SUPPLEMENTARY FIGURES

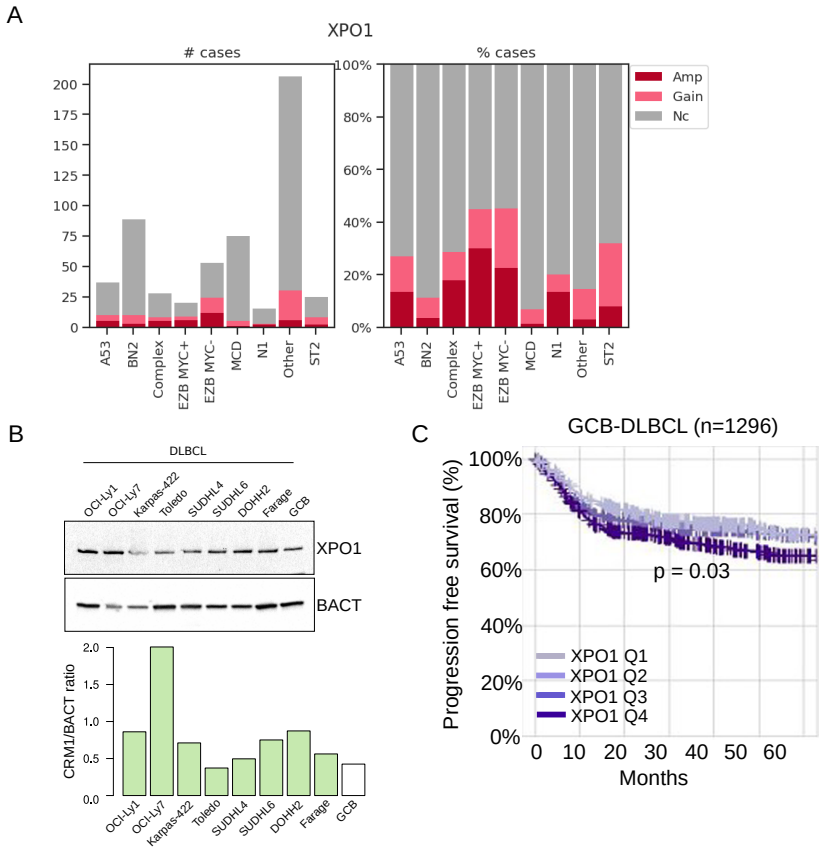

Figure S1. A: Distribution of XPO1 amplifications and gains according to LymphGen genetic subtypes. **B:** XPO1 protein expression in DLBCL cell lines (OCI-Ly7, OCI-Ly1, DoHH2, Toledo, Karpas422, Farage, SU-DHL6, SU-DHL4) and normal germinal center B cells (GCB) isolated from tonsils. Left panel: quantification. **C:** Kaplan-Meier survival curves of progression-free survival of 1,296 GCB-DLBCL patients stratified by XPO1 gene expression (RNA-sequencing) in quartiles (Q1: lowest, Q4: highest).

