

Supplementary Table 1 Background hematologic disease in this study

	Total patients (n=194)	Total HD-MTX cycles (n=517)
Disease, n (%)		
Malignant lymphoma	162 (83.5)	437 (84.5)
B-cell lymphoma	147 (75.8)	406 (78.5)
DLBCL	110 (56.7)	295 (57.1)
PCNSL	16 (8.2)	63 (12.2)
IVLBCL	10 (5.1)	26 (5.0)
Burkitt lymphoma	5 (2.6)	13 (2.5)
Others	6 (3.1)	9 (1.7)
T/NK cell lymphoma and HL	15 (7.7)	31 (6.0)
Acute lymphoblastic leukemia	32 (16.5)	80 (15.5)

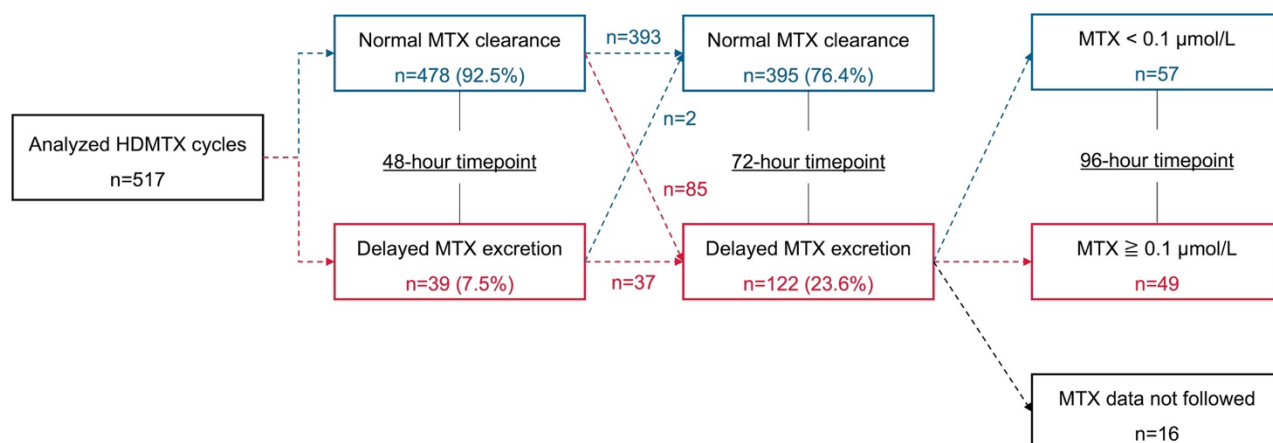
Abbreviations: DLBCL, diffuse large B-cell lymphoma; PCNSL, primary central nervous system lymphoma; IVLBCL, intravascular large B-cell lymphoma; HL, Hodgkin's lymphoma.

Supplementary Table 2 Multivariate analysis for predicting delayed methotrexate excretion after excluding pleural effusion

	Multivariate analysis		
	OR	95% CI	P-value
Patient and disease factors			
R/R disease status	2.16	1.26–3.72	0.005
MTX administration details			
Cycle counts (continuous variables)	0.764	0.664–0.879	<0.001
Treatment intent	1.88	1.08–3.27	0.024
Laboratory data (all continuous variables)			
Alb	0.504	0.332–0.765	0.001
CrCl	0.992	0.985–0.999	0.023
GGT	1.005	1.002–1.008	0.004

Abbreviations: OR, odds ratio; CI, confidence interval; R/R, relapsed/refractory; MTX, methotrexate; Alb, albumin; CrCl, creatinine clearance; GGT, γ -glutamyl transpeptidase.

Supplementary Fig. 1 Transition of MTX clearance status from 48, 72 and 96 h after HDMTX initiation

