Five-Year Analysis of an Asia Subpopulation with Previously Untreated DLBCL Confirms Pola-R-CHP Benefit on Outcomes: The POLARIX Study

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Disclosures

- **Yuqin Song, M.D., PhD**

➢ Consultancy/advisory board participation (past 12 months):

- AbbVie, BeiGene, AstraZeneca, MSD, Johnson & Johnson, Roche

➢ Research support (managed by institution):

- Janssen, BeiGene, MSD, Takeda

POLARIX study design

Patients

- Previously untreated DLBCL
- Age 18–80 years
- IPI 2–5
- ECOG PS 0–2

Stratification factors

- IPI score (2 vs 3–5)
- Bulky disease (<7.5 vs ≥7.5cm)
- Geographic region (Western Europe, US, Canada, & Australia vs Asia vs rest of world)

Randomize 1:1

Pola-R-CHP

Polatuzumab vedotin (1.8mg/kg)*
R-CHP + vincristine placebo

R-CHOP

R-CHOP† +
polatuzumab vedotin placebo

Cycles 1–6
(1 cycle=21 days)

Rituximab
375mg/m^2

Cycles 7 & 8

Primary endpoint: PFS by INV

Key secondary endpoints: EFS_{eff} by INV, PET CR at EOT by BICR, OS

		Pola-R-CHP	R-CHOP	Total
Asia Subpopulation‡	Intent-to-Treat§	141	140	281
	Safety evaluable¶	140	139	279
	Median PFS follow-up (months)	54.4	54.1	54.1
	Median OS follow-up (months)	60.3	59.8	60.0

*IV on Day 1; †R-CHOP: IV rituximab 375mg/m^2, cyclophosphamide 750mg/m^2, doxorubicin 50mg/m^2, and vincristine 1.4mg/m^2 (max. 2mg) on Day 1, plus oral prednisone 100mg once daily on Days 1–5; ‡The Asia subpopulation includes 281 patients enrolled from Asian countries/regions (mainland China, Japan, South Korea, and Taiwan) during the global phase (160 patients) and patients from the China extension cohort (121 patients); §Asian randomized population; ¶Asian treated population.

BICR, blinded independent central review; CR, complete response; DLBCL, diffuse large B-cell lymphoma; ECOG PS, Eastern Cooperative Oncology Group performance status; EFS_{eff}, event-free survival (efficacy); EOT, end of treatment; INV, investigator; IPI, International Prognostic Index; OS, overall survival; PET, positron emission tomography; PFS, progression-free survival; Pola-R-CHP, polatuzumab vedotin, rituximab, cyclophosphamide, doxorubicin and prednisolone; R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine and prednisone.

Tilly H, et al. *N Eng J Med* 2022;386:351–63.

Patient baseline characteristics of Asia subpopulation

n (%), unless otherwise stated		Pola-R-CHP (n=141)	R-CHOP (n=140)
Age	Median, years (min–max) ≥65 years	63 (19–79) 58 (41.1)	64 (23–78) 67 (47.9)
Sex	Male	71 (50.4)	78 (55.7)
ECOG PS	0–1 2	116 (82.3) 25 (17.7)	121 (86.4) 19 (13.6)
Stratification - IPI score (IxRS)	2 3–5	54 (38.3) 87 (61.7)	53 (37.9) 87 (62.1)
Stratification - bulky disease (IxRS)	Absent Present	98 (69.5) 43 (30.5)	98 (70.0) 42 (30.0)
Ann Arbor stage	I–II III IV	19 (13.5) 40 (28.4) 82 (58.2)	21 (15.0) 52 (37.1) 67 (47.9)
Baseline LDH	≤1xULN >1xULN	45 (31.9) 96 (68.1)	41 (29.3) 99 (70.7)
Number of extranodal sites	≥2	64 (45.4)	58 (41.4)
NHL histologic diagnosis (eCRF)	DLBCL NOS, ABC, GCB HGBL, NOS, DHL/THL Other large B-cell	131 (92.9) 6 (4.3) 4 (2.8)	128 (91.4) 3 (2.1) 9 (6.4)
COO centrally reported by NanoString	ABC GCB Unclassified Unknown	55 (55.0) 30 (30.0) 15 (15.0) 41	46 (46.0) 40 (40.0) 14 (14.0) 40

ABC, activated B-cell; COO, cell of origin; DHL/THL, double-hit/triple-hit lymphoma; GCB, germinal center B-cell; HGBCL, high-grade B-cell lymphoma; LDH, lactate dehydrogenase; NOS, not otherwise specified; ULN, upper limit of normal.

