Oncologic Drugs Advisory Committee (ODAC) Meeting

March 09, 2023

BLA# 761121/Supplement 008

Drug name: Polatuzumab vedotin-piiq

Applicant: Genentech, Inc.

ERRATA

To the combined FDA and Applicant ODAC Briefing Document

This document contains an erratum to the ODAC Briefing Document for one table, and formatting corrections without content change for three tables.

A. FDA Appendix 4, Table 27

The original table is followed by a table with corrections in red. The conclusions are unchanged.

Table 1 Results of PFS and OS by NHL Subgroups (Original)

NHL Subtype	Parameter	Pola + R-CHP	R-CHOP
Overall	**N**	440	439
	PFS		
	1-year rate (95% CI)	83.9% (80.1, 87.1)	79.8% (75.6, 83.3)
	diff	4.1% (-1.0, 9.3)	
	2-year rate (95% CI)	76.7% (72.3, 80.5)	70.2% (65.5, 74.4)
	diff	6.5% (-1.8, 10.1)	
	HR (95% CI)	**0.73 (0.57, 0.95)**	
	OS		
	1-year rate (95% CI)	92.2% (89.2, 94.3)	94.6% (92.0, 96.4)
	diff	-2.4% (-5.8, 0.9)	
	2-year rate (95% CI)	88.7% (85.3, 91.3)	88.6% (85.2, 91.3)
	diff	0.1% (-6.7, 1.8)	
	HR (95% CI)	**0.94 (0.65, 1.37)**	
DLBCL NOS	**N**	373	367
	PFS		
	1-year rate (95% CI)	84.0% (79.8, 87.4)	81.0% (76.5, 84.7)
	diff	3.0% (-2.6, 8.6)	
	2-year rate (95% CI)	77.3% (72.6, 81.3)	70.9% (65.8, 75.3)
	diff	6.4% (-3.5, 9.5)	
	HR (95% CI)	**0.75 (0.57, 0.99)**	
	OS		
	1-year rate (95% CI)	91.8% (88.5, 94.2)	95.5% (92.8, 97.2)
	diff	-3.7% (-7.2, -0.2)	
	2-year rate (95% CI)	88.0% (84.2, 90.9)	89.6% (85.9, 92.3)
	diff	-1.6% (-8.3, 0.9)	
	HR (95% CI)	**1.02 (0.70, 1.49)**	
HGBL (NOS or DH/TH)	**N**	43	50
	PFS		
	1-year rate (95% CI)	86.0% (71.6, 93.5)	67.4% (51.8, 79.0)
	diff	18.6% (1.5, 35.7)	
	2-year rate (95% CI)	81.4% (66.2, 90.2)	62.7% (46.9, 75.0)
	diff	18.7% (0.3, 36.9)	
	HR (95% CI)	**0.48 (0.21, 1.08)**	

NHL Subtype	Parameter	Pola + R-CHP	R-CHOP
	OS		
	1-year rate (95% CI)	95.2% (82.3, 98.8)	85.3% (71.6, 92.7)
	diff	9.9% (-2.0, 21.8)	
	2-year rate (95% CI)	95.2% (82.3, 98.8)	81.1% (66.8, 89.7)
	diff	14.2% (-3.0, 22.8)	
	HR (95% CI)	**0.42 (0.15, 1.19)**	
Other LBCL [a]	**N**	24	22
	PFS		
	1-year rate (95% CI)	78.4% (55.6, 90.4)	85.7% (62.0, 95.2)
	diff	-7.3% (-29.8, 15.2)	
	2-year rate (95% CI)	58.4% (34.8, 76.1)	76.2% (51.9, 89.3)
	diff	-17.8% (-35.3, 20.7)	
	HR (95% CI)	**1.93 (0.66, 5.64)**	
	OS		
	1-year rate (95% CI)	91.7% (70.6, 97.8)	100.0% (100.0, 100.0)
	diff	-8.3% (-19.4, 2.7)	
	2-year rate (95% CI)	87.5% (66.1, 95.8)	90.9% (68.3, 97.6)
	diff	-3.4% (-26.2, 9.5)	
	HR (95% CI)	**1.89 (0.35, 10.33)**	

[a] T-cell/histiocyte-rich LBCL (n=28) and EBV+ DLBCL (n=18)
Source: FDA analysis. OS based on the 6/15/2022 CCOD.

