Impact of the total lesion glycolysis (TLG) in predicting response of follicular lymphoma to rituximab

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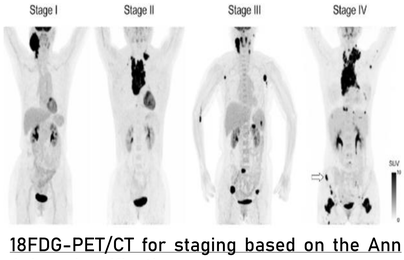
ABSTRACT

18-Fluorodeoxyglucose positron emission tomography, allowing to evaluate the tumour volume of follicular lymphoma (FL), can be enhanced by taking into account the total lesion glycolysis (TLG). Here, this parameter was evaluated retrospectively in a cohort of 81 patients. Among patients with a good prognosis,i.e. TMTV<510cm^3, a subgroup with a worse prognosis was identified with a TLG above 237. Although all received rituximab monotherapy, those with higher TLG values had a 3-year relapse rate of 56%, compared to 22% in the lower TLG group (p=0.009). These data suggest that this new threshold could prompt earlier initiation of immunochemotherapy.

INTRODUCTION

Follicular Lymphoma (FL) is a common type of indolent non-Hodgkin lymphoma, characterized by t(14;18) translocation, leading to BCL2 overexpression. FL is an indolent disease, and the goal in management is often to delay chemotherapy for as long as possible to minimize toxicity. The management of FL varies between low-tumor-burden and high-tumor-burden cases, with immunochemotherapy (ICT) being standard for high burden, while low burden may involve various strategies including watchful waiting or rituximab monotherapy.

Positron emission tomography, using 18 F-Fluorodeoxyglucose (18 F-FDG PET), allows to precisely quantify the metabolic activity of all tissues using their standardized uptake value (SUV). Actually, the PET-Scanner is used to obtain the Ann Arbor clasification, and to differentiate FL varies based on low and high tumor burden according to the Total Metabolic Tumor Volume (TMTV) with the cut off of 510cm^3. The Total Lesion Glycolysis is then calculated by multiplying the TMTV by the mean of these voxels SUV.



18FDG-PET/CT for staging based on the Ann Arbor classification

The current FLIPI prognostic classification for follicular lymphoma was established before the widespread use of rituximab. As a result, it is no longer fully relevant in an era where rituximab alone can be used as first-line therapy for some patients.

ISSUE



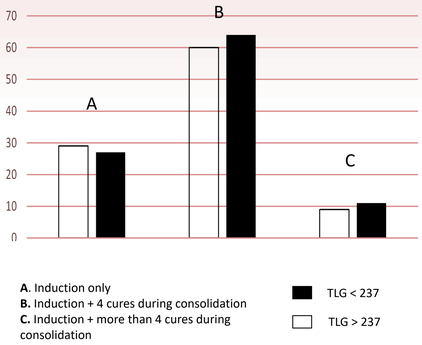
Can we predict in advance which patients with low-burden follicular lymphoma will respond well to Rituximab as monotherapy ?

RESULTS

Variable	TLG < 237 cm³ (n = 45)	TLG > 237 cm³ (n = 36)	p-value
Age, year, median (IQR)	61 (54–69)	62 (54.75–75.25)	0.546
Sex, *n* (%)			
Male	26 (57.78%)	17 (47.22%)	0.470
Female	19 (42.22%)	19 (52.78%)	
Performance status, *n* (%)			
0	37 (82.22%)	26 (72.22%)	0.420
1	8 (17.78%)	10 (27.78%)	
Ann Arbor, *n* (%)			
I/II	24 (53.33%)	10 (27.72%)	**0.033**
III/IV	21 (46.67%)	26 (72.28%)	
Diagnosis to induction time, year, median (IQR)	2 (0–4)	1 (0–1)	**0.028**
SUV max, median (IQR)	8.3 (5.8–10.11)	10.85 (8.78–13.28)	**<0.001**
TMTV (41% threshold), cm³ median (IQR)	20.8 (9.41–40.9)	106.89 (64.23–168.6)	**<0.001**
TLG (41% threshold), cm³ median (IQR)	77.16 (35.66–144.43)	420.35 (281.23–623.21)	**<0.001**
Number of nodal groups ≥4, *n* (%)	9 (20.00%)	20 (57.14%)	**0.001**
Increased LDH *n* (%)	10 (24.39%)	13 (37.14%)	0.339
Morphological response to induction, *n* (%)			
CR	23 (51.11%)	14 (38.89%)	0.757
PR	17 (37.78%)	18 (50.00%)	
SD	3 (6.67%)	2 (5.56%)	
Progression	2 (4.44%)	2 (5.56%)	
Metabolic response to induction, *n* (%)			
CR	27 (60.00%)	16 (44.44%)	0.327
PR	13 (28.89%)	17 (47.22%)	
SD	3 (6.67%)	1 (2.78%)	
Progression	2 (4.44%)	2 (5.56%)	
Consolidation, *n* (%)	32 (71.11%)	26 (72.22%)	1.000
Morphological response to consolidation, *n* (%)	(*N* = 32)	(*N* = 26)	0.845
CR	27 (84.38%)	20 (76.92%)	
PR	1 (3.12%)	2 (7.69%)	
SD	1 (3.12%)	0 (0.00%)	
Progression	3 (9.38%)	4 (15.38%)	
Metabolic response to consolidation, *n* (%)	(*N* = 32)	(*N* = 26)	0.738
CR	27 (84.38%)	20 (76.92%)	
PR	1 (3.12%)	0 (0.00%)	
SD	1 (3.12%)	0 (0.00%)	
Progression	3 (9.38%)	5 (19.23%)	
Treatment duration, days, median (IQR)	250 (22–273)	246 (21.75–271.5)	0.924

