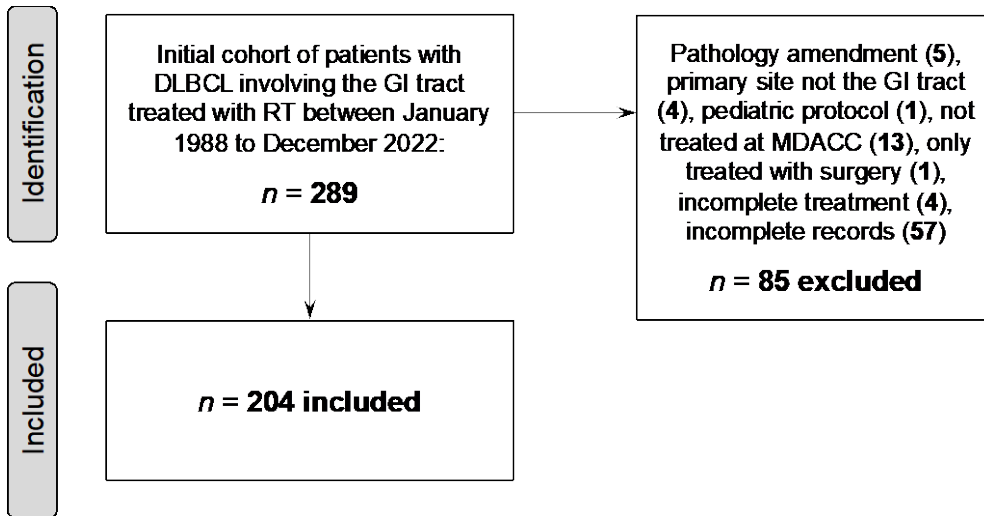
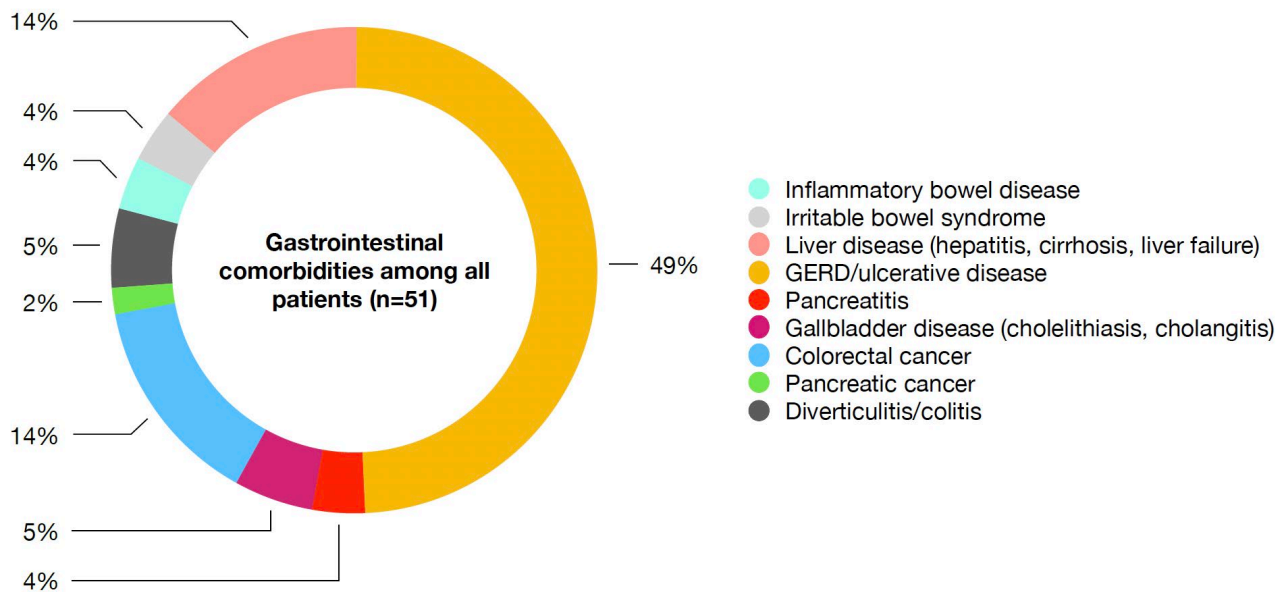


## Supplementary Material

**Supplementary Figure 1. Patient inclusion and exclusion criteria.** 85 patients were excluded owing to a number of factors, yielding a final cohort of 204 patients who were analyzed. *Abbreviations:* RT = radiation therapy.

