

Sponsor

Novartis Pharmaceuticals

Generic Drug Name

CAR-T cell therapy

Trial Indication(s)

Diffuse large B-cell lymphoma and Acute Lymphoblastic Leukemia

Protocol Number

CCTL019A0FR02

Protocol Title

CAR-T Cells – Real Life Study Of Care Pathway And Total Cost Of Care For Patients under Car T-Cell Treatment Based On The PMSI French Database

Clinical Trial Phase

NA

Phase of Drug Development

NA

Study Start/End Dates

Study start date: 12/09/2020

Study Completion date: 28/08/2021

Reason for Termination

NA

Study Design/Methodology

A retrospective database analysis was performed using the French national hospital claims database (Medicalized Information System Program - PMSI, 2015-2019), which includes discharge summaries for all hospital admissions in France (~99% of French residents).

The patients were identified based on the CAR-T administration hospital stay, between 2017 and 2019. Based on the exhaustivity of the database, all patients treated with CAR-T (since 2018) were identified.

The study design included multiple periods of analysis based on the CAR-T process. Three main periods were defined: the historical period, the CAR-T period, and the post CAR-T period. The CAR-T period was divided in 2 sub-periods: pre CAR-T (including the apheresis procedure and 15 days before this procedure) and per CAR-T (including the lymphodepletion and CAR-T cell injection hospital stay until the end at the discharge date related to CAR-T cell injection hospital stay). The follow-up period started at the end of CAR-T hospital stay.

CAR-T populations:

KYMRIAH® DLBCL cohort:

- Adult patients (≥ 18 years of age) with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) after two or more lines of systemic therapy.
- Patient with a CAR-T administration hospital stay of Kymriah between 2017 and 2019

YESCARTA®DLBCL cohort:

- Adult patients (≥ 18 years of age) with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) after two or more lines of systemic therapy:
- Patient with a CAR-T administration hospital stay of Yescarta between 2017 and 2019

KYMRIAH® ALL cohort:

- Pediatric and young adult patients (≤ 25 years of age) with B-cell acute lymphoblastic leukemia (ALL) that is refractory, in relapse post-transplant or in second or later relapse:
- Patient with a CAR-T administration hospital stay of Kymriah between 2017 and 2019

Centers

Novartis Investigative Site

Objectives:**Primary objective(s)**

To describe the care pathway, the cost of care, and the treatment effectiveness of patients treated with chimeric antigen receptor T (CAR-T) cells in hospital, identified between 2017 and 2019, in each of the CAR T populations.

Test Product (s), Dose(s), and Mode(s) of Administration

NA

Statistical Methods

The data analysis was performed using R software.

For DLBCL and ALL population, descriptive analyses were implemented to understand the treatment and patient's management and presented split by the three CAR T periods, the pre, per and post-CAR-T. Effectiveness endpoints (OS, TTNT) were evaluated with Kaplan-Meier survival method. Cost assessment was realized for the CAR-T hospital stay and for the patient follow-up cost using specific health-economics methods reflecting censored data.

Study Population: Key Inclusion/Exclusion Criteria

Inclusion criteria

- Patients treated with CAR-T cells from 2017 to 2019 and informed as such in the PMSI And
- Patients diagnosed with ALL or DLBCL when administering CAR-T cells and
- up to 25 years for patients with ALL

Exclusion criteria

- All patients treated outside the two types of indications presented in the inclusion criteria will be excluded

Participant Flow

Between 2017 and 2019, 239 patients treated with a CAR-T post clinical trials in DLBCL were identified, 77 patients treated with Kymriah and 162 with Yescarta.

Baseline Characteristics

Socio-demographic characteristics and care consumption before matching

	Adult R/R DLBCL cohort Before matching	
	KYMRIAH® N= 77	YESCARTA® N= 162
Age:		
Mean (SD)	59 (12.59)	56 (13.71)
Median [Q1, Q3]	63 [53, 69]	60 [48, 67]
Min-Max	28, 77	18, 76
Gender:		
Male N (%)	55 (71.43%)	93 (57.41%)
Female N (%)	22 (28.57%)	69 (42.59%)
Number of MSO hospitalizations over the historical period*:		
Mean (SD)	25 (13.45)	23 (11.57)
Median [Q1, Q3]	21 [16, 34]	21 [17, 28]
Min-Max	3, 70	0, 71

*2 years before index date

Socio-demographic characteristics and care consumption after matching

	Adult R/R DLBCL cohort After matching 1:1		
	KYMRIAH® N= 72	YESCARTA® N= 72	P-value
Age:			
Mean (SD)	59 (12.94)	58 (12.46)	0.675
Median [Q1, Q3]	63 [49, 69]	62 [52, 68]	
Min-Max	28, 77	23, 74	
Gender:			
Male N (%)	50 (69%)	51 (70%)	>0.999
Female N (%)	22 (31%)	21 (30%)	
Number of MSO hospitalizations over the historical period*:			
Mean (SD)	25 (12.71)	26 (12.31)	0.545
Median [Q1, Q3]	21 [16, 33]	22.50 [18, 34]	
Min-Max	3, 70	3, 68	

*2 years before index date

The matching method allowed the matching of the majority of the Kymriah cohort patients (72 patients of 77).

The above table presents the characteristics of the patients after matching. The proportion of men, the average age and