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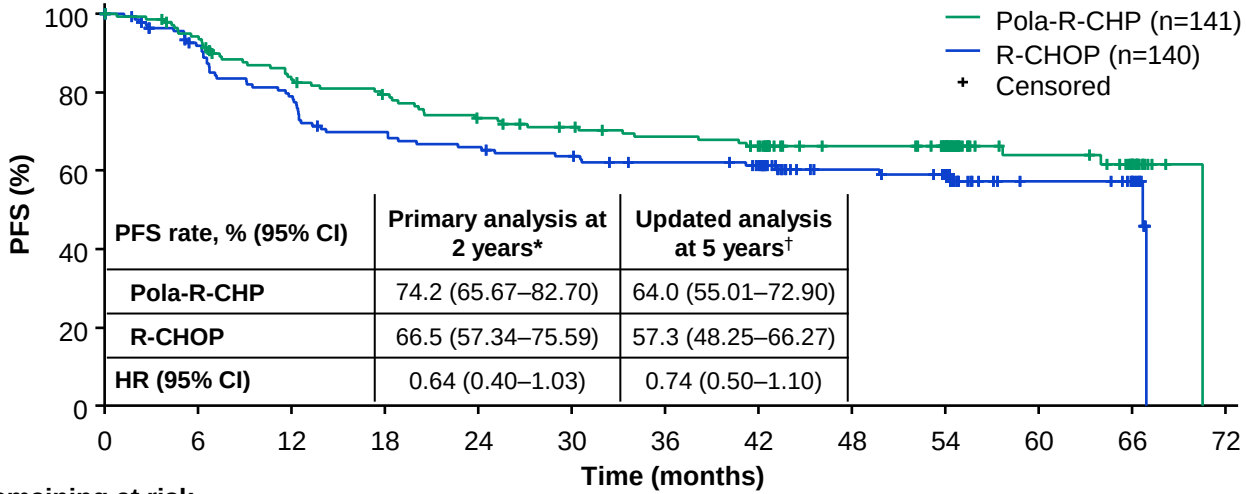
Initial PFS benefit of Pola-R-CHP over R-CHOP is maintained at 5 years



PFS rate, % (95% CI)	Primary analysis at 2 years*	Updated analysis at 5 years†
Pola-R-CHP	74.2 (65.67–82.70)	64.0 (55.01–72.90)
R-CHOP	66.5 (57.34–75.59)	57.3 (48.25–66.27)
HR (95% CI)	0.64 (0.40–1.03)	0.74 (0.50–1.10)

Patients remaining at risk

Pola-R-CHP	141	130	112	105	96	90	85	79	64	55	28	20	NE
R-CHOP	140	121	104	91	86	82	77	73	48	42	16	12	NE

After the 5-year follow up, Pola-R-CHP had a sustained and clinically meaningful PFS benefit in the Asia subpopulation (HR: 0.74)

*Data cut-off: June 28, 2021;
†Data cut-off: July 5, 2024.
Hazard ratio (HR): unstratified.