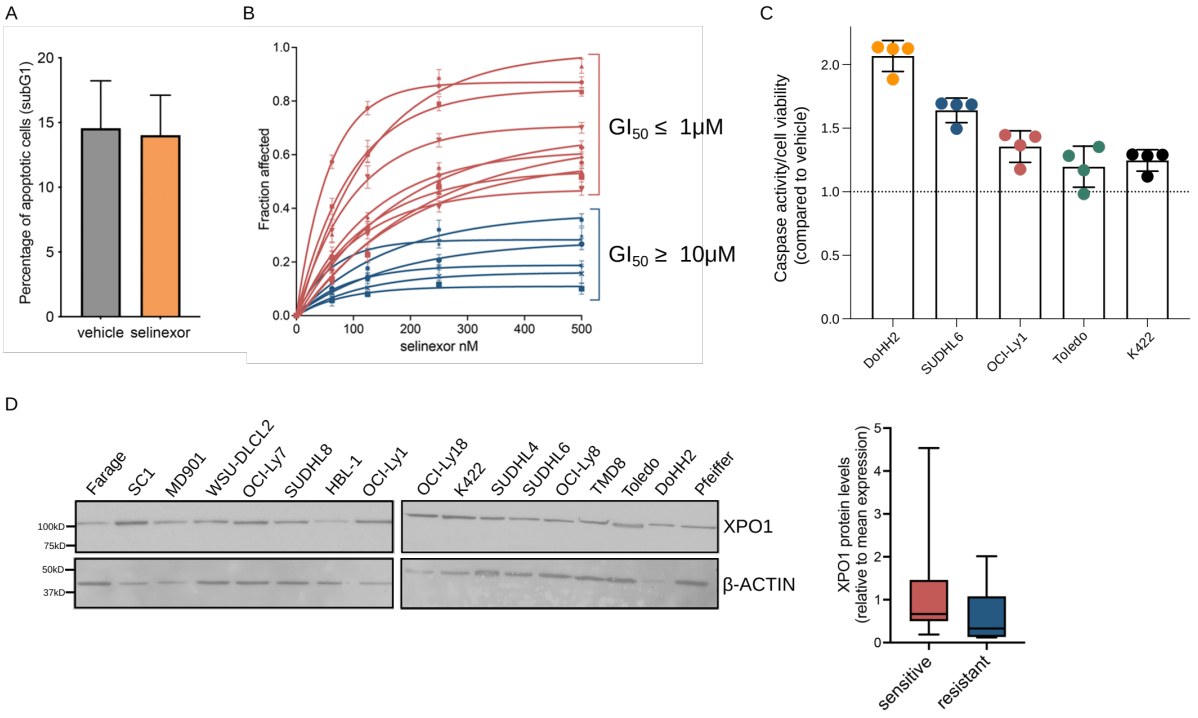

Figure S2. A: Apoptotic cells in P493-6 lymphoblastoid B cells upon MYC transgene induction followed by exposure to vehicle vs. selinexor. **B:** Dose-response curves of selinexor in a panel of 16 DLBCL cell lines. Growth inhibitory concentration 50% (GI_{50}) for responsive (red) and resistant (blue) cell lines is indicated. **C**: Apoptosis (by caspase 7/3 activity) in selected DLBCL cell lines treated with selinexor 1 μM. **D**: XPO1 expression in a panel of DLBCL cell lines and quantification of XPO1 expression in DLBCL cell lines segregated as sensitive or resistant to selinexor according to C.

