For this analysis:
  - Outcomes by age <60 and ≥60 years, gender, and PTCL subtype (PTCL-not otherwise specified [NOS], angioimmunoblastic T-cell lymphoma [AITL], and sALCL by IPI categories) were assessed.
- Kaplan-Meier curves were generated to estimate the OS and PFS of patients within treatment arms.
- BV dosing at 1.8 mg/kg 21-day cycle for 6-8 cycles
- All p-values are nominal

Demographics by Age and Gender:

Baseline demographics and disease characteristics were balanced and consistent with the ITT population

	Age <60 Years		Age ≥60 Years	
	A+CHP (n=123)	CHOP (n=126)	A+CHP (n=103)	CHOP (n=100)
Age, mean (range)	44.7 (18, 59)	43.8 (18, 59)	68.0 (60, 85)	68.6 (60, 83)
Female, n (%)	59 (48)	43 (34)	34 (33)	32 (32)
ECOG, n (%)				
0	42 (34)	50 (40)	42 (41)	43 (43)
1	49 (40)	47 (37)	41 (40)	39 (39)
2	31 (25)	29 (23)	20 (19)	18 (18)

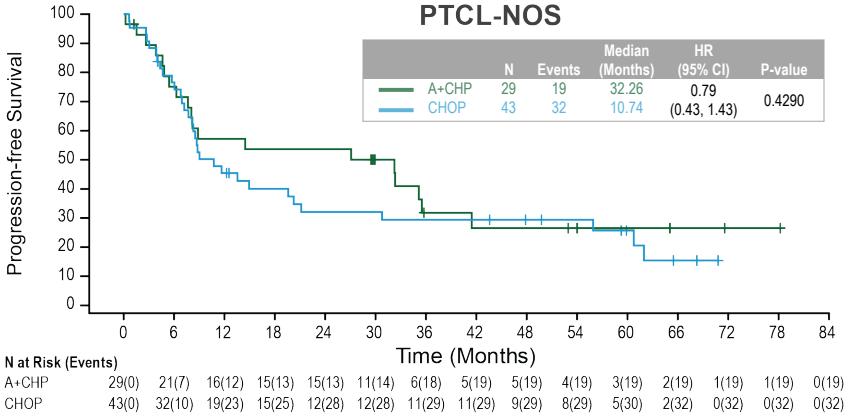
	Males		Females	
	A+CHP (n=133)	CHOP (n=151)	A+CHP (n=93)	CHOP (n=75)
Age, mean (range)	56.5 (18, 81)	55.7 (18, 83)	53.7 (18, 85)	53.1 (18, 82)
ECOG, n (%)				
0	50 (38)	66 (44)	34 (37)	27 (36)
1	54 (41)	58 (38)	36 (39)	28 (37)
2	28 (21)	27 (18)	23 (25)	20 (27)

Analysis by Subtypes: Estimated 5-year PFS and OS rates in prespecified subgroups