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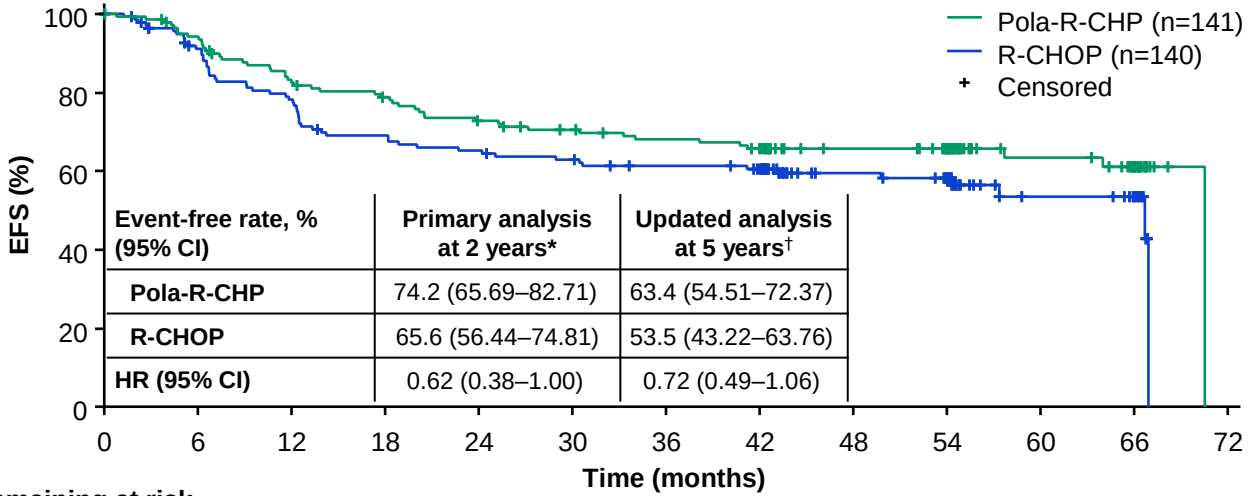
EFS shows similar treatment effect as PFS at 5 years



Event-free rate, % (95% CI)	Primary analysis at 2 years*	Updated analysis at 5 years†
Pola-R-CHP	74.2 (65.69–82.71)	63.4 (54.51–72.37)
R-CHOP	65.6 (56.44–74.81)	53.5 (43.22–63.76)
HR (95% CI)	0.62 (0.38–1.00)	0.72 (0.49–1.06)

Patients remaining at risk

Pola-R-CHP	141	130	112	105	96	90	85	79	64	55	28	20	NE
R-CHOP	140	120	103	90	85	81	76	72	47	41	16	12	NE

After the 5-year follow up, EFS outcomes were consistent with results of the primary endpoint (PFS) suggesting clinical benefit for Pola-R-CHP vs R-CHOP in the Asia subpopulation

*Data cut-off: June 28, 2021;
†Data cut-off: July 5, 2024.
HR: unstratified.

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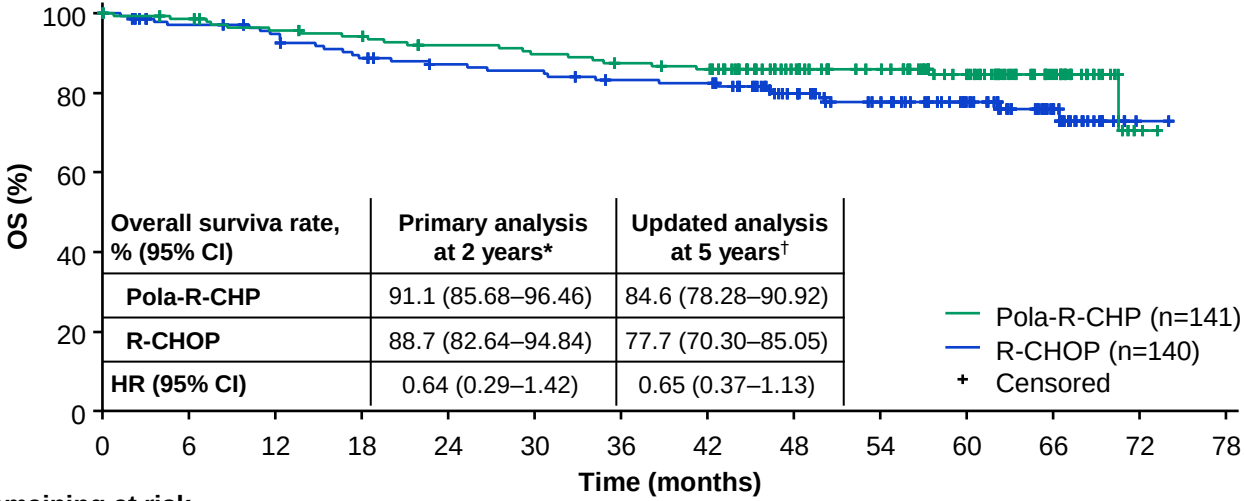
5-year OS shows favorable results for Pola-R-CHP-treated patients



