Retrospective analysis of Follicular Lymphoma Treatments (Fly-T study)

Note publication plateforme HDH

Introduction

There are various treatment options for follicular lymphoma (FL) based on the severity of associated symptoms and cancer growth rate. Treatment for relapsed or refractory disease is influenced by proposed first-line therapy for FL, the duration and quality of the response.
An accurate estimation of the target population size and market shares of comparators is crucial for the reimbursement dossier analyses, which will as well be factored in the regulatory framework for price setting.
Currently, no data source is available to properly document the market shares & population size of FL in France. Other comparators which accessed to the French market for FL over the past years (2015 to 2020) mainly used the overall incidence of FL, in addition with international publications and expert opinions to document the proportion of patients who would ultimately reach the additional treatment sequences. There is a lot of uncertainty behind these estimates, since the therapeutic indications are rather specific (e.g., relapse within 6 months) and the therapeutic patterns are complex (watchful waiting in first sequence, stem cell transplant, radiotherapy, new anti-neoplastic agents ...).
This project aims to document the target FL population of KYMRIAH® and its management in the upcoming indication from the French hospital claims database (PMSI); and to understand to which extent its therapeutic management differs from that of the overall third-line (and more) treatment population. A secondary objective seeks to identify the geographic disparities in terms of access to CAR-T cells treatments, since these regimens can only be administered in a specific list of specialized hospitals. This additional objective aims to anticipate such questions raised by the French National Authority for Health (HAS) during the assessment of Kymriah® in follicular lymphoma, since geographic access to CAR-Ts therapies was questioned in the prior assessment of these therapeutic options (Kymriah® and Yescarta®).

Study objectives

Primary objective
To describe the characteristics and care management of FL population initiating a new treatment sequence in 2018 and to identify among them:

- Patients in third sequence or more
- Patients in third sequence or more, whose prior relapse occurred within 2 years following the end of the prior sequence

Secondary objective
To describe access to CAR-Ts treatments and associated hospitals for FL patients based on the region of residence and the region of CAR-T care management.

1.1. Population

This is a retrospective cohort study, based on French hospital claims data (PMSI), over the 2015 to 2020 period, describing therapeutic patterns in adult patients with follicular lymphoma.

1.1.1. Inclusion criteria

The study will include adult patients (> 18 years old) having at least one hospitalization (MSO or HAD) for follicular lymphoma in 2018 (**included population**). These hospitalizations will be identified via the ICD-10 code and sub-codes for follicular lymphoma (C82) as main, related or associated diagnosis.
Our **analysis target population** consists of adult patients, initiating a new treatment sequence in 2018, who received at least two treatment sequences during previous period.

Sub - groups of interest
Subgroups of the analysis target population were defined according to the timing of the prior relapse; they were aligned with the key thresholds considered by the ESMO clinical guidelines (6 months, 12 months and 24 months).
Sub - groups of patients defined by the time between current and prior sequence, called further prior relapse: [0-6] months;]6-12] months;]12-24] months; and more than 24 months.