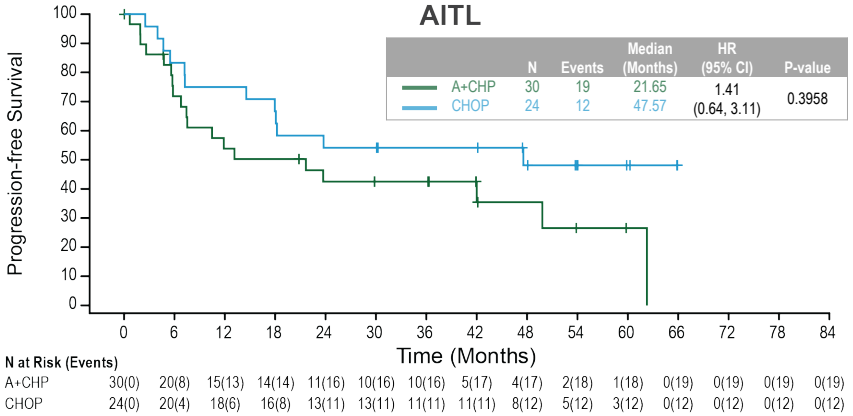
Subgroup	Estimated 5-year PFS rate		HR (95% CI)	P-value*	Estimated 5-year OS rate		HR (95% CI)	P-value*
	A+CHP	CHOP			A+CHP	CHOP		
PTCL subtype								
PTCL-NOS, % (n)	26.5 (29)	25.7 (43)	0.79 (0.43, 1.43)	0.4	46.2 (29)	35.9 (43)	0.75 (0.37, 1.48)	0.4003
AITL, % (n)	26.6 (30)	48.1 (24)	1.41 (0.64, 3.11)	0.3958	67.8 (30)	62.5 (24)	1.01 (0.40, 2.55)	0.9855
sALCL								
Overall, % (n)	60.6 (162)	48.4 (154)	0.55 (0.39, 0.79)	0.0009	75.8 (162)	68.7 (154)	0.66 (0.43, 1.01)	0.0529
ALK+ % (n)	87 (49)	67 (49)	0.40 (0.17, 0.98)	0.0372	91.5 (26)	79.6 (27)	0.48 (0.16, 1.40)	0.1688
ALK– % (n)	49 (113)	39 (105)	0.58 (0.40, 0.86)	0.0054	68.7 (50)	63.3 (41)	0.71 (0.44, 1.12)	0.1373
sALCL, IPI Score								
0–1, % (n)	59.5 (41)	47.6 (32)	0.42 (0.18, 0.94)	0.0301	87.0 (41)	86.2 (32)	0.73 (0.20, 2.73)	0.6411
2–3, % (n)	68.5 (95)	50.9 (100)	0.57 (0.35, 0.90)	0.0158	80.6 (95)	68.7 (100)	0.57 (0.32, 1.01)	0.0496
4–5, % (n)	27.2 (26)	36.4 (22)	0.73 (0.35, 1.50)	0.3839	38.0 (26)	43.2 (22)	0.89 (0.42, 1.89)	0.7606

ITT, intent-to-treat; IPI, International Prognostic Index. *All p-values are nominal

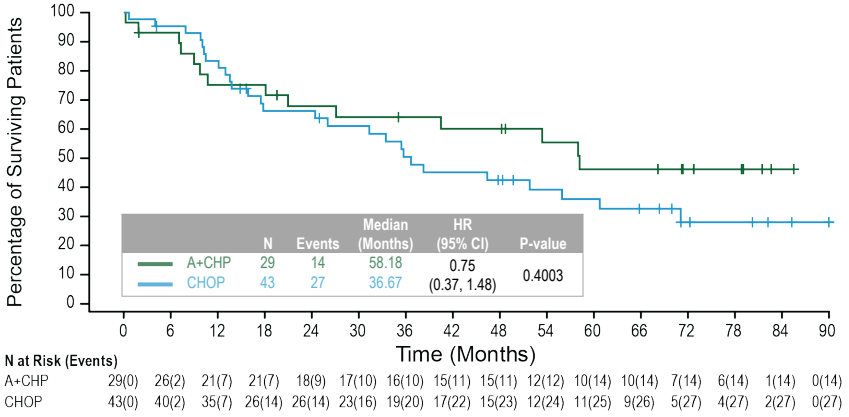
Summary of PFS per Investigator and OS (PTCL-NOS and AITL)



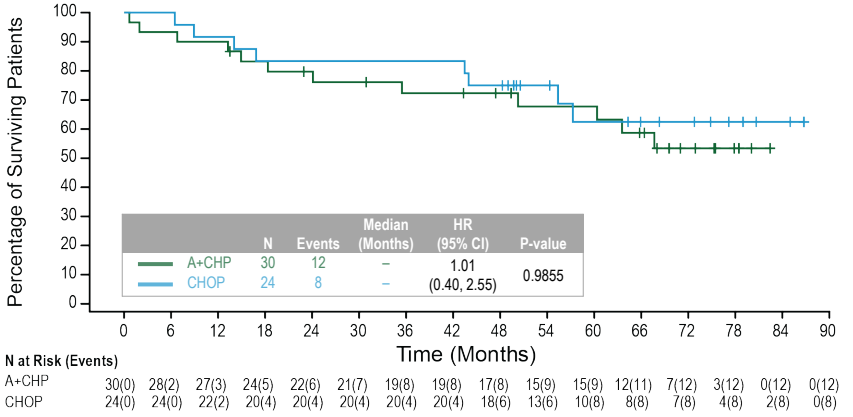
	N	Events	Median (Months)	HR (95% CI)	P-value
A+CHP	29	19	32.26	0.79 (0.43, 1.43)	0.4290
CHOP	43	32	10.74		