Overall survival rate, % (95% CI)	Primary analysis at 2 years*	Updated analysis at 5 years†
Pola-R-CHP	91.1 (85.68–96.46)	84.6 (78.28–90.92)
R-CHOP	88.7 (82.64–94.84)	77.7 (70.30–85.05)
HR (95% CI)	0.64 (0.29–1.42)	0.65 (0.37–1.13)

Patients remaining at risk

Pola-R-CHP	141	137	131	128	122	119	115	112	92	80	61	30	2	NE
R-CHOP	140	130	125	116	111	109	104	103	83	69	52	27	1	NE

After the 5-year follow up, the risk of death was reduced by 35% following treatment with Pola-R-CHP vs R-CHOP in the Asia subpopulation

*Data cut-off: June 28, 2021;
†Data cut-off: July 5, 2024.
HR: unstratified.

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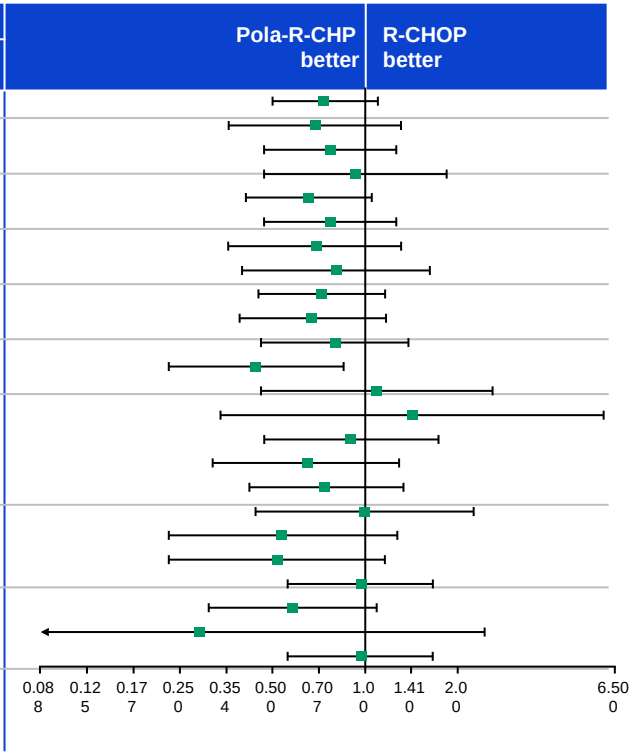
5-year PFS outcomes show consistent treatment effect of Pola-R-CHP across subgroups in the Asia subpopulation

