Treatment-Related Costs of Pharmacologic Regimens for Patients with Relapsed or Refractory Diffuse Large B-Cell Lymphoma (R/R DLBCL) Who Have Received Two or More Prior Lines of Therapies

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Background and Objectives

- Diffuse large b-cell lymphoma (DLBCL) accounts for approximately one third of all new cases of non-Hodgkin lymphoma.[1] It is estimated that approximately 30% to 50% of patients are refractory to the first-line treatment or relapse after achieving a complete remission.[2]
- Patients who develop relapse or refractory (R/R) DLBCL may be treated with high-dose chemotherapy consolidated with autologous stem cell transplant. However, not all patients are eligible for these subsequent treatments or respond to them, or relapse after responding to the treatment.[3]
- Several treatments have been approved by Food and Drug Administration (FDA) recently for treating R/R DLBCL, including loncastuximab tesirine-lpyl (loncastuximab), polatuzumab vedotin-piiq in combination with bendamustine and rituximab (pola + BR), tafasitamab-cxix + lenalidomide, selinexor, and chimeric antigen receptor T therapies.
- Loncastuximab was granted approval by the FDA based on a multicenter open-label single arm Phase 2 clinical trial (NCT 03589469) that showed an objective response rate of 48.3% associated with loncastuximab.[4-6]
- This analysis was performed to estimate treatment-related costs associated with loncastuximab in comparison with other newer targeted pharmacologic treatments that were approved after 2019 for the treatment of patients with R/R DLBCL who have received two or more prior lines of therapies.

Methods

- A model was developed to assess treatment-related costs during the treatment course for the following treatments: loncastuximab, pola + BR, tafasitamab-cxix + lenalidomide, and selinexor.
- Cost components included costs associated with drug administration, premedication, monitoring, and prophylactic treatments, as well as adverse event (AE) costs.
- All costs were incurred throughout the treatment and were estimated as monthly costs, except for grade 3/4 AEs, which were assumed to incur one-time costs.
- All costs were estimated in 2021 USD.

Methods

- Administration Costs
  - Drug administration costs were considered for intravenous infusion (IV) administered pharmacological drugs only, and were estimated based on administration time[4,7-10], dosing schedule[4,7,11,12], median treatment duration[10,13-15], and unit administration costs which were obtained based on Healthcare Common Procedure Coding System (HCPCS) codes from the CMS Physician Fee Schedule 2021[16] (**Table 1**).
  - Monthly administration costs = (administration costs per infusion * number of infusions per month) + (additional costs associated with first dose(s) / median treatment duration)

Table 1. Administration time and median treatment duration

Treatments	Drugs	Administration time	Median treatment duration (months)	Sources
Loncastuximab	Loncastuximab	IV 30 mins	2.07	**Administration time:** PIs[4,7-9] and literature[10] **Drug dosing schedule:** PIs[4,7,11,12] **Median treatment duration:** Literature[10,13-15]
Pola + BR	Polatuzumab vedotin-piiq	Initial dose: IV 90 mins; subsequent dose: IV 30 mins	3.45	
	Bendamustine	IV 60 mins		
	Rituximab	IV 90 mins		
Tafasitamab-cxix + lenalidomide	Co-administration			
	Tafasitamab-cxix	IV 120 mins	6.20	
	Lenalidomide	Oral		
	Tafasitamab-cxix monotherapy	IV 120 mins	4.10	
Selinexor	Selinexor	Oral	2.07	

Methods

- Premedication Costs
  - Premedication costs were estimated based on premedication costs per infusion/day and premedication frequencies (**Table 2**).
  - Monthly premedication costs = sum of (premedication costs per infusion/day * frequencies per month)