	N	Events	Median (Months)	HR (95% CI)	P-value
A+CHP	30	19	21.65	1.41 (0.64, 3.11)	0.3958
CHOP	24	12	47.57		

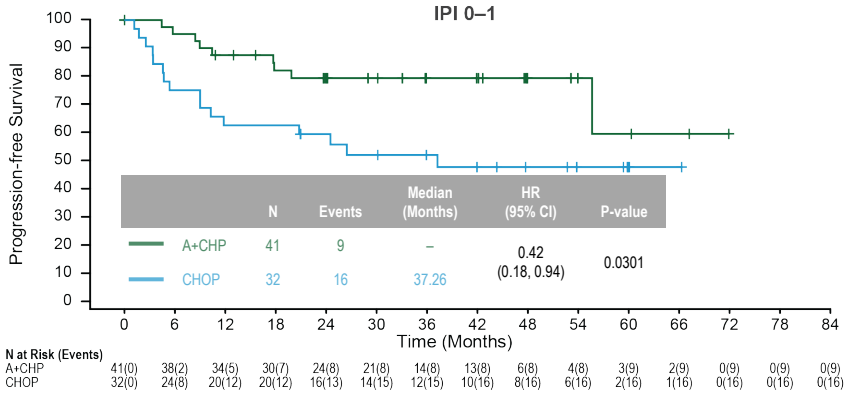


	N	Events	Median (Months)	HR (95% CI)	P-value
A+CHP	29	14	58.18	0.75 (0.37, 1.48)	0.4003
CHOP	43	27	36.67		

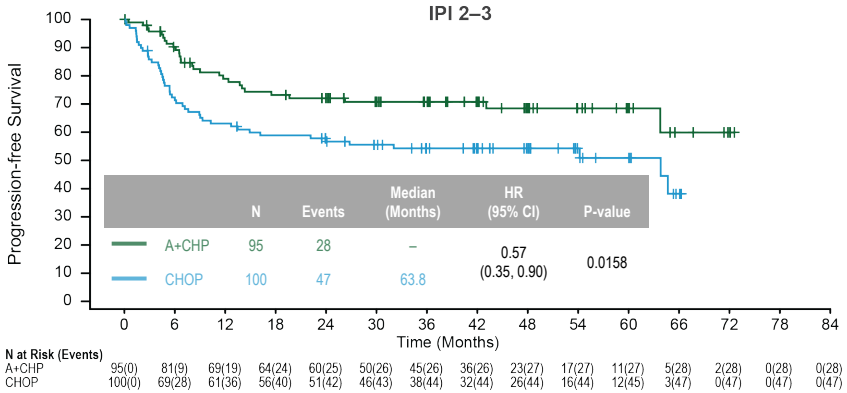


	N	Events	Median (Months)	HR (95% CI)	P-value
A+CHP	30	12	–	1.01 (0.40, 2.55)	0.9855
CHOP	24	8	–		

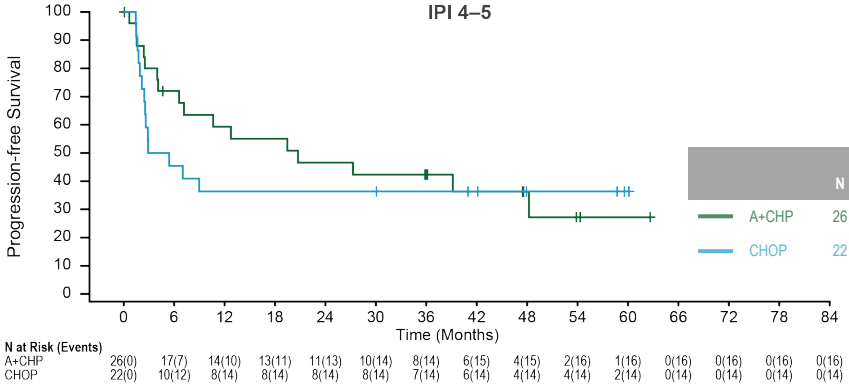
Summary of PFS per Investigator (sALCL by IPI score)