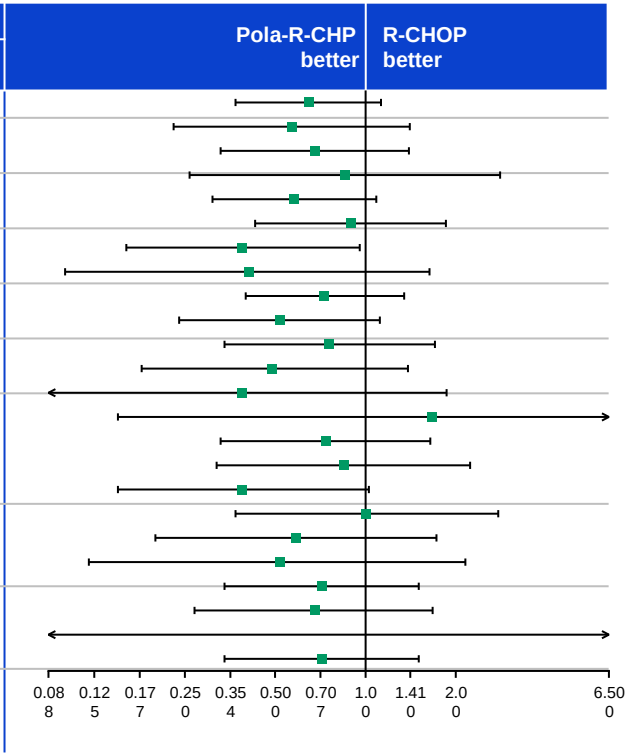
Baseline characteristics	Subgroups	Total	R-CHOP (n=140)			Pola-R-CHP (n=141)				
		n	n	Events	5 years rate	n	Events	5 years rate	HR	95% Wald CI
Overall		281	140	56	57.26	141	48	63.95	**0.74**	0.5−1.1
Age group	>65	112	60	25	57.46	52	15	65.69	**0.69**	0.36−1.31
	18–65	169	80	31	57.97	89	33	63.73	**0.77**	0.47−1.26
IPI score	IPI 2	107	53	17	65.03	54	16	69.98	**0.93**	0.47−1.84
	IPI 3–5	174	87	39	52.21	87	32	60.74	**0.66**	0.41−1.05
Bulky disease	Absent	196	98	35	62.66	98	31	69.11	**0.77**	0.47−1.26
	Present	85	42	21	44.6	43	17	49.4	**0.69**	0.36−1.31
Baseline LDH	≤1xULN	84	39	16	51.39	45	16	63.94	**0.81**	0.4−1.62
	>1xULN	197	101	40	58.97	96	32	63.9	**0.72**	0.45−1.16
No. of extranodal sites	≥2	122	58	27	47.57	64	25	57.87	**0.67**	0.39−1.17
	0–1	159	82	29	63.7	77	23	69.8	**0.8**	0.46−1.38
COO	ABC	101	46	22	51.91	55	16	73.14	**0.44**	0.23−0.85
	GCB	70	40	12	69.28	30	9	67.61	**1.09**	0.46−2.6
	Unclassified	29	14	4	72.92	15	5	66.67	**1.42**	0.34−5.96
	Unknown	81	40	18	43.81	41	18	46.54	**0.9**	0.47−1.73
Double expressor by IHC	DEL	76	41	21	51.1	35	13	58.34	**0.65**	0.32−1.29
	Non-DEL	147	72	24	61.26	75	23	71.12	**0.74**	0.42−1.33
	Unknown	58	27	11	57.69	31	12	54.85	**1**	0.44−2.26
M1 macrophage	High	72	41	16	59.87	31	9	72.77	**0.54**	0.23−1.27
	Low	73	34	15	58.82	39	10	73.49	**0.52**	0.23−1.16
	Unknown	136	65	25	52.36	71	29	51.61	**0.97**	0.56−1.66
Dark Zone Signature	Negative	120	58	24	58	62	18	71.3	**0.58**	0.31−1.09
	Positive	25	17	7	62.5	8	1	87.5	**0.29**	0.04−2.44
	Unknown	136	65	25	52.36	71	29	51.61	**0.97**	0.56−1.66



Please note that subgroup analysis of the Asia subpopulation is not a pre-specified analysis, and the sample size is very limited, translating univariate subgroup results into patient care should be applied with caution

5-year OS outcomes show consistent treatment effect of Pola-R-CHP across subgroups in the Asia subpopulation