Table 2. Premedication costs and frequencies

Premedication categories	Drug costs per infusion/day ($)	Premedication frequencies per month				Source
		Loncastuximab	Pola + BR	Tafasitamab-cxix + lenalidomide	Selinexor	
Dexamethasone	$17.82	4.35	-	-	-	**Premedication requirements:** PIs[4,7-9,11,12,17] * If the same premedication was required for two or more drugs in a combination therapy, the highest frequency required was applied to avoid double counting. **Dosing schedule of premedication drugs**: PIs[4,18-22] **Unit costs of premedication drugs**: WAC in RedBook 2020[23]; CPI[24] * All premedication drugs were oral; no administration costs were considered
Antipyretic/Acetaminophen (Acetaminophen)	$0.06	-	1.45	2.17	-	
Histamine H1 receptor blockers (Diphenhydramine)	$1.27	-	1.45	2.17	-	
Histamine H2 receptor blockers (Cimetidine or ranitidine)	$0.20	-	-	2.17	-	
Glucocorticosteroids (Methylprednisolone)	$8.30	-	-	2.17	-	

Methods

- Monitoring Costs
  - Monitoring costs were estimated based on monitoring costs per test and monitoring frequencies (**Table 3**).
  - Monthly monitoring costs = sum of (monitoring costs per test * frequencies per month) + (one-time monitoring costs / median treatment duration)

Table 3. Monitoring costs per test and monthly monitoring frequencies

Procedures and monitoring services	Unit cost ($)	Monitoring frequencies per month				Source
		Loncastuximab	Pola + BR**	Tafasitamab-cxix + lenalidomide	Selinexor	
Physician visit	$183.19	1.45	1.45	2.17	8.70	**Monitoring requirements:** PIs[4,7-9,11,12,17] *If the monitoring frequency was not specified, it was assumed to be the same frequency as specified in the dosing schedule. If the same monitoring test was required for two or more drugs in a combination therapy, the highest test frequency was applied to avoid double counting. **Monitoring unit cost:** CMS Physician Fee Schedule 2021[16];CMS Laboratory Fee Schedule 2021[25]
Hematology test	$7.77	1.45	1.45	2.17	8.70	
Total bilirubin	$5.02	-	1.45	1.09	-	
Aspartate aminotransferase test	$5.18	-	1.45	1.09	-	
Alanine aminotransferase test	$5.30	-	1.45	1.09	-	
Serum creatinine	$5.12	-	1.45	-	-	
Serum sodium	$4.81	-	-	-	8.70	
HBV infection	$22.38	-	1.45	-	-	

** Pola + BR incurred one-time monitoring costs of two hematology tests, and one HBV infection.

Methods

- Prophylactic Treatment Costs
  - Prophylactic treatment costs were considered if prophylactic treatments were mandatory in PIs. The costs were estimated based on prophylactic treatment costs per infusion/day and prophylactic treatment frequencies (**Table 4**).
  - Monthly prophylactic treatment costs = sum of (prophylactic treatment costs per infusion/day * frequencies per month)

Table 4. Prophylactic treatment costs and frequencies

Prophylactic treatment categories	Drug cost per day/infusion ($)	Prophylactic treatment frequencies per month				Source
		Loncastuximab	Pola + BR	Tafasitamab-cxix + lenalidomide	Selinexor	
Pneumocystis jiroveci pneumonia prophylaxis	$34.73	-	1.45	-	-	**Prophylactic treatment requirements:** PIs[4,7-9,11,12,17] * If the prophylactic treatment frequency was not specified, it was assumed to be the same frequency as specified in the dosing schedule. If the same prophylactic treatment was required for two or more drugs in a combination therapy, the highest prophylactic treatment frequency was applied to avoid double counting. **Selection of drugs used for prophylactic treatments**: Disease management guidelines[30,31] literature[32,33]; expert opinions **Dosing schedule of prophylactic treatment drugs**: PIs[26-29]; disease management guidelines[30] **Unit costs of prophylactic treatment drugs**: WAC in RedBook 2020[23]; CPI[24] * All drugs for prophylactic treatment were oral; no administration costs were considered
Herpesvirus prophylaxis	$42.52	-	1.45	-	-	
Tumor lysis syndrome prophylaxis	$8.30	-	1.45	-	-	
Infection prophylaxis	$77.25	-	1.45	-	-	
Nausea prophylaxis	$113.46	-	-	-	8.70	