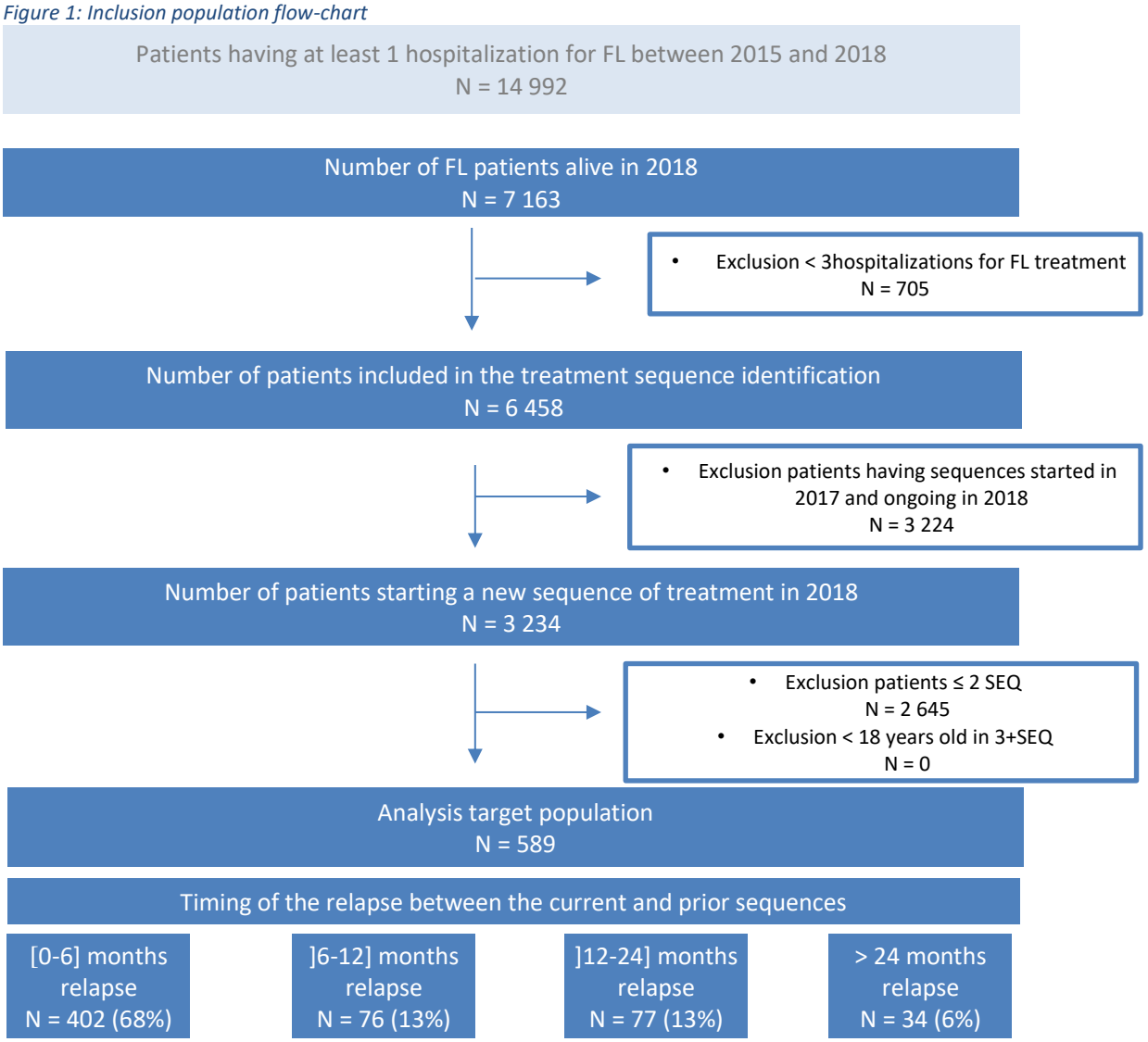
1.1.2. Study design

The study period from **2015 to 2020**.
The **inclusion period** consists in 1 year period, 2018. Index date (month and year) is defined as the first hospitalization for FL in 2018.
A **historical period** of up to 4 years will be used to identify prior treatment history of follicular lymphoma in included patients.
A 3-year follow-up period is considered.

Results

1.2. Flow chart

Figure 1: Inclusion population flow-chart



1.3. Target population analysis

The target population analysis is equal to 589 patients. The following analyses relate to this target population.

1.3.1. Population sequences visualization

Figure 2: Treatment sequences distribution plot, visualization over a maximum of 50 FL treatment hospitalizations, target population