Baseline characteristics	Subgroups	Total	R-CHOP (n=140)			Pola-R-CHP (n=141)				
		n	n	Events	5 years rate	n	Events	5 years rate	HR	95% Wald CI
Overall		281	140	30	77.67	141	21	84.6	**0.65**	0.37−1.13
Age group	>65	112	60	14	75.79	52	7	84.24	**0.57**	0.23−1.41
	18–65	169	80	16	79.12	89	14	85.05	**0.68**	0.33−1.4
IPI score	IPI 2	107	53	6	88.06	54	5	90	**0.86**	0.26−2.82
	IPI 3–5	174	87	24	70.87	87	16	81.52	**0.58**	0.31−1.09
Bulky disease	Absent	196	98	15	85.31	98	14	86.26	**0.9**	0.43−1.86
	Present	85	42	15	58.8	43	7	80.47	**0.39**	0.16−0.96
Baseline LDH	≤1xULN	84	39	6	86.29	45	3	92.9	**0.41**	0.1−1.64
	>1xULN	197	101	24	74.44	96	18	80.81	**0.73**	0.4−1.35
No. of extranodal sites	≥2	122	58	16	70.9	64	11	82.77	**0.52**	0.24−1.12
	0-1	159	82	14	81.77	77	10	86.24	**0.76**	0.34−1.71
COO	ABC	101	46	9	77.54	55	6	90.73	**0.49**	0.18−1.39
	GCB	70	40	7	84.93	30	2	92.31	**0.39**	0.08−1.87
	Unclassified	29	14	1	91.67	15	2	86.67	**1.67**	0.15−18.45
	Unknown	81	40	13	65.79	41	11	70.03	**0.74**	0.33−1.65
Double expressor by IHC	DEL	76	41	10	76.41	35	7	77.92	**0.85**	0.32−2.24
	Non-DEL	147	72	13	80.64	75	6	93.03	**0.39**	0.15−1.03
	Unknown	58	27	7	73.08	31	8	71.92	**1.01**	0.37−2.78
M1 macrophage	High	72	41	10	73.68	31	5	86.21	**0.59**	0.2−1.73
	Low	73	34	5	87.53	39	3	91.96	**0.52**	0.12−2.16
	Unknown	136	65	15	75.84	71	13	78.09	**0.72**	0.34−1.51
Dark Zone Signature	Negative	120	58	11	81.5	62	8	88.01	**0.68**	0.27−1.68
	Positive	25	17	4	75	8	0	100	**0**	0−Inf
	Unknown	136	65	15	75.84	71	13	78.09	**0.72**	0.34−1.51



Please note that subgroup analysis of the Asia subpopulation is not a pre-specified analysis, and the sample size is very limited, translating univariate subgroup results into patient care should be applied with caution

Causes of death

n (%), unless otherwise stated	Pola-R-CHP (n=141)	R-CHOP (n=140)
Total number of deaths	22 (15.6)	32 (22.9)
Primary cause of death		
Disease progression	14 (9.9)	22 (15.7)
Not disease related	5 (3.5)	5 (3.6)
Cardiovascular	1 (0.7)	1 (0.7)
COVID-19	1 (0.7)	1 (0.7)
Infection	1 (0.7)	1 (0.7)
Liver failure	0	1 (0.7)
Secondary malignancy*	2 (1.4)	1 (0.7)
Unknown†	3 (2.1)	5 (3.6)

Deaths associated with lymphoma progression are fewer with Pola-R-CHP in the Asia subpopulation

*Carcinogenicity includes treatment-emergent adverse events (TEAEs) with onset during the AE reporting period and after the TEAE reporting window. The TEAE period is defined as new or worsening AEs from the first dose of any study drug through 90 days after the last dose or prior to new anti-lymphoma therapy (NALT), whichever occurs first. Carcinogenicity events included acute myeloid leukemia and glottis carcinoma (R-CHOP arm), and colorectal cancer (Pola-R-CHP arm; 1 patient each). †Deaths due to unknown reasons refer to those reported via public records without cause of death, per reporting standards.