	N	Events	Median (Months)	HR (95% CI)	P-value
A+CHP	41	9	–	0.42 (0.18, 0.94)	0.0301
CHOP	32	16	37.26		

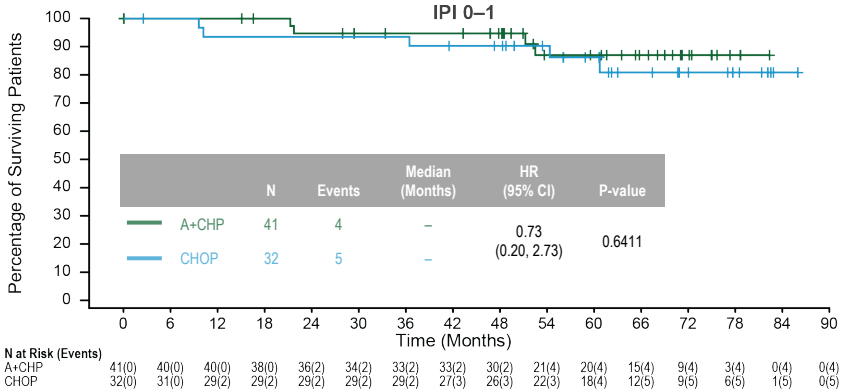


	N	Events	Median (Months)	HR (95% CI)	P-value
A+CHP	95	28	–	0.57 (0.35, 0.90)	0.0158
CHOP	100	47	63.8		

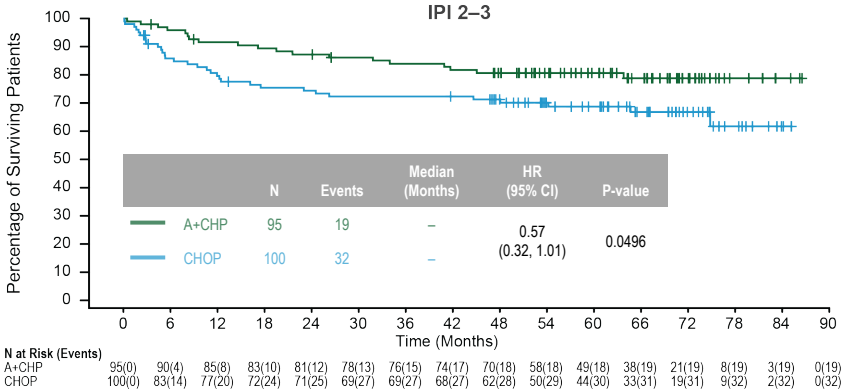


	N	Events	Median (Months)	HR (95% CI)	P-value
A+CHP	26	16	20.7	0.73 (0.35, 1.50)	0.3839
CHOP	22	14	4.11		

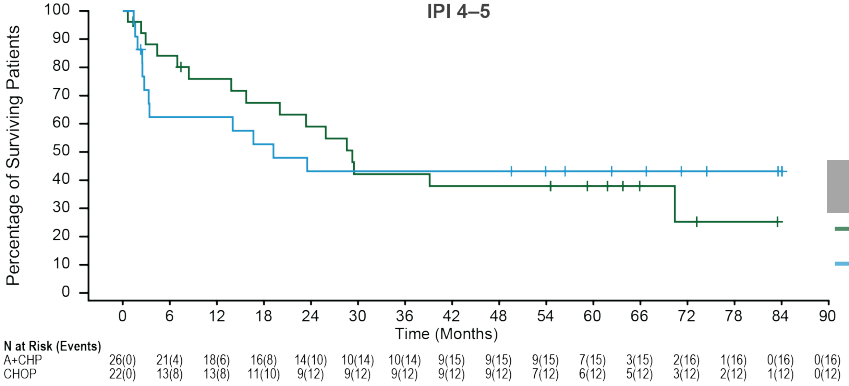
Summary of OS (sALCL by IPI score)