Corrected to read as:

Table 2 Results of PFS and OS by NHL Subgroups (Corrected)

NHL Subtype	Parameter	Pola + R-CHP	R-CHOP
Overall	**N**	440	439
	PFS		
	1-year rate (95% CI)	83.9% (80.1, 87.1)	79.8% (75.6, 83.3)
	diff	4.1% (-1.0, 9.3)	
	2-year rate (95% CI)	76.7% (72.3, 80.5)	70.2% (65.5, 74.4)
	diff	6.5% (0.5, 12.5)	
	HR (95% CI)	**0.73 (0.57, 0.95)**	
	OS		
	1-year rate (95% CI)	92.2% (89.2, 94.3)	94.6% (92.0, 96.4)
	diff	-2.4% (-5.8, 0.8)	
	2-year rate (95% CI)	88.7% (85.3, 91.3)	88.7% (85.3, 91.4)
	diff	0.0% (-4.3, 4.2)	
	HR (95% CI)	**0.94 (0.67, 1.33)**	
DLBCL NOS	**N**	373	367
	PFS		
	1-year rate (95% CI)	84.0% (79.8, 87.4)	81.0% (76.5, 84.7)
	diff	3.0% (-2.6, 8.6)	
	2-year rate (95% CI)	77.3% (72.6, 81.3)	70.9% (65.8, 75.3)
	diff	6.4% (0.0, 12.9)	
	HR (95% CI)	**0.75 (0.57, 0.99)**	
	OS		
	1-year rate (95% CI)	91.8% (88.5, 94.2)	95.5% (92.8, 97.2)
	diff	-3.7% (-7.2, -0.2)	
	2-year rate (95% CI)	88.0% (84.2, 90.9)	89.6% (85.9, 92.3)
	diff	-1.6% (-6.2, 3.0)	
	HR (95% CI)	**1.02 (0.70, 1.49)**	
HGBL (NOS or DH/TH)	**N**	43	50
	PFS		
	1-year rate (95% CI)	86.0% (71.6, 93.5)	67.4% (51.8, 79.0)
	diff	18.6% (1.5, 35.7)	
	2-year rate (95% CI)	81.4% (66.2, 90.2)	62.7% (46.9, 75.0)
	diff	18.7% (0.4, 37.0)	
	HR (95% CI)	**0.48 (0.21, 1.08)**	
	OS		
	1-year rate (95% CI)	95.2% (82.3, 98.8)	85.3% (71.6, 92.7)
	diff	9.9% (-2.0, 21.8)	
	2-year rate (95% CI)	95.2% (82.3, 98.8)	81.1% (66.8, 89.7)

NHL Subtype	Parameter	Pola + R-CHP	R-CHOP
	diff	14.2% (1.3, 27.0)	
	HR (95% CI)	**0.42 (0.15, 1.19)**	
Other LBCL [a]	**N**	24	22
	PFS		
	1-year rate (95% CI)	78.4% (55.6, 90.4)	85.7% (62.0, 95.2)
	diff	-7.3% (-29.8, 15.2)	
	2-year rate (95% CI)	58.4% (34.8, 76.1)	76.2% (51.9, 89.3)
	diff	-17.8% (-45.7, 10.2)	
	HR (95% CI)	**1.93 (0.66, 5.64)**	
	OS		
	1-year rate (95% CI)	91.7% (70.6, 97.8)	100.0% (100.0, 100.0)
	diff	-8.3% (-19.4, 2.7)	
	2-year rate (95% CI)	87.5% (66.1, 95.8)	90.9% (68.3, 97.6)
	diff	-3.4% (-21.3, 14.5)	
	HR (95% CI)	**1.89 (0.35, 10.33)**	

[a] T-cell/histiocyte-rich LBCL (n=28) and EBV+ DLBCL (n=18)
Source: FDA analysis. OS based on the 6/15/2022 CCOD.

B. Table formatting

Tables 20, 22, and 25 in the Applicant's Appendix had lost the column formatting of the treatment arms. The tables are provided below with corrected formatting.

Table 20 Summary of Adverse Events Leading to Dose Reduction for Any Study Drug by System Organ Class (Safety Evaluable Patients)

Summary of Adverse Events Leading to Dose Reduction for Any Study Drug by System Organ Class,
Safety-Evaluable Patients, Protocol: GO39942

MedDRA System Organ Class	R-CHOP (N=438)	Pola+R-CHP (N=435)
Total number of patients with at least one adverse event	57 (13.0%)	40 (9.2%)
Overall total number of events	78	47
Nervous system disorders		
Total number of patients with at least one adverse event	36 (8.2%)	20 (4.6%)
Total number of events	38	20
Blood and lymphatic system disorders		
Total number of patients with at least one adverse event	6 (1.4%)	7 (1.6%)
Total number of events	14	7
Investigations		
Total number of patients with at least one adverse event	6 (1.4%)	4 (0.9%)
Total number of events	7	7
Gastrointestinal disorders		
Total number of patients with at least one adverse event	6 (1.4%)	3 (0.7%)
Total number of events	6	3
General disorders and administration site conditions		
Total number of patients with at least one adverse event	3 (0.7%)	2 (0.5%)
Total number of events	4	2
Infections and infestations		
Total number of patients with at least one adverse event	4 (0.9%)	1 (0.2%)
Total number of events	4	1
Metabolism and nutrition disorders		
Total number of patients with at least one adverse event	0	3 (0.7%)
Total number of events	0	4
Cardiac disorders		
Total number of patients with at least one adverse event	1 (0.2%)	1 (0.2%)
Total number of events	1	1
Ear and labyrinth disorders		
Total number of patients with at least one adverse event	1 (0.2%)	1 (0.2%)
Total number of events	1	1
Psychiatric disorders		
Total number of patients with at least one adverse event	2 (0.5%)	0
Total number of events	2	0
Hepatobiliary disorders		
Total number of patients with at least one adverse event	0	1 (0.2%)
Total number of events	0	1
Vascular disorders		
Total number of patients with at least one adverse event	1 (0.2%)	0
Total number of events	1	0