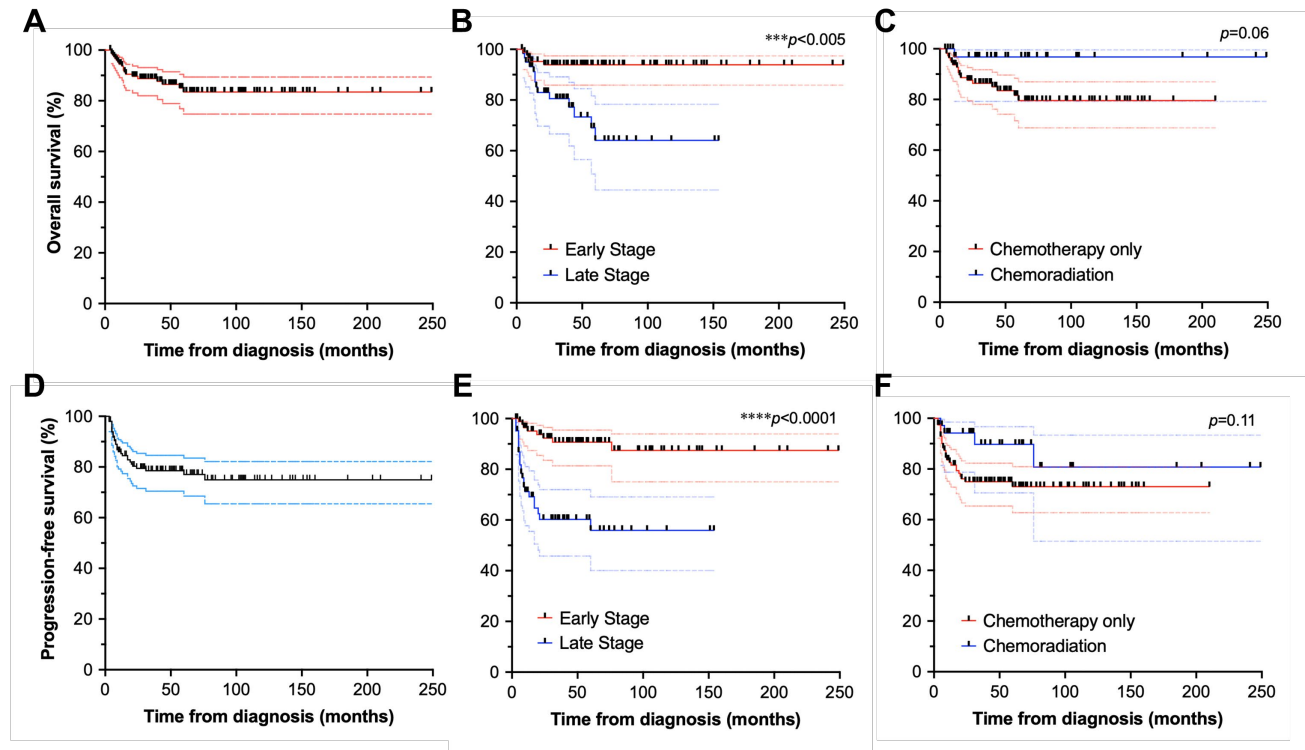


**Supplementary Figure 2. Gastrointestinal comorbidities among all patients.** The most common comorbidities included GERD, followed by colorectal cancer, and liver disease.