Methods

- AE Costs
  - The model considered costs associated with grade 3/4 AEs that affected ≥ 5% patients in any treatment. Grade 3/4 AE rates were obtained from PIs.[4,7,11,12]
  - The unit costs for the grade 3/4 AEs were estimated as follows (**Table 5**):
    - Grade 3/4 laboratory abnormalities that did not require any hospitalization based on National Cancer Institute Common Terminology Criteria for Adverse Events Version 4.0[34] were considered not requiring substantial resource use, and thus were assigned zero cost.
    - For the rest of the grade 3/4 AEs, the costs were estimated based on Healthcare Cost and Utilization Project (HCUP) 2016 National Inpatient Sample[35] or Wong 2018 (a claims analysis estimating the AE costs in adult patients with cancers of lymphatic and hematopoietic tissue).[36]
      - If the costs were reported for an AE in both Wong 2018[36] and HCUP 2016[35], the lower costs of the two was used. Otherwise, the costs reported in HCUP 2016 was used.
      - Furthermore, based on expert opinions, for the grade 3/4 AEs that were normally treated in an outpatient setting, a 75% discount was further applied to the selected costs from Wong 2018 or HCUP 2016.[35,36]
      - Febrile neutropenia is a severe form of neutropenia requiring hospitalization. However, the cost for febrile neutropenia and neutropenia were not reported separately in Wong 2018 and HCUP 2016 due to lack of separate International Classification of Diseases (ICD) -10. Based on expert opinions, the cost for neutropenia was assumed to be the same as those for leukopenia and the cost for febrile neutropenia was estimated with the higher costs reported for neutropenia in Wong 201836 and HCUP 201635, given its severity.
  - Total AE costs = sum of (grade 3/4 AE costs * grade 3/4 AE rates)