	N	Events	Median (Months)	HR (95% CI)	P-value
A+CHP	41	4	–	0.73 (0.20, 2.73)	0.6411
CHOP	32	5	–		

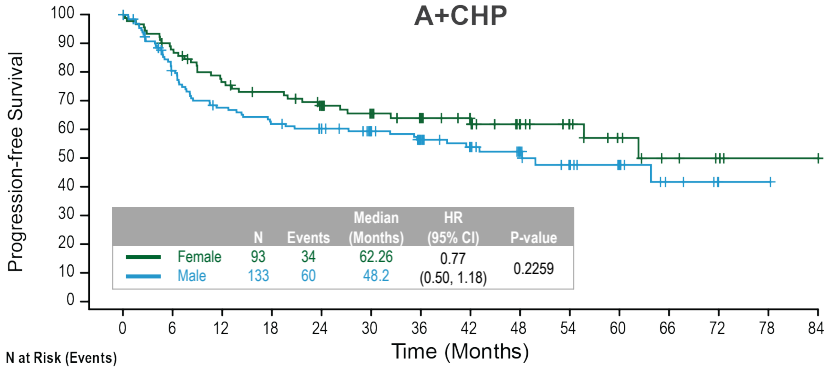


	N	Events	Median (Months)	HR (95% CI)	P-value
A+CHP	95	19	–	0.57 (0.32, 1.01)	0.0496
CHOP	100	32	–		



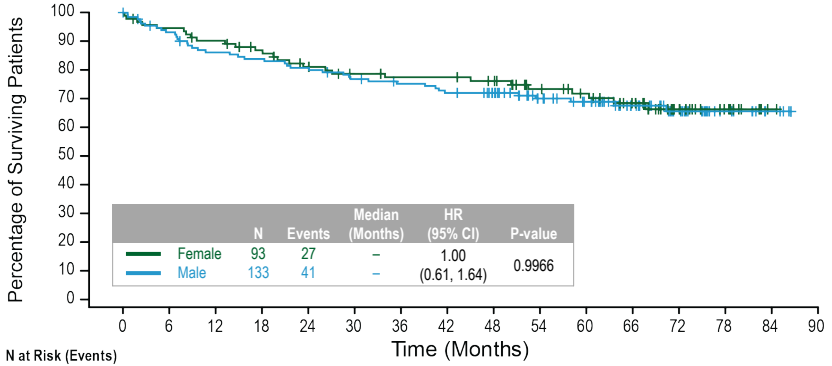
	N	Events	Median (Months)	HR (95% CI)	P-value
A+CHP	26	16	29.27	0.89 (0.42, 1.89)	0.7606
CHOP	22	12	19.19		

Summary of PFS per Investigator and OS (by gender, within arm)



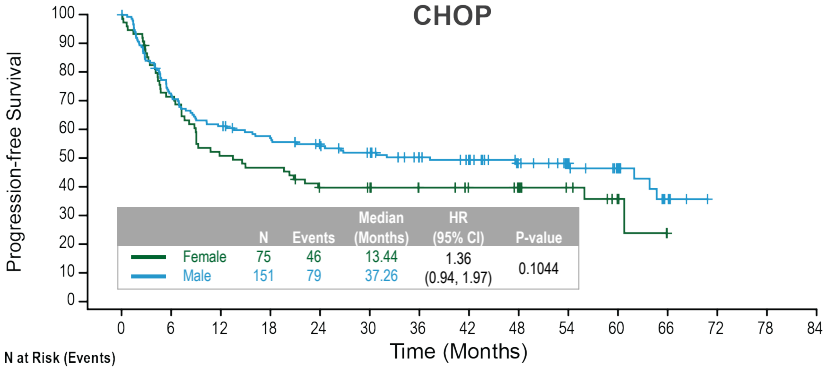
N at Risk (Events)