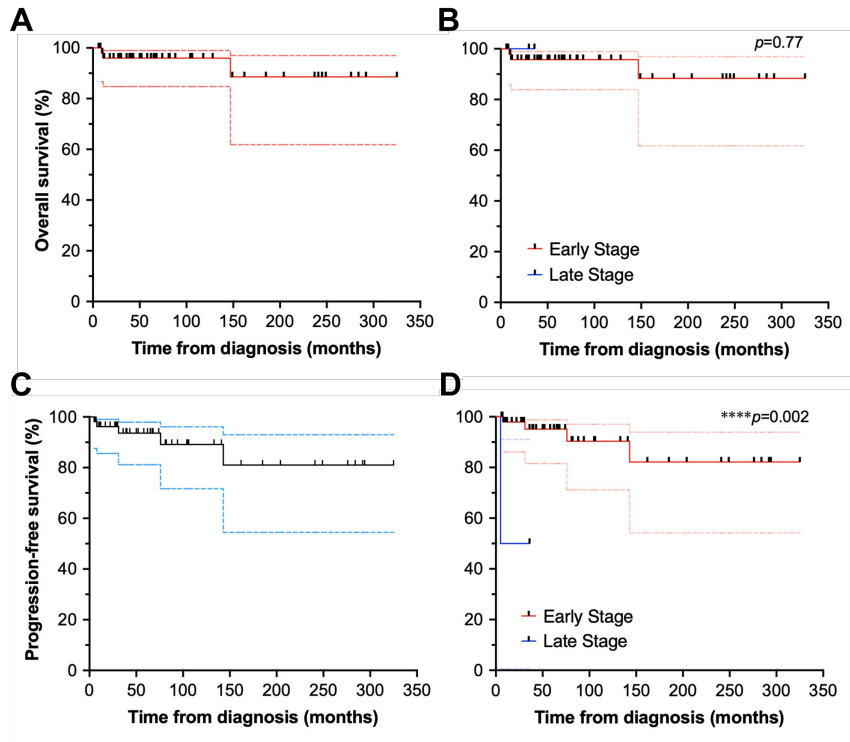
**Supplementary Figure 3. Survival outcomes of patients with DLBCL of the GI tract treated only in the post-rituximab era.** Overall survival of the full post-rituximab cohort (A), stratified by stage (B), and receipt of chemotherapy vs. chemoradiation (C). Also depicted are progression-free survival of the full post-rituximab cohort (D), as well as analyses stratified by stage (E), and chemotherapy vs. chemoradiation disposition (F). \* $p < 0.05$ , \*\* $p < 0.01$ , \*\*\* $p < 0.001$ , \*\*\*\* $p < 0.0001$ .

## POST-RITUXIMAB COHORT ONLY



**Supplementary Figure 4. Survival outcomes of patients with DLBCL of the GI tract treated with CMT.** Patients treated with systemic therapy alone were excluded from this analysis. Overall survival of the full CMT cohort (A), also stratified by stage (B). Also depicted are progression-free survival of the full CMT cohort (C), as well as an analysis stratified by stage (D). \* $p < 0.05$ , \*\* $p < 0.01$ , \*\*\* $p < 0.001$ , \*\*\*\* $p < 0.0001$ .

COMBINED MODALITY THERAPY (CMT) COHORT ONLY



Supplementary Table 1. Summary of chemotherapies received.