Investigator text for AEs encoded using MedDRA version 24.0. Percentages are based on N in the column headings.
For frequency counts by preferred term, multiple occurrences of the same AE in an individual are counted only once.
For frequency counts of "Total number of events" rows, multiple occurrences of the same AE in an individual are counted separately. Includes treatment-emergent AEs during AE reporting period only, which is defined as new or worsening AE from the first dose of any study drug through 90 days after the last dose of any study drug or prior to NALT, whichever is earlier.
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Table 22 Overall Adverse Event Profile - Febrile Neutropenia (Safety Evaluable Patients)

Overall AE Profile - Febrile Neutropenia, Safety-Evaluable Patients
Protocol: GO39942

	R-CHOP (N=438)	Pola+R-CHP (N=435)
Total number of patients with at least one AE	35 (8.0%)	62 (14.3%)
Total number of AEs	41	84
Total number of patients with at least one		
Grade 5 AE	0	0
Grade 3-5 AE	35 (8.0%)	60 (13.8%)
Serious AE	28 (6.4%)	43 (9.9%)
Serious Related AE to any study drug	25 (5.7%)	42 (9.7%)
AE leading to study discontinuation	0	0
AE leading to any study treatment dose discontinuation	0	0
AE leading to any study treatment dose reduction	2 (0.5%)	5 (1.1%)
AE leading to any study treatment dose interruption	1 (0.2%)	3 (0.7%)
AE leading to polatuzumab vedotin/placebo discontinuation	0	0
AE leading to polatuzumab vedotin/placebo dose reduction	1 (0.2%)	2 (0.5%)
AE leading to polatuzumab vedotin/placebo dose interruption	0	3 (0.7%)
AE leading to vincristine/placebo discontinuation	0	0
AE leading to vincristine/placebo dose reduction	1 (0.2%)	1 (0.2%)
AE leading to vincristine/placebo dose interruption	0	3 (0.7%)

Investigator text for AEs encoded using MedDRA version 24.0. Percentages are based on N in the column headings. Multiple occurrences of the same AE in one individual are counted only once except for "Total number of AEs" row in which multiple occurrences of the same AE are counted separately. Includes treatment-emergent AEs during AE reporting period only, which is defined as new or worsening AE from the first dose of any study drug through 90 days after the last dose of any study drug or prior to NALT, whichever is earlier.
CCOD: 28JUN2021 Data Extract Date: 02AUG2021

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Table 3 Summary of Resolution Profile for Peripheral Neuropathy, Neutropenia, Thrombocytopenia, Anemia, and Infections (Safety Evaluable Population)

Summary of AEPI Resolution Profile, Safety-Evaluable Patients
Protocol: GO39942

	R-CHOP (N=438)	Pola+R-CHP (N=435)
Peripheral Neuropathy		
Patients with at least one event	236 (53.9%)	230 (52.9%)
Patients with all AEs resolved	158 (66.9%)	133 (57.8%)
Patients with at least one event ongoing/unresolved	78 (33.1%)	97 (42.2%)
Total number of events	292	301
Number of events resolved	201 (68.8%)	195 (64.8%)
Neutropenia		
Patients with at least one event	187 (42.7%)	200 (46.0%)
Patients with all AEs resolved	183 (97.9%)	196 (98.0%)
Patients with at least one event ongoing/unresolved	4 (2.1%)	4 (2.0%)
Total number of events	443	456
Number of events resolved	439 (99.1%)	452 (99.1%)
Thrombocytopenia		
Patients with at least one event	58 (13.2%)	58 (13.3%)
Patients with all AEs resolved	50 (86.2%)	55 (94.8%)
Patients with at least one event ongoing/unresolved	8 (13.8%)	3 (5.2%)
Total number of events	123	102
Number of events resolved	115 (93.5%)	99 (97.1%)
Anemia		
Patients with at least one event	118 (26.9%)	125 (28.7%)
Patients with all AEs resolved	102 (86.4%)	106 (84.8%)
Patients with at least one event ongoing/unresolved	16 (13.6%)	19 (15.2%)
Total number of events	178	190
Number of events resolved	162 (91.0%)	171 (90.0%)
Infections and infestations		
Patients with at least one event	187 (42.7%)	216 (49.7%)
Patients with all AEs resolved	158 (84.5%)	188 (87.0%)
Patients with at least one event ongoing/unresolved	29 (15.5%)	28 (13.0%)
Total number of events	343	409
Number of events resolved	309 (90.1%)	380 (92.9%)

Investigator text for AEs encoded using MedDRA version 24.0.
Includes treatment-emergent AE during AE reporting period only, which is defined as new or worsening AE from the first dose of any study drug through 90 days after the last dose of any study drug or prior to NALT, whichever is earlier.
CCOD: 28JUN2021 Data Extract Date: 02AUG2021

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