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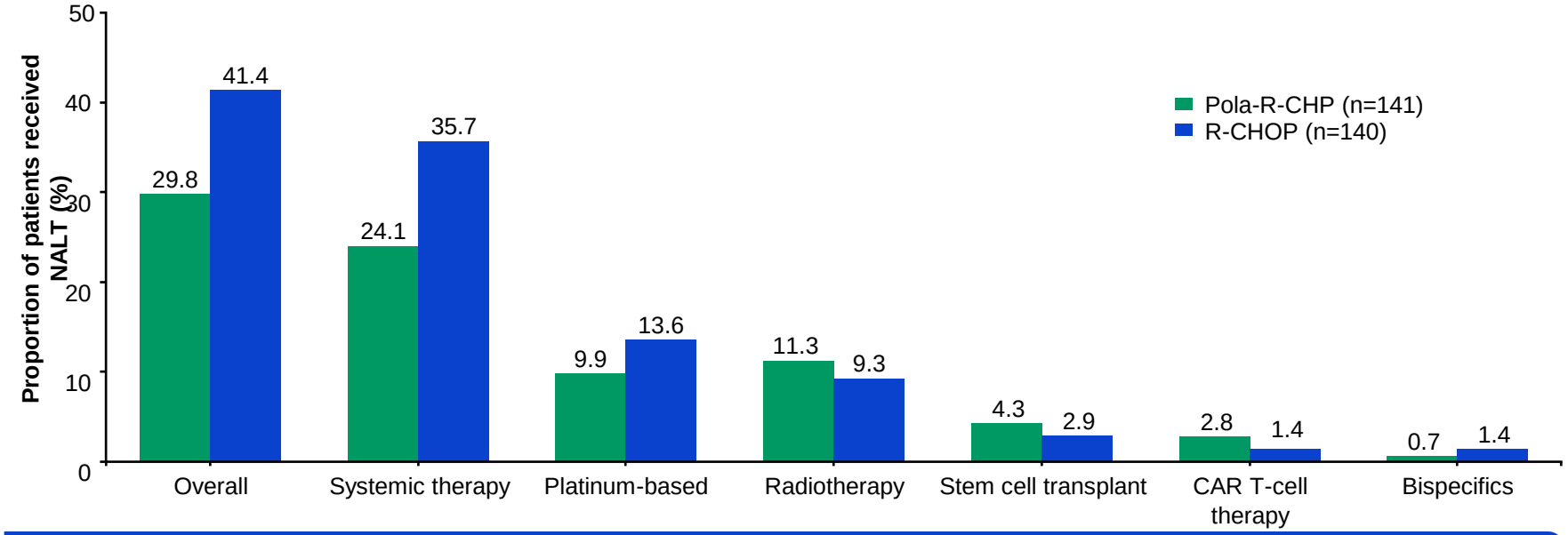
Fewer patients treated with Pola-R-CHP required subsequent therapies vs patients treated with R-CHOP



Patterns of subsequent therapies in Asia subpopulation mirror routine clinical care at the time of study conduct

CAR, chimeric antigen receptor.

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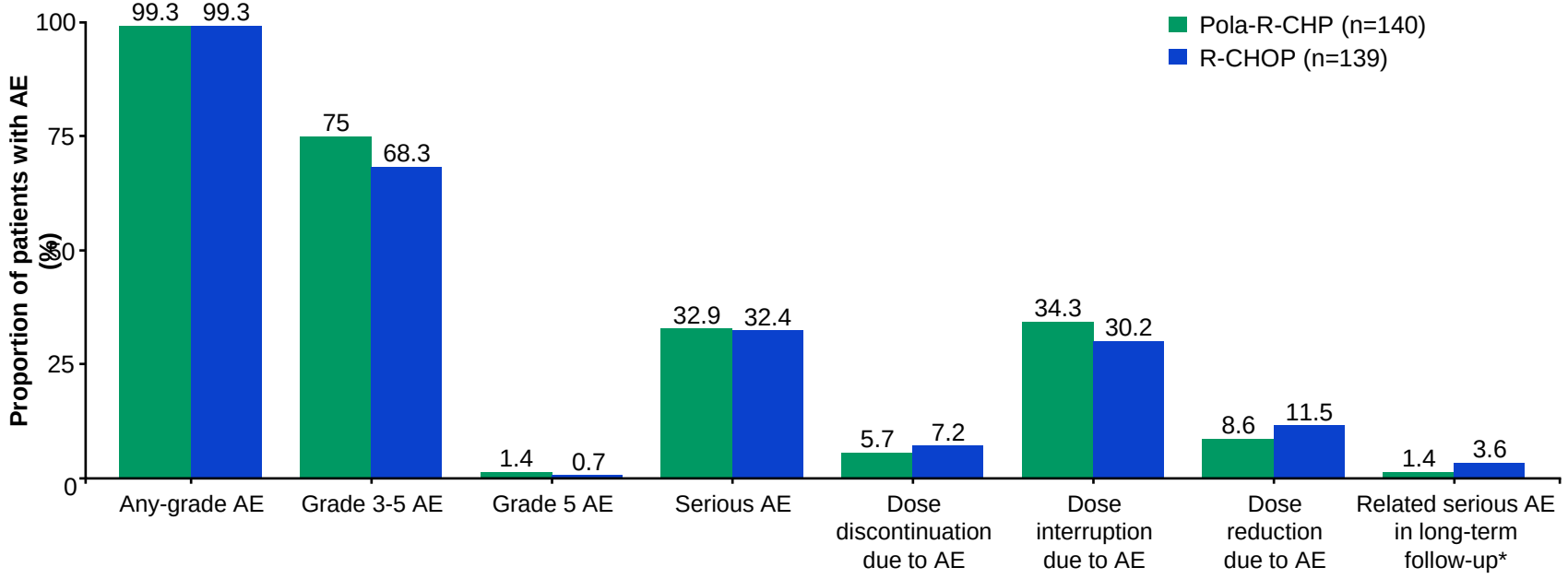
Safety profile remained comparable between arms