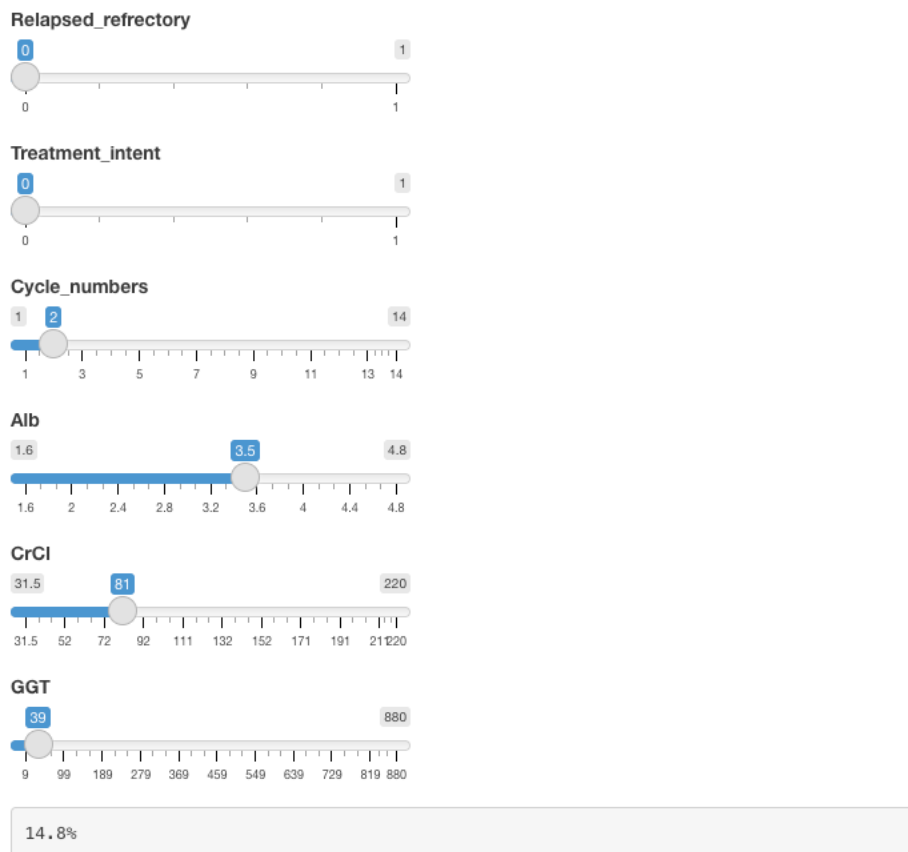


Abbreviation: HDMTX, high-dose methotrexate.

Supplementary Fig. 2 Examples of individual delayed MTX excretion prediction using the web-based nomogram.

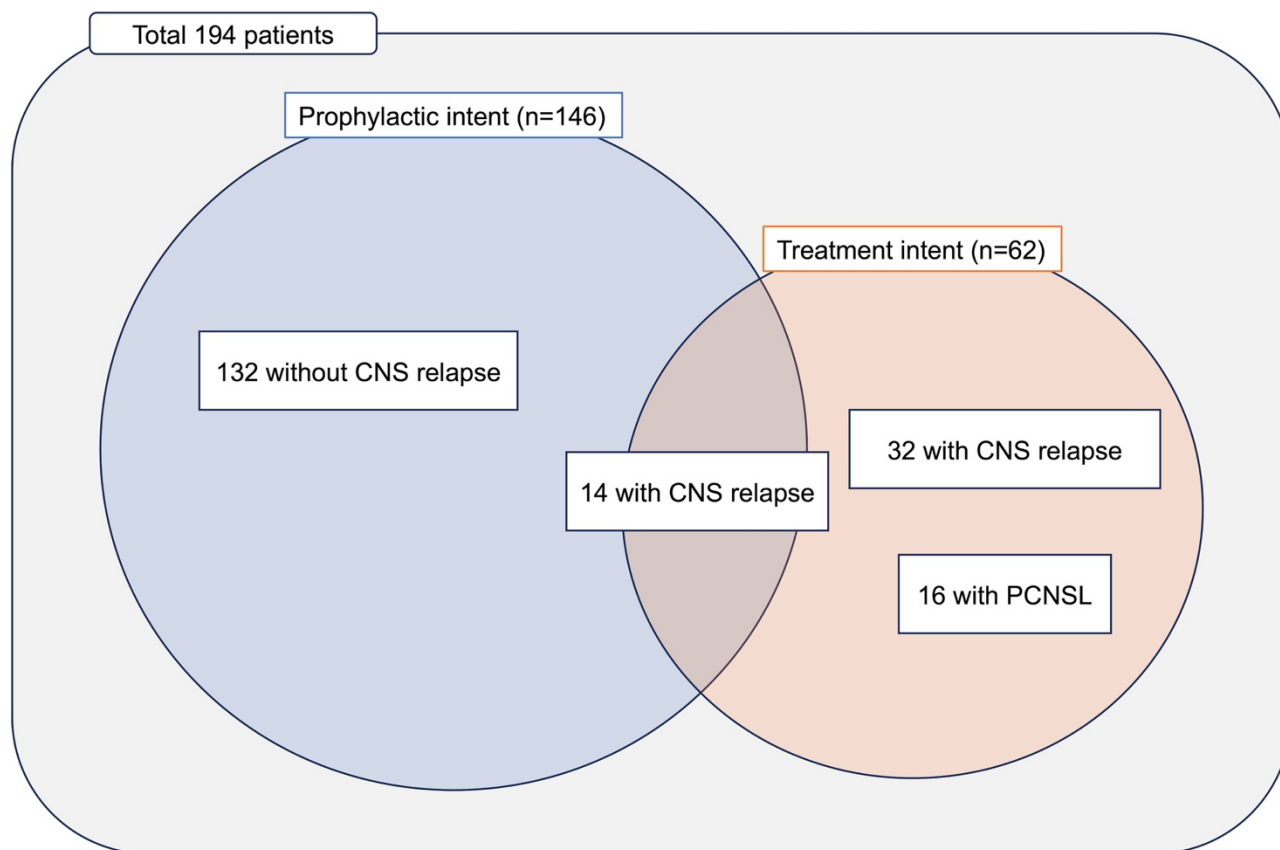
The nomogram is available on the following URL https://predicting-delayed-mtx-excretion.shinyapps.io/MTX_shiny/. The users scored each predictor by moving the slider to the value closest to the patient's actual measurements. In this case, the patient had a newly diagnosed disease, received prophylactic HDMTX during the second cycle, and had an albumin level of 3.5 g/dL, CrCl (Cockcroft-Gault) level of 81 mL/min, and GGT level of 39 U/L. The predicted probability was 14.8%.