Female	93(0)	79(11)	67(21)	62(24)	53(28)	43(30)	36(31)	29(32)	20(32)	14(32)	9(33)	5(34)	3(34)	1(34)	0(34)
Male	133(0)	100(25)	83(41)	76(48)	70(50)	61(51)	49(54)	38(56)	24(57)	17(59)	12(59)	5(60)	1(60)	1(60)	0(60)



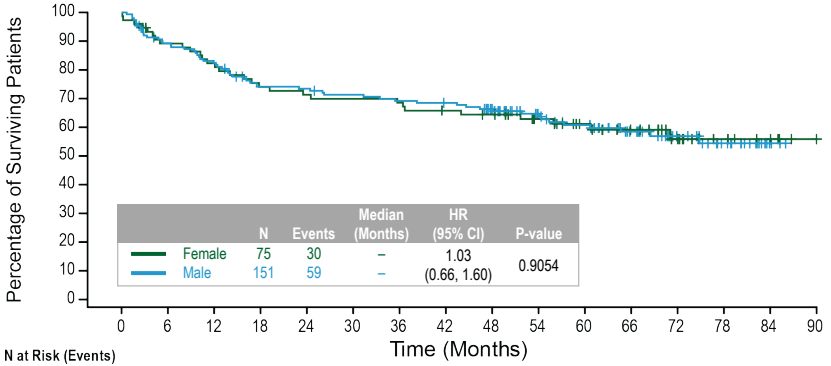
N at Risk (Events)

Female	93(0)	87(5)	82(9)	76(12)	69(17)	64(19)	62(20)	62(20)	59(21)	50(23)	44(24)	37(26)	21(27)	11(27)	1(27)	0(27)
Male	133(0)	121(9)	111(18)	108(21)	104(25)	98(30)	94(32)	90(36)	84(36)	67(38)	59(39)	43(40)	27(41)	12(41)	4(41)	0(41)



N at Risk (Events)

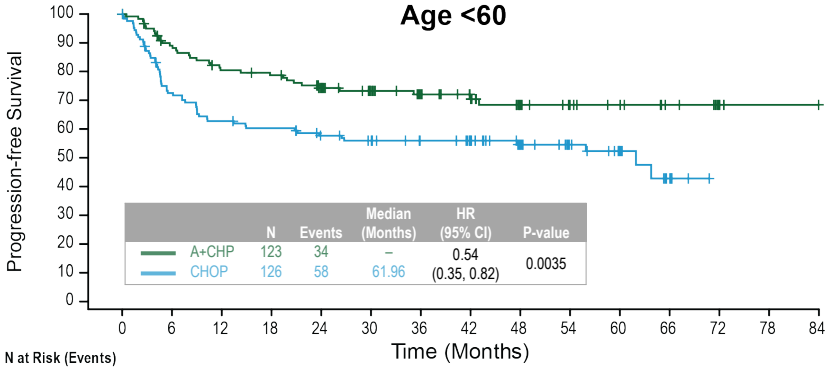
Female	75(0)	52(21)	37(36)	34(39)	27(44)	26(44)	22(44)	19(44)	17(44)	11(44)	5(45)	0(46)	0(46)	0(46)	0(46)
Male	151(0)	107(42)	91(58)	82(64)	74(68)	68(71)	57(73)	51(74)	38(75)	28(75)	19(76)	6(79)	0(79)	0(79)	0(79)



N at Risk (Events)