Methods

Table 5. AE unit costs

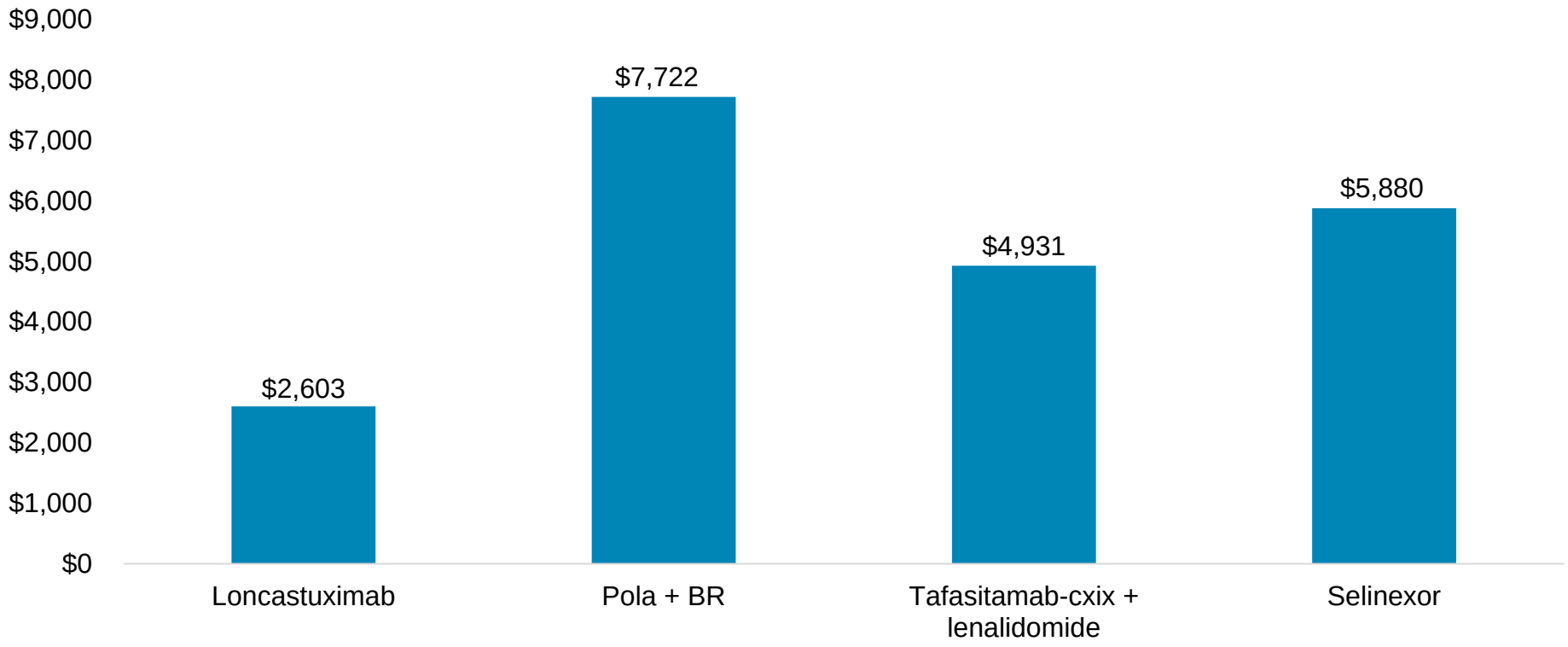
Grade 3/4 AEs	AE cost inputs	Grade 3/4 AEs	AE cost inputs	Source
Abdominal Pain	$7,240	**Hypotension**	$8,655	
Anaemia	$1,944	**Infection**	$1,468	
Calcium decreased	$7,714	**Lymphopenia**	$1,719	
Diarrhea	$7,689	**Nausea**	$3,945	HCUP 2016[35];Wong 2018[36]; expert opinions
Dyspnea	$7,131	**Neutropenia**	$1,719	
Febrile neutropenia	$14,224	**Pneumonia**	$10,260	
Glucose increased	$7,498	**Pyrexia**	$1,923	
Hypokalemia	$7,484	**Renal disorder**	$10,112	
Hyponatremia	$2,036	**Thrombocytopenia**	$2,712	

Results – Total AE costs over the treatment course

- Among the newer targeted pharmacologic treatments indicated for R/R DLBCL, loncastuximab had the lowest AE costs over the treatment course. (**Figure 1**)

Results – Total AE costs over the treatment course

Figure 1. Total AE costs over the treatment course (2021 USD)