All bold values are statistically significant.

Patients characteristics according to total lesion glycolysis (TLG) value

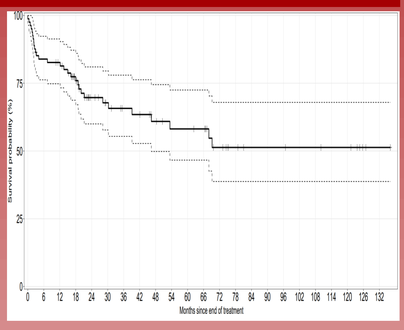


A. Induction only
B. Induction + 4 cures during consolidation
C. Induction + more than 4 cures during consolidation

Treatment Schedule according to total lesion glycolysis (TLG) value

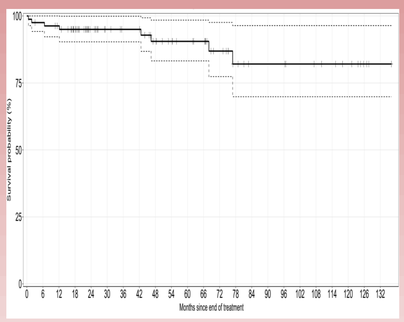
All of them were treated with rituximab monotherapy :

- 4 cures during induction
- +/- 4 cures during consolidation



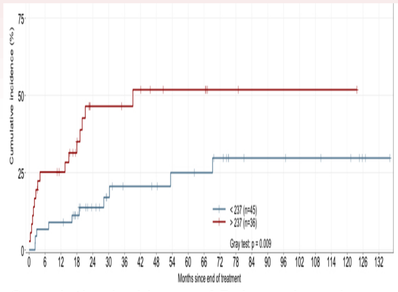
Progression Free Survival

The 3-year Progression Free Survival was 65,72%



Overall Survival

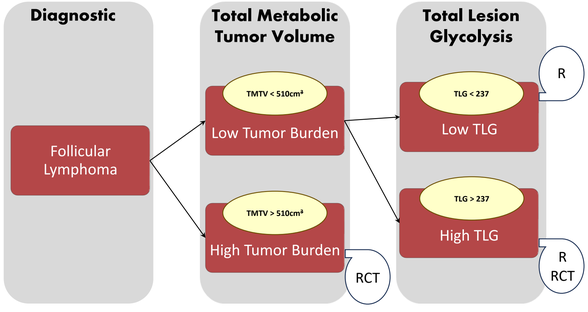
The 3-year Overall Survival was 95%



Cumulative incidence of Relapse based on total lesion glycolysis (TLG) value

The 3-year relapse rate is significantly higher at 56% versus 22% (subdistribution hazard ratio 3.10, 95% CI 1.45–6.64; p=0.009) characterized patients with a higher TLG

INTERPRETATION



First line therapy :

- RCT : RITUXIMAB + Chemotherapy
- R : RITUXIMAB as monotherapy

- 18FDG-PET/CT is essential for classifying follicular lymphoma
- TLG, with a cut-off of 237, can predict either good or poor response
- RITUXIMAB is effective in the population with a low tumor burden and a TLG<237.

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