	All patients, <i>n</i> =204 <i>n</i> (%)	Early stage DLBCL, <i>n</i> =125 (61.3%) <i>n</i> (%)	Advanced stage DLBCL, <i>n</i> =75 (36.8%) <i>n</i> (%)
<b>Systemic line 1</b>			
<i>Without rituximab</i>	<u>Subtotal: 38 (18.6)</u>	<u>Subtotal: 31 (24.8)</u>	<u>Subtotal: 8 (10.7)</u>
<b>CHOP</b>	31 (15.2)	27 (21.6)	4 (5.3)
<b>EPOCH</b>	3 (1.5)	1 (0.8)	2 (2.7)
<b>HCVAD</b>	4 (2.0)	3 (2.4)	2 (2.7)
<i>With rituximab</i>	<u>Subtotal: 151 (74.0)</u>	<u>Subtotal: 87 (69.6)</u>	<u>Subtotal: 61 (81.3)</u>
<b>R-CHOP</b>	114 (55.9)	75 (60.0)	37 (49.3)
<b>R-EPOCH</b>	31 (15.2)	9 (7.2)	22 (29.3)
<b>R-HCVAD</b>	6 (2.9)	3 (2.4)	2 (2.7)
<i>Other</i>	15 (7.4)	5 (4.0)	6 (8.0)
<b>Systemic line 2</b>			
<i>Without rituximab</i>	<u>Subtotal: 2 (1.0)</u>	<u>Subtotal: 1 (0.8)</u>	<u>Subtotal: 1 (1.3)</u>
<b>CHOP</b>	2 (1.0)	1 (0.8)	1 (1.3)
<b>EPOCH</b>	0 (0.0)	0 (0.0)	0 (0.0)
<b>HCVAD</b>	0 (0.0)	0 (0.0)	0 (0.0)
<i>With rituximab</i>	<u>Subtotal: 8 (3.9)</u>	<u>Subtotal: 3 (2.4)</u>	<u>Subtotal: 5 (6.7)</u>
<b>R-CHOP</b>	3 (1.5)	1 (0.8)	2 (2.7)
<b>R-EPOCH</b>	5 (2.5)	2 (1.6)	3 (4.0)
<b>R-HCVAD</b>	0 (0.0)	0 (0.0)	0 (0.0)
<i>Other</i>	37 (18.1)	13 (10.4)	24 (32.0)

Supplementary Table 2. Presenting symptoms at diagnosis by GI-DLBCL subsite.

GI-DLBCL LOCATION	Stomach ( <i>n</i> =124)	Small Intestine ( <i>n</i> =44)	Large Intestine ( <i>n</i> =23)	
<b>INITIAL PRESENTATION</b> <i>n</i> (%)	Obstruction***	5 (4.1%)	11 (25%)	—
	GI bleeding	19 (15.4%)	5 (11.4%)	4 (17.4%)
	Abdominal pain	45 (36.6%)	13 (29.5%)	8 (34.8%)
	GERD	3 (2.4%)	—	2 (8.7%)
	Perforation	—	2 (4.5%)	—
	Nausea/vomiting	2 (1.6%)	1 (2.3%)	—
	Chronic anemia	1 (0.8%)	—	—
	Weight loss	—	—	1 (4.3%)
	Misc.	—	—	1 (4.3%) <sup>†</sup>

\*\*\**p*<0.001, <sup>†</sup>Ulcerative colitis requiring elective colectomy upon which GI-DLBCL was identified

**Supplementary Table 3.** Radiation treatment details.

		<b>All patients, n=65 n (%)</b>	<b>Early stage DLBCL, n=54 (83.1%) n (%)</b>	<b>Advanced stage DLBCL, n=9 (13.8%) n (%)</b>
<b>Radiation intent</b>	<b>Curative</b>	55 (84.6)	50 (92.6)	4 (44.4)
	<b>Palliative</b>	8 (12.3)	4 (7.4)	4 (44.4)
	<b>Missing</b>	2 (3.1)	0 (0.0)	1 (11.1)
<b>Radiation context</b>	<b>Initial therapy (upfront)</b>	57 (87.7)	52 (96.3)	4 (44.4)
	<b>Disease recurrence</b>	5 (7.7)	1 (1.9)	4 (44.4)
	<b>Missing</b>	3 (4.6)	1 (1.9)	1 (11.1)
	<b>Consolidation</b>	51 (78.5)	47 (87.0)	2 (22.2)
	<b>Gross disease</b>	14 (21.5)	7 (13.0)	6 (66.7)
	<b>Missing</b>	0 (0.0)	0 (0.0)	1 (11.1)
<b>Site(s) of radiation</b>	<b>Stomach</b>	50 (76.9)	45 (83.3)	2 (22.2)
	<b>Small intestines</b>	2 (3.1)	2 (3.7)	0 (0.0)
	<b>Pancreas</b>	1 (1.5)	1 (1.9)	0 (0.0)
	<b>Abdomen/pelvis, nodes</b>	9 (13.8)	8 (14.8)	1 (11.1)
	<b>Other (thorax, scrotum, bone, CNS)</b>	6 (9.2)	0 (0.0)	6 (66.7)
	<b>Missing</b>	1 (1.5)	0 (0.0)	1 (11.1)
<b>Concurrent chemotherapy</b>	<b>Yes</b>	0 (0.0)	0 (0.0)	0 (0.0)
	<b>No</b>	63 (96.9)	54 (100.0)	8 (88.9)
	<b>Missing</b>	2 (3.1)	0 (0.0)	1 (11.1)
<b>Dose of RT</b>	<b>Median (IQR)</b>	36 (30.6-39.6)	36 (30.6-39.6)	34 (30.5-37)
	<b>Missing</b>	7 (10.8)	5 (9.3)	1 (11.1)
<b>Fractionation</b>	<b>Median (IQR)</b>	18 (17-22)	20 (17-22)	16.5 (15-15)
	<b>Missing</b>	7 (10.8)	5 (9.3)	1 (11.1)
<b>Technique</b>	<b>2D/3D</b>	33 (50.8)	27 (50.0)	5 (55.6)
	<b>IMRT/VMAT</b>	25 (38.5)	22 (40.7)	3 (33.3)
	<b>Missing</b>	9 (13.8)	6 (11.1)	2 (22.2)