Nomogram for predicting delayed MTX excretion



Abbreviation: HDMTX, high-dose methotrexate; CrCl, creatinine clearance; GGT, γ -glutamyl transpeptidase.

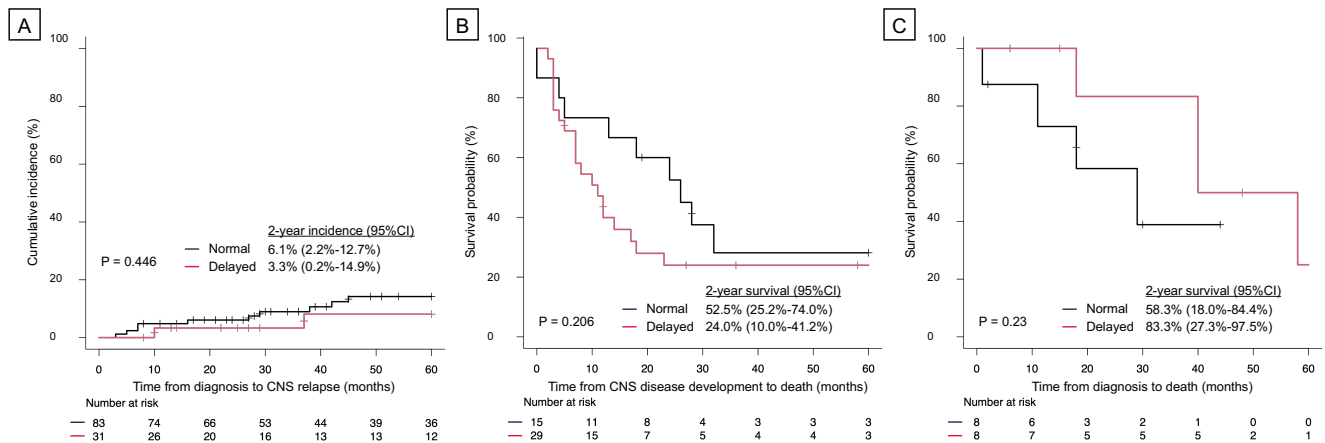
Supplementary Fig. 3 Venn diagram representing intention to administer HDMTX and CNS recurrence



Abbreviation: CNS, central nervous system; PCNSL, primary central nervous system lymphoma; HDMTX, high-dose methotrexate.

Supplementary Fig. 4 Subgroup survival analysis confined to patients with malignant lymphoma

A) Cumulative incidence of CNS relapse in patients with malignant lymphoma, B) survival time from SCNSL development and C) Survival time from PCNSL diagnosis according to MTX clearance status.



Abbreviation: CNS, central nervous system; SCNSL, secondary central nervous system lymphoma; PCNSL, primary central nervous system lymphoma.