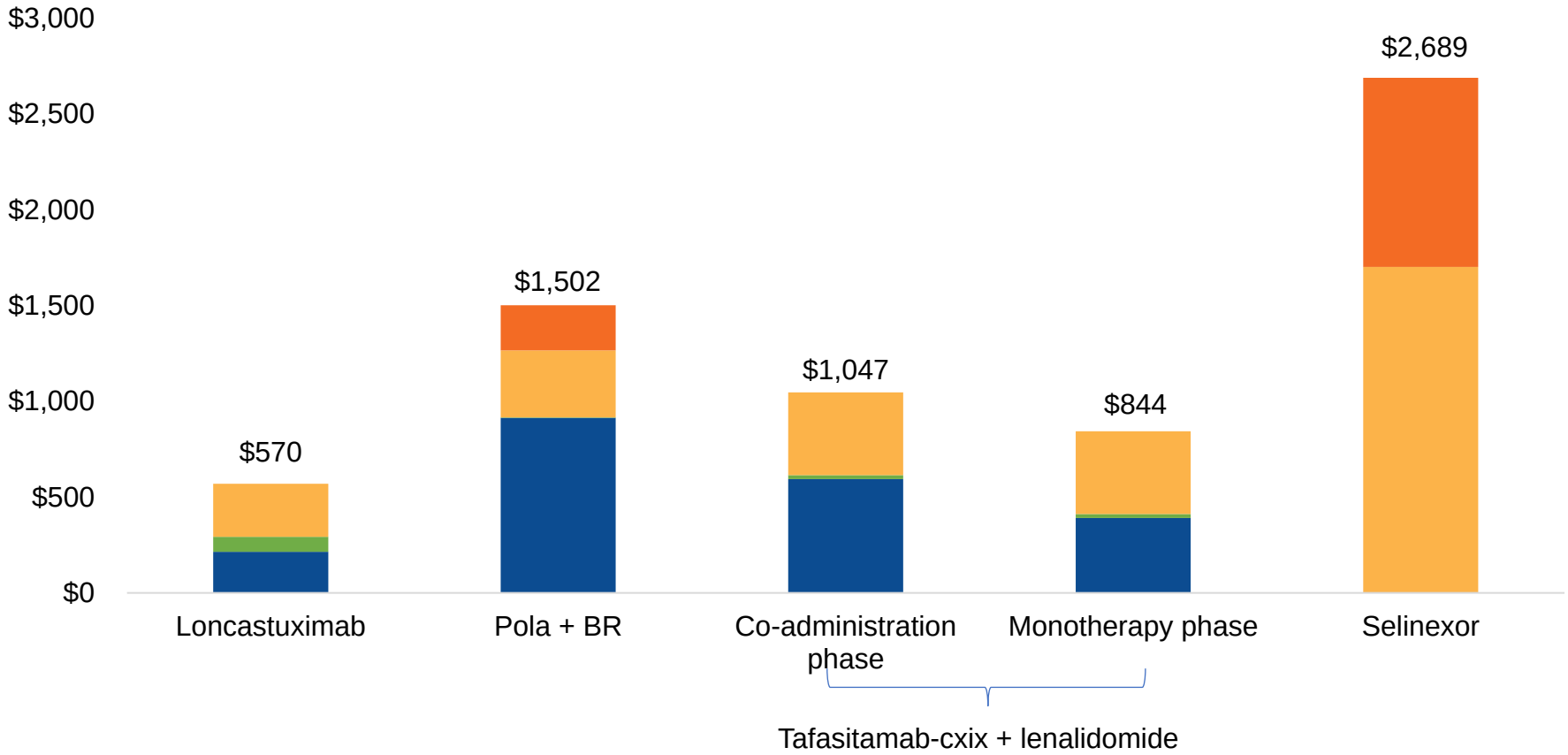


Results – Monthly treatment-related costs

- Among the newer targeted pharmacologic treatments indicated for R/R DLBCL, loncastuximab had the lowest monthly treatment-related costs (administration costs, premedication costs, monitoring costs, and prophylactic treatment costs). (**Figure 2**)

Results – Monthly treatment-related costs

Figure 2. Monthly treatment-related costs (2021 USD)



Monthly administration costs	$215	$914	$594	$391	$0
Monthly premedication costs	$78	$2	$21	$21	$0
Monthly monitoring costs	$277	$350	$432	$432	$1,702
Monthly prophylactic treatment costs	$0	$236	$0	$0	$987

Limitation

- Median treatment duration and AE rates in clinical trials were used to estimate treatment costs. Data observed in clinical trials may be different from the real-world clinical practice. Participants of clinical trials are likely to have received closer management and had better adherence to therapies than patients who would have been treated in a real-world setting.
- Costs associated with other grade 3/4 AEs that affected less than 5% were not included in the analysis. Thus, the estimated AE cost may underestimate the costs for all treatments.
- Some AE costs were not available in the literature or public data sources. However, we made conservative assumptions on the per event costs for the selected AEs, which led to smaller reduction in total AE costs for loncastuximab than other treatments.

Conclusions

- Compared with all other newer targeted pharmacologic treatments, loncastuximab was associated with the lowest treatment-related costs due to its ease of administration and the lowest AE costs.

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