**Supplementary Table 4.** Multivariate analysis of patient, disease, and treatment factors associated with decrements in overall and progression-free survival among patients treated with rituximab.

Characteristic	OS HR	95% CI	<i>p</i> -value	PFS HR	95% CI	<i>p</i> -value
<b>Stage</b>						
I	<i>Ref</i>			<i>Ref</i>		
II	12.2	1.34 – 112.34	<b>0.027</b>	2.4	0.63 – 9.12	0.200
III	20.2	1.75 – 233.05	<b>0.016</b>	7.1	1.65 – 30.35	<b>0.008</b>
IV	12.9	1.62 – 102.22	<b>0.016</b>	5.8	2.15 – 15.85	<b>&lt;0.001</b>
<b>Achieved CR?</b>						
Yes	0.1	0.05 – 0.38	<b>&lt;0.001</b>	0.2	0.10 – 0.47	<b>&lt;0.001</b>

**Supplementary Table 5.** Multivariate analysis of patient, disease, and treatment factors associated with decrements in progression-free survival among patients treated with combined modality therapy.

Characteristic	PFS <sup>†</sup> HR	95% CI	<i>p</i> -value
<b>Achieved CR?</b>			
Yes	0.02	0.002 – 0.254	<b>0.002</b>

<sup>†</sup>No variables associated with OS decrements among the CMT cohort (*n*=55), hence only PFS is shown

**Supplementary Table 6.** Late treatment-related complications by GI-DLBCL subsite.

GI-DLBCL LOCATION	Stomach ( <i>n</i> =124)	Small Intestine ( <i>n</i> =44)	Large Intestine ( <i>n</i> =23)	
<b>TREATMENT COMPLICATION</b> <i>n</i> (%)	Perforation	3 (2.4%)	1 (2.3%)	—
	Obstruction	8 (6.5%)	5 (11.4%)	2 (8.7%)
	Bleeding	4 (3.2%)	4 (9.1%)	1 (4.3%)
	Pyloric Stenosis	1 (0.8%)	—	—
	Malabsorption	1 (0.8%)	—	—
	Chronic Anemia	1 (0.8%)	4 (9.1%)	2 (8.7%)
	Dysphagia	1 (0.8%)	—	—
	Fistula	—	1 (2.3%)	1 (2.3%)
	Surgical Intervention	<b><i>n</i>=9</b> ; Dilation ( <i>n</i> =1), Partial gastrectomy ( <i>n</i> =2), Jejunostomy or Gastrostomy ( <i>n</i> =2), Unknown ( <i>n</i> =4)	<b><i>n</i>=4</b> ; Venting Tube/J-tube/gastrojejunostomy ( <i>n</i> =1), Unknown ( <i>n</i> =3)	Not specified ( <b><i>n</i>=2</b> )