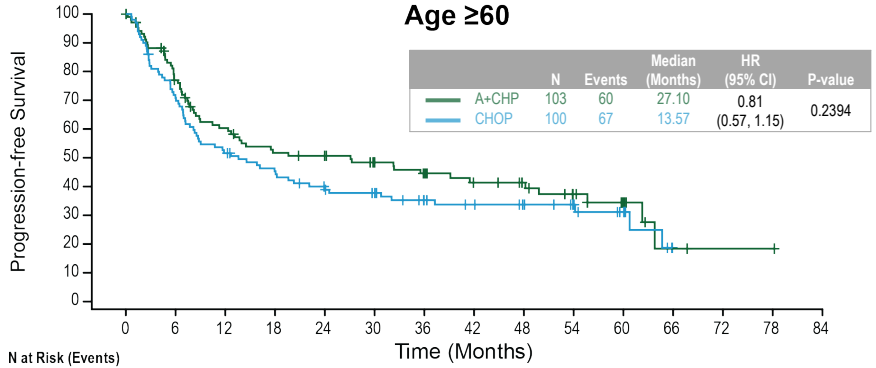
Female	75(0)	65(8)	60(13)	54(19)	52(21)	51(22)	50(23)	47(25)	45(26)	37(27)	30(28)	24(29)	16(30)	8(30)	5(30)	0(30)
Male	151(0)	131(16)	121(26)	106(38)	105(39)	101(42)	98(45)	96(46)	87(49)	68(51)	60(55)	44(57)	27(58)	17(59)	3(59)	0(59)

Summary of PFS per Investigator and OS (by age within arm)



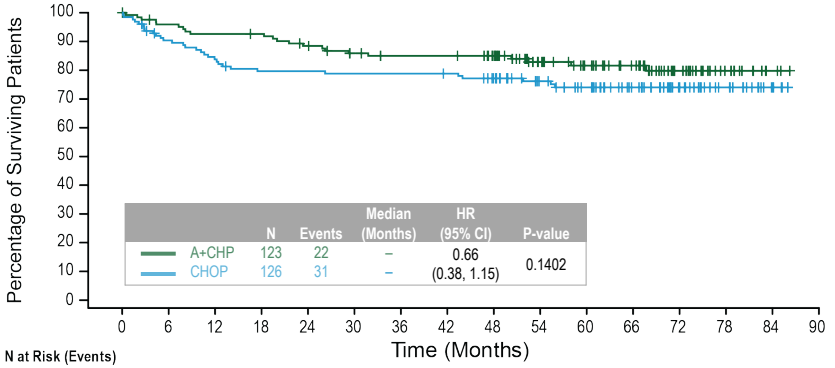
N at Risk (Events)

A+CHP	123(0)	104(13)	93(23)	90(25)	78(30)	66(31)	53(32)	43(33)	23(34)	17(34)	13(34)	8(34)	3(34)	1(34)	0(34)
CHOP	126(0)	89(34)	77(46)	73(49)	66(52)	62(54)	55(54)	49(54)	37(55)	25(55)	15(56)	6(58)	0(58)	0(58)	0(58)



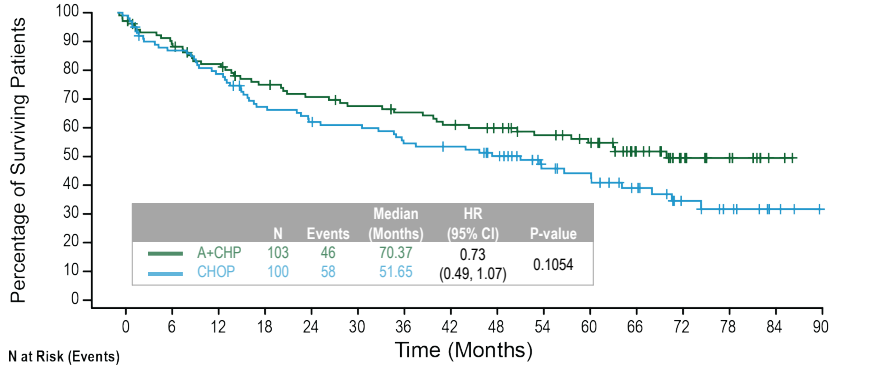
N at Risk (Events)

A+CHP	103(0)	75(23)	57(39)	48(47)	45(48)	38(50)	32(53)	24(55)	21(55)	14(57)	8(58)	2(60)	1(60)	1(60)	0(60)
CHOP	100(0)	70(29)	51(48)	43(54)	35(60)	32(61)	24(63)	21(64)	18(64)	14(64)	9(65)	0(67)	0(67)	0(67)	0(67)



N at Risk (Events)

A+CHP	123(0)	116(5)	112(9)	111(9)	105(14)	99(17)	96(18)	96(18)	90(18)	71(20)	61(21)	51(21)	30(22)	14(22)	3(22)	0(22)
CHOP	126(0)	110(12)	102(20)	96(25)	96(25)	95(26)	95(26)	94(26)	88(28)	72(29)	63(31)	48(31)	30(31)	17(31)	5(31)	0(31)



N at Risk (Events)

A+CHP	103(0)	92(9)	81(18)	73(24)	68(28)	63(32)	60(34)	56(38)	53(39)	46(41)	42(42)	29(45)	18(46)	9(46)	2(46)	0(46)
CHOP	100(0)	86(12)	79(19)	64(32)	61(35)	57(38)	53(42)	49(45)	44(47)	33(49)	27(52)	20(55)	13(57)	8(58)	3(58)	0(58)

Summary of Incidence of Select Adverse Events by Age

	Age <60 Years		Age ≥60 Years	
	A+CHP (n=120)	CHOP (n=126)	A+CHP (n=103)	CHOP (n=100)
Pre-existing PN, n (%)	8 (7)	8 (6)	16 (16)	16 (16)
Treatment-emergent PN, n (%)	63 (53)	68 (54)	54 (52)	56 (56)
Worst severity Grade 2	14 (12)	8 (6)	19 (18)	18 (18)
Worst severity Grade 3	4 (3)	8 (6)	4 (4)	2 (2)
Worst severity Grade 4	0	0	1 (1)	0
Complete resolution of PN[a], n (%)	47 (75)	48 (71)	24 (44)	34 (61)
Improvement of PN[b], n (%)	3 (5)	8 (12)	10 (19)	7 (13)
Neutropenia	50 (42)	46 (37)	35 (34)	39 (39)
Febrile neutropenia	11 (9)	11 (9)	30 (29)	22 (22)

a. Resolution was defined as resolved/recovered with or without sequelae; or return to baseline or lower severity as of the latest assessment for pre-existing events.
b. Improvement was defined as decrease by at least 1 grade from the worst grade with no higher grade thereafter. Pts with improvement in any event at last follow up were those with at least one improved event and the date of improvement was before last follow up date. Subjects with all events resolved were excluded.

Conclusions

- A+CHP was the first frontline regimen to demonstrate an OS benefit vs CHOP for patients with PTCL.
- This is the largest prospective study of patients with untreated PTCL.
- ECHELON-2 5-year data have redefined efficacy outcomes for this population and provided an important benchmark data to inform future studies.
- This detailed analysis of subgroups of clinical interest could be used to inform the next series of trials in these patients.

Disclosures

Horwitz: Acrotech Biopharma, Affimed, ADC Therapeutics, Astex, Merck, Portola Pharma, C4 Therapeutics, Celgene, Janssen, Kura Oncology, Kyowa Hakko Kirin, Myeloid Therapeutics, ONO Pharmaceuticals, Seagen Inc., Shoreline Biosciences, Inc, Takeda, Trillium Th, Daiichi Sankyo, Forty Seven Inc., Millennium/Takeda, Verastem/SecuraBio. Astra Zeneca Rare Disease, Alexion. **Savage**: Seagen Inc., Bristol-Myers Squibb, Merck, AbbVie, AstraZeneca, Servier, Roche, Takeda, Beigene, Kwoya, Janssen, Novartis. **Illidge**: Seagen Inc. **Iyer**: N/A. **Advani**: Seagen Inc. **Shustov**: Seagen Inc. **Bartlett**: ADC Therapeutics, Roche/Genentech, Seagen Inc., Autolus, Bristol-Myers Squibb, Celgene, Forty Seven, Janssen, Kite, Merck, Millennium, Pharmacyclics. **Pro**: N/A. **Jacobsen**: Takeda, Syros, Janssen, Novartis, Pharmacyclics, Acerta. **Koch**: Seagen Inc. **Domenech**: Takeda. **Fanale**: Seagen Inc. **Fenton**: Seagen Inc. **Campana**: Seagen, Inc. **Dong**: Seagen Inc. **Truemper**: Seagen Inc.

References:

1. Horwitz S, et al. ASH 2020