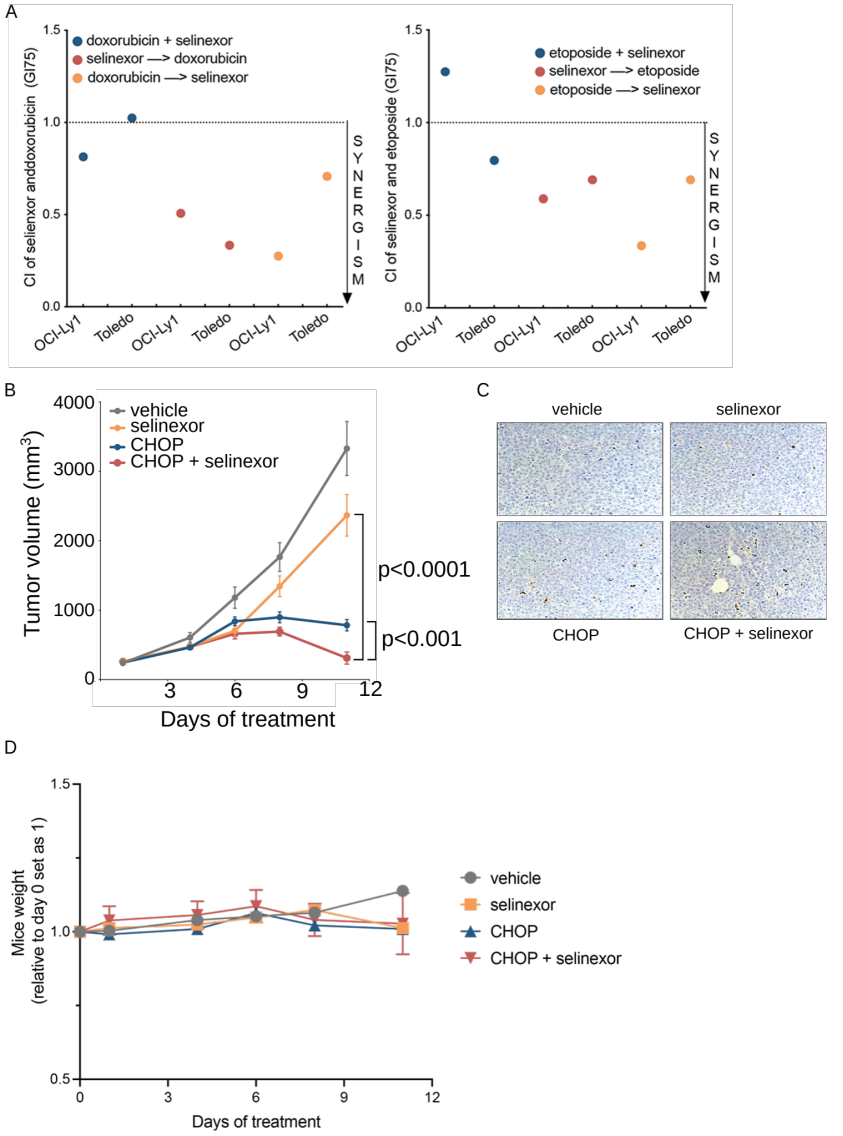

Figure S3. A: Combination index (CI) at GI_{75} for selinexor with doxorubicin (left) or with etoposide (right) with three different administration schedules in two MYC-driven DLBCL cell lines Toledo and OCI-Ly1. **B:** normalized tumor growth curves of a MYC-driven XPO1-amplified DLBCL PDTX treated with vehicle, selinexor, CHOP or their combination. **C:** Representative apoptotic index (TUNEL) images from the experiment in B. **D:** Normalized mice weight from the mice in B.

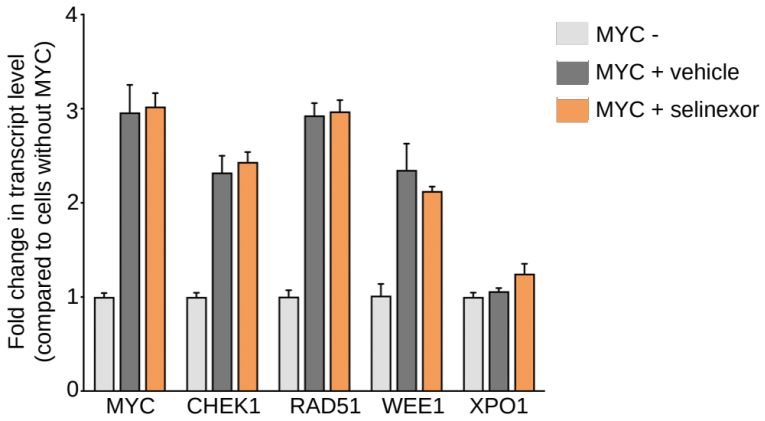

Figure S4. Expression levels of *MYC, XPO1* and DNA damage repair transcripts encoding for *CHEK1, RAD51* and *WEE1* in P493-6 lymphoblastoid B cell line after MYC induction followed by exposure to vehicle or selinexor for 6 h.

