



Updated results of a phase 2 study from GELTAMO investigating the combination of ibrutinib with R-GEMOX in patients with relapsed or refractory diffuse large B-cell lymphoma



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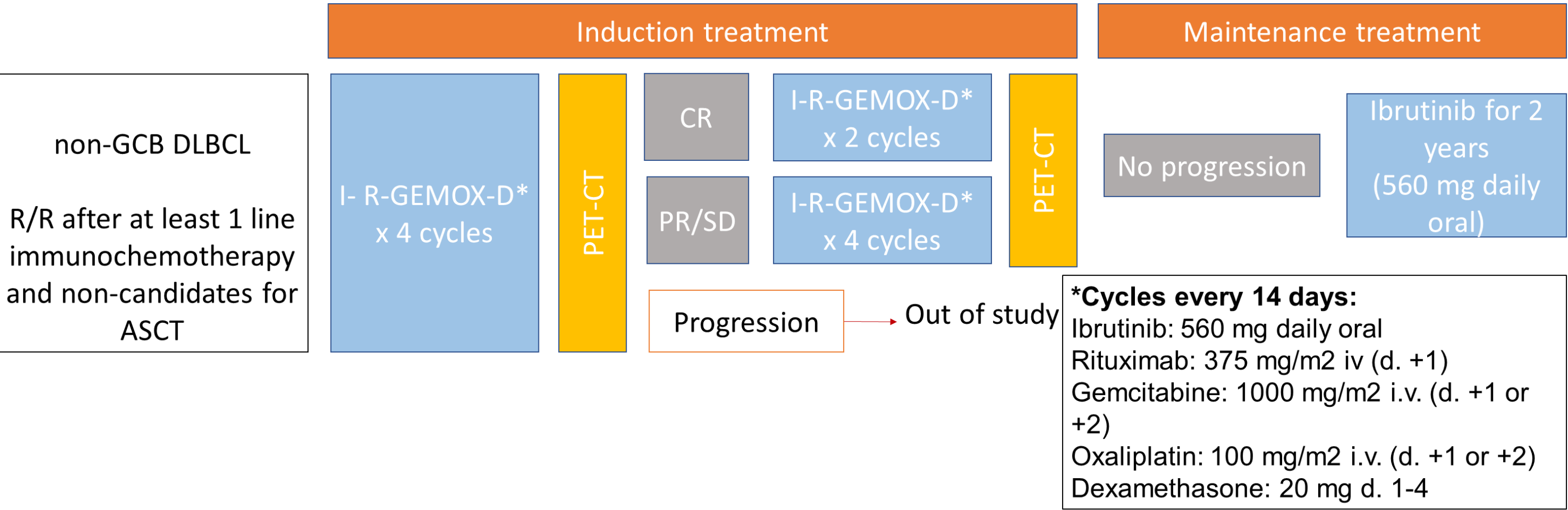
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Background

Patients with relapsed or refractory diffuse large B-cell lymphoma (R/R DLBCL), non-candidates for autologous stem-cell transplantation (ASCT), have few treatment options. Ibrutinib is an oral Bruton’s tyrosine kinase inhibitor that has shown increased antitumor activity in patients with DLBCL of different subtype from germinal center B-cell like (non-GCB).

In the present phase II clinical trial (NCT02692248), we investigated the efficacy and toxicity of the combination of Ibrutinib with R-GEMOX-D (rituximab, gemcitabine, oxaliplatin and dexamethasone), in patients with non-germinal center B-cell like (non-GCB) diffuse large B-cell lymphoma (DLBCL).

Materials & Methods



Key inclusion criteria: Histological diagnosis of non-GCB DLBCL (according to Hans algorithm). Relapsed or refractory disease after at least 1 line of immunotherapy (containing rituximab and anthracyclines). Non-candidates for ASCT. Age ≥18 years. ECOG ≤2. Measurable disease with PET+ lessions

Primary objective: overall response rate (ORR) after 4 cycles.

Secondary objectives: complete remission (CR) rate, progression-free survival (PFS), overall survival (OS) and toxicity.

Analyses were performed in the intention to treat population (data cut-off 16th January 2021).

Table 1. Baseline characteristics		n=64
Age, median (range)		67 (25-84)
Age >60 years, n (%)		45 (70.3%)
Sex, n (%)	Female	26 (40.6%)
	Male	38 (59.4%)
Local diagnosis, n (%)		Non-GCB DLBCL 64 (100%)
Central diagnosis, n(%)	Non-GCB DLBCL	45 (70.3%)
	GCB DLBCL	4 (6.3%)
	No data	15 (23.4%)
	ABC	17 (26.6%)
Nanostring, n (%)	GCB	3 (4.7%)
	Intermediate	3 (4.7%)
	No data	41 (64.1%)
Previous lines, n (%)	1	22 (34.4%)
	2	26 (40.6%)
	≥3	16 (24%)
Previos lines, median (range)		2 (1-5)
Previous ASCT, n (%)	Yes	10 (15.6%)
	No	54 (84.4%)
History of primary refractory disease, n (%)	Yes	17 (26.6%)
	No	47 (73.4%)
Status of lymphoma at study entry, n (%)	Refractory	39 (61%)
	Non refractory	24 (39%)
IPI at study entry, n (%)	0-1	6 (9.4%)
	2-3	43 (67.2%)
	4-5	13 (20.3%)
	No data	2 (3.1%)