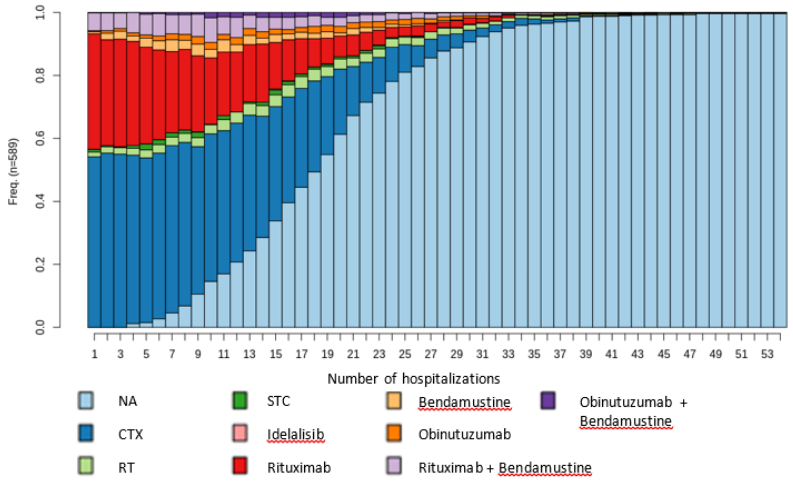
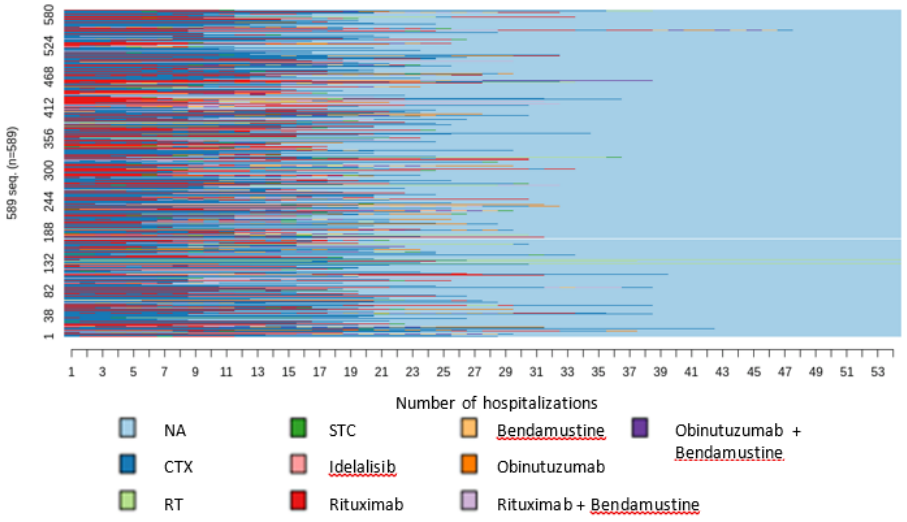


Figure 3: Treatment sequences individual plot, visualization over a maximum of 50 FL treatment hospitalizations, target population



1.3.2. Access to CAR-Ts treatments

Among the patients selected in the target population (N = 589), 1% of patients have the residential area in French overseas departments and territories (DOM-TOM) or abroad. Knowing that patients must be lodged at maximum 2 hours from the CAR-T center, we decided to proceed the distance estimation analysis only on the patients living in continental France.

Table 1: Distance estimation to access to FL treatments based on the region of residence and the region of the care center - Haversine method

			Timing of the relapse between the current and prior sequences		
	All patients	**[0-6] months**	**]6-12] months**	**]12-24] months**	**>24 months**
Number of patients living in France and abroad (DOM-TOM or other countries)	589	402	76	77	34
Number of patients living in continental (Metropolitan) France	582	395	76	77	34
Distance to the closest CAR-T center (in kilometers)					
Mean (SD)	51 (44)	50 (44)	50 (44)	51 (46)	65 (45)
Median (IQR)	43 (69)	42 (67)	42 (69)	40 (71)	69 (71)
Q1, Q3	12, 81	12, 79	10, 79	11, 82	26, 97
Min, Max	0, 217	0, 217	0, 182	0, 211	0, 141
Missing (DOM-TOM or other countries)	7	7	0	0	0
Distance to the current FL treatment hospital center (in kilometers)					
Mean (SD)	31 (39)	31 (42)	29 (28)	32 (34)	30 (26)
Median (IQR)	18 (38)	18 (36)	15 (38)	17 (47)	27 (44)
Q1, Q3	6, 44	6, 42	6, 44	7, 54	5, 49
Min, Max	0, 393	0, 393	0, 116	0, 149	0, 91
Missing (DOM-TOM or other countries)	7	7	0	0	0
Difference in distance between the hospital and the closest CAR-T center (as ratio of the distance to the hospital center; %), for patients with a residence area different that the current FL treatment hospital area and CAR T-cells hospital area					
Number of patients	501	339 (68%)	67 (13%)	68 (14%)	27 (5%)

Mean (SD)	206 (524)	220 (548)	146 (386)	204 (518)	186 (552)
Median (IQR)	0 (140)	0 (149)	0 (145)	0 (116)	19 (108)
Q1, Q3	0, 140	0, 149	0, 145	0, 116	0, 108
Min, Max	-98, 4166	-98, 4166	-63, 2204	-63, 2676	-15, 2804
Missing	88	63	9	9	7

***Legend**: All patients: on average the distance between a patient residence and that of a CART center is 2 times higher than the distance of the current treatment center (2018);*

- The maximum difference of 4166*% means that for a patient the current distance is 1 and the minimum distance to a CART center is 41 km (the distance increase 41 times).*

- *138 patients have ratios equals to 0 because they have equal distance to the current FL treatment and to CAR-T center*

Conclusion

This study allowed to identify the target FL population of KYMRIAH® and it health management in the upcoming indications well as to identify the geographic disparities in terms of access to CAR-T cells treatments.