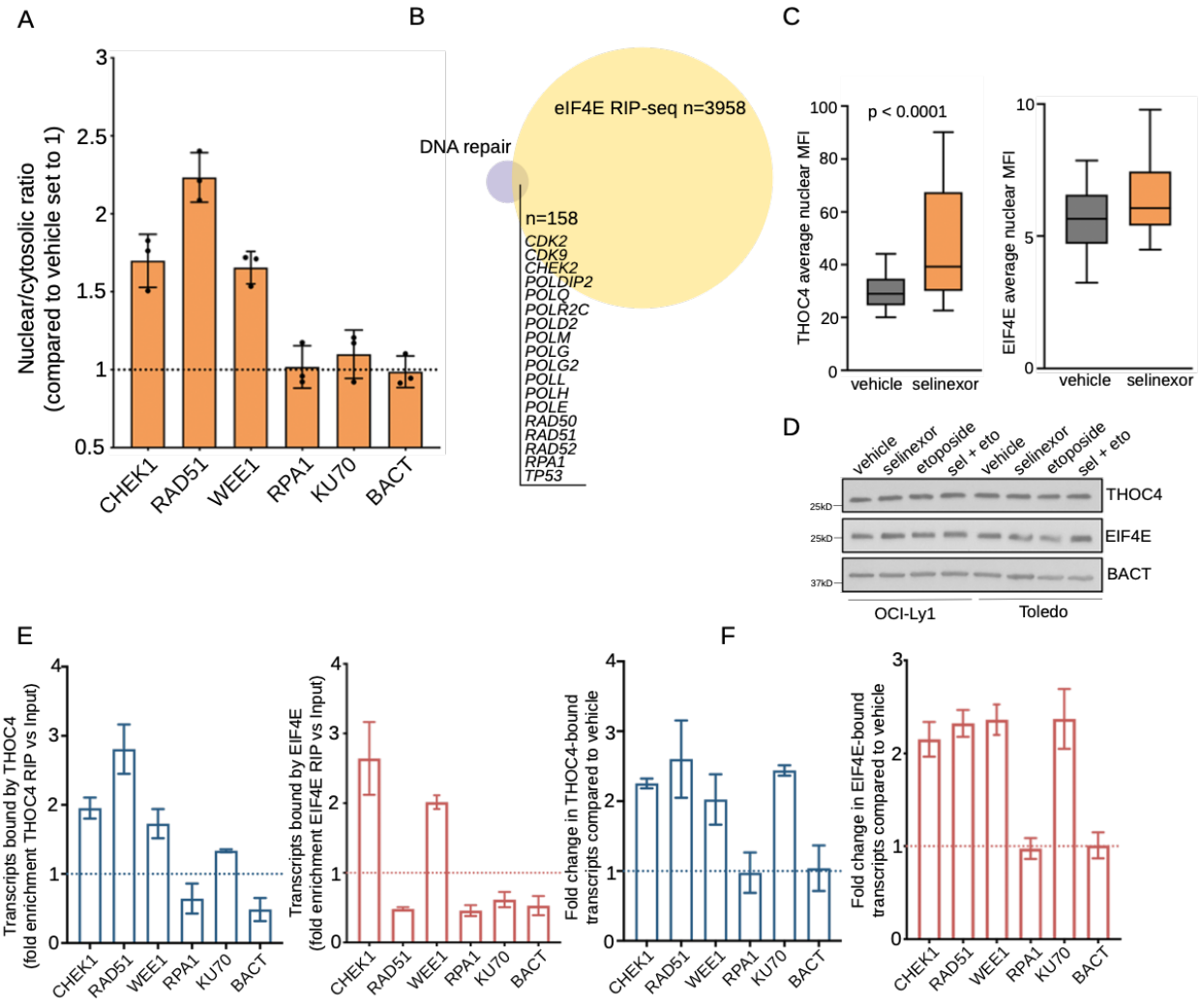

Figure S5. A: nuclear/cytoplasmic ratio of selected DNA damage repair transcripts (i.e., CHEK1, RAD51, WEE1, RPA1 and KU70) and BACT (control) in OCI-Ly1 cells exposed to vehicle or selinexor (1 μM) for 6 h. **B:** Re-analysis of EIF4E RIP-sequencing in baseline OCI-Ly1 cells to show significantly bound transcripts (vs. IgG RIP-sequencing) belonging to the "DNA repair" category (n = 158). Selected transcripts names shown. **C:** nuclear levels of THOC4 and EIF4E in OCI-Ly1 cells exposed to vehicle or selinexor (1 μM) for 6 h. **D:** immunoblotting of THOC4 and EIF4E in OCI-Ly1 and Toledo cells exposed to vehicle or selinexor (1 μM), etoposide or their combination for 6 h. **E:** Ribonucleoprotein immunoprecipitation assays of DNA damage repair transcripts (i.e., CHEK1, RAD51, WEE1, RPA1 and KU70) bound by THOC4 (left) or EIF4E (right) in the nuclear fraction of OCI-Ly1 cells. Data are presented as fold enrichment over input. **F:** Change in the amount of DNA damage repair transcripts CHEK1, RAD51, WEE1, RPA1 and KU70 (and actin as control) bound by THOC4 (left) and EIF4E (right) in OCI-Ly1 lymphoma cells exposed to vehicle or etoposide for 6 h. Data are presented as fold enrichment over vehicle (normalized by their respective inputs).