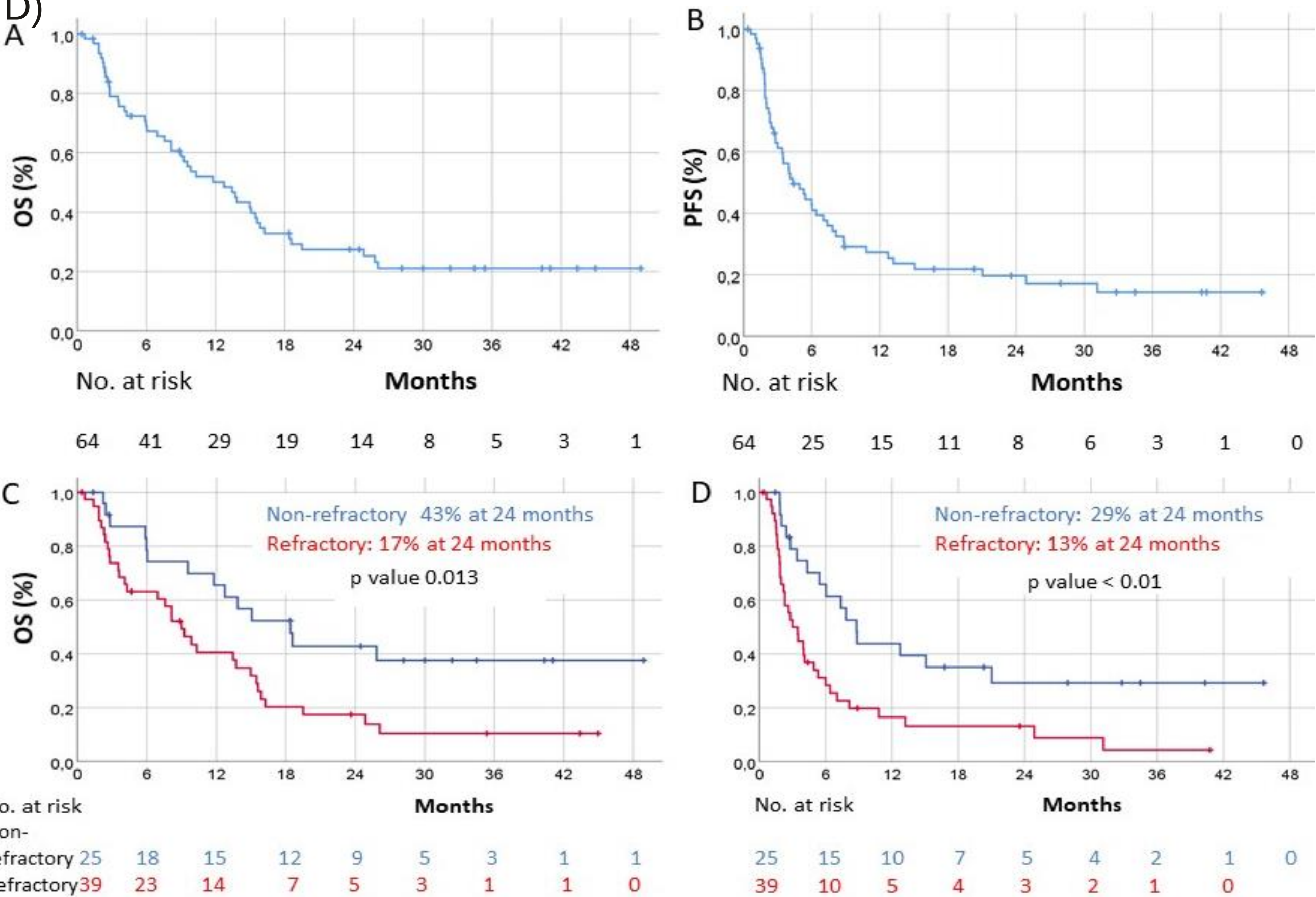
Abbr: GCB, germinal center B-cell; IPI, international prognosis index; DLBCL, diffuse large B-cell lymphoma; ASCT, autologous stem cell transplantation.

Table 2. Response rates	After 4 cycle, n (%)	End of induction, n (%)
Complete remission	22 (34.4)	19 (29.7)
Partial response	12 (18.8)	4 (6.2)
Overall response rate	34 (53.1)	23 (35.9)
Stable disease	5 (7.8)	1 (1.6)
Progression	13 (20.3)	11 (17,2)
Not evaluated	12* (20.3)	29* (45.4)
Total	64 (100)	64 (100)

*Early discontinuation before assessment of the response

Results

Figure 1. Overall survival (OS) and progression free survival (PFS) in the overall series (A, B) and according to status of lymphoma at sudy entry (C, D)



In the multivariate analysis, status of lymphoma at study entry significantly influenced PFS (HR 3.03; 95% CI 1.6-5.7; p<0.01) and OS (HR 2.2; 95% CI 1.2-4.2; p=0.016)

Table 3. Most frequent adverse events

Present in at least 10% of patients	n (%)
Thrombocytopenia	46 (71.9)
Neutropenia	35 (54.7)
Diarhea	34 (53.1)
Anemia	29 (45.3)
Fatigue	23 (35.9)
Nausea	20 (31.3)
Upper respiratory infection	13 (20.3)
Paresthesia	13 (20.3)
Adverse events with grade ≥3	n (%)
Thrombocytopenia	33 (51.6)
Neutropenia	30 (46.9)
Anemia	14 (21.9)
Lymphocyte count decreased	11 (17.2)
Diarrhea	10 (15.6)
Fatigue	6 (9.4)
Adverse events GRADE 5 (n=4)	
Aspergilosis (related), pneumonia (n=2, related); heart failure (unrelated)	

Conclusions

The combination of ibrutinib with R-GEMOX-D as salvage therapy for patients with non-GCB DLBCL is associated with high response rates, especially in relapsed patients. The vast majority of refractory patients progress very early, so this regimen could be considered as a bridge to other consolidation therapies. Biological studies analyzing cell of origin by gene expression profiling, minimal residual disease and mutational spectrum are in progress.