Safety profile remains consistent with primary analysis in Asia subpopulation.
No new safety signals were detected during long-term follow-up

*TEAEs are defined as new or worsening AE from the first dose of study drug through 90 days after the last dose of any study drug or prior to NALT, whichever is earlier. After this TEAE period, the post-TEAE period (i.e. long-term safety follow up) reporting requirement is only for serious AEs that the investigator believes to be related to prior study drug treatment.

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Select AEs of particular interest are consistent with the identified risks associated with polatuzumab vedotin

Patients, n (%)	R-CHOP (N=139)	Pola-R-CHP (N=140)
Peripheral neuropathy		
All grade	72 (51.8)	63 (45.0)
Grade 3–5	1 (0.7)	0
Infections and infestations		
All grade	67 (48.2)	58 (41.4)
Grade 3–5	22 (15.8)	15 (10.7)
Cardiac arrhythmia		
All grade	10 (7.2)	5 (3.6)
Grade 3–5	2 (1.4)	1 (0.7)
Neutropenia		
All grade	85 (61.2)	96 (68.6)
Grade 3–5	71 (51.1)	85 (60.7)

Patients, n (%)	R-CHOP (N=139)	Pola-R-CHP (N=140)
Anemia		
All grade	59 (42.4)	63 (45.0)
Grade 3–5	18 (12.9)	12 (8.6)
Thrombocytopenia		
All grade	46 (33.1)	53 (37.9)
Grade 3–5	15 (10.8)	13 (9.3)
Carcinogenicity*		
All grade	1 (0.7)	2 (1.4)
Grade 3–5	1 (0.7)	2 (1.4)

The AEPIs remain comparable between arms, and consistent with the identified risks associated with polatuzumab vedotin in Asia subpopulation

Data cut-off: July 5, 2024. *Carcinogenicity includes TEAEs with onset during the AE reporting period and after the TEAE reporting window. The TEAE period is defined as new or worsening AEs from the first dose of any study drug through 90 days after the last dose or prior to NALT, whichever occurs first. Carcinogenicity events included acute myeloid leukemia and glottis carcinoma (R-CHOP arm), and colorectal cancer (Pola-R-CHP arm; 1 patient each).

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Conclusions

- Pola-R-CHP continues to show a clinically meaningful improvement in INV-assessed PFS versus R-CHOP in the Asia subpopulation
- With longer follow-up, the reduction in risk of death following treatment with Pola-R-CHP was maintained, suggesting a sustained effect of OS
- Favorable outcomes were seen in Pola-R-CHP across exploratory subgroups in the Asia subpopulation, but cautious interpretation is strongly advised
- The safety profile remained comparable between the two regimens, and no new safety signals were identified
- In general, 5-year data support Pola-R-CHP as the standard of care in frontline LBCL in Asia