SUPPLEMENTARY TABLES

Table S2: Patient Characteristics

Age (years)		Median 67 (34-79)
Sex	Male: Female	14:8
Stage	I-II	6
	III	7
	IV	9
International Prognostic Index	Low	5
	Low Intermediate	9
	High Intermediate	5
	High	3
Diagnosis[1]	DLBCL NOS[2]	12
	DH-HGL[3]	4
	TiNHL[4]	2
	PMBCL[5]	1
	RT[6]	3

[1]One subject with RT did not receive selinexor; [2]Diffuse large B-cell lymphoma not otherwise specified; [3]Double-hit high-grade lymphoma; [4]Transformed indolent non-Hodgkin lymphoma; [5]Primary mediastinal large B-cell lymphoma; [6]Richter's transformation (chronic lymphocytic leukemia to DLBCL)

Table S3: Adverse Events, Grade 1-2 in ≥ 10% of Patients and All Grade 3-5 (n = 21)

(Number of patients according to highest grade experienced)

Adverse Event (# of patients)	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Platelet count decreased	22 (2)	10 (1)	16 (3)	17 (13)	
Lymphocyte count decreased	6 (0)	13 (0)	23 (7)	10 (7)	
Neutrophil count decreased	2 (1)	3 (0)	9 (3)	11 (10)	
Anemia	14 (3)	20 (6)	10 (7)		
Fatigue	15 (9)	6 (5)			
Hyponatremia	8 (3)		13 (8)		
Alanine aminotransferase increase	7 (3)		2 (2)		
Aspartate aminotransferase increase	4 (1)	1 (0)	2 (2)		
WBC count decreased		5 (0)	4 (1)	8 (7)	
Nausea	8 (5)	7 (5)	1 (1)		
Creatinine increase	8 (3)	5 (3)	2 (1)		
Hypoalbuminemia	6 (2)	9 (6)			
Hypocalcemia	11 (5)	3 (3)			
Anorexia	8 (8)	4 (3)			
Altered mental status	1 (1)	3 (2)	4 (4)		
Constipation	6 (2)	2 (2)			
Hypokalemia	7 (5)				
Abdominal pain	4 (3)	1 (1)	1 (1)		
Sensory neuropathy	4 (3)	2 (2)			
Hyperglycemia	6 (3)				
Diarrhea	4 (4)	1 (1)			
Hypomagnesemia	5 (5)				
Alopecia	4 (3)	1 (1)			
Alkaline phosphatase increase	3 (1)	1 (1)			
Febrile neutropenia			3 (3)		1 (1)
Hypophosphatemia	1 (1)	1 (0)	2 (2)		
Weakness	4 (3)				
Abdominal infection			3 (1)		
Blood bilirubin increased	1 (1)	2 (2)			
Dyspnea	3 (3)				
Fever	3 (3)				
Acid reflux		2 (2)			
Back pain	1 (1)		1 (1)		
Bone pain	2 (1)				

Adverse Event (# of patients)	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Confusion		2 (2)			
Chills		2 (2)			
Cough	2 (2)				
Edema (limbs)	2 (2)				
Epistaxis	1 (1)	1 (1)			
Fall	1 (1)	1 (1)			
Gait problem	2 (2)				
Hypermagnesemia	2 (2)				
Hypotension	1 (1)		1 (1)		
Sepsis				1 (1)	1 (1)
Syncope			2 (2)		
Urinary frequency	2 (2)				
Urinary incontinence		2 (2)			
Coronavirus (non COVID-19)			1 (1)		
Dehydration			1 (1)		
Hypertension			1 (1)		
Left shoulder weakness			1 (1)		
Thromboembolic event			1 (1)		

Table S4: Stem cell information for those subjects in whom mobilization and collection was attempted

Subject	Number of mobilization attempts	Number of collection attempts	Number of $CD34^+$ cells (x 10^6/kg)	Underwent ASCT
1	1	1	4.17	No (allogeneic SCT)
2	1	1	4.37	Yes
3	2	2	5.66	Yes
4	3	3	9.73	Yes
5	2	2	2.18	No (allogeneic SCT)
6	2	0	Not applicable	No
7	1	0	Not applicable	No
8	1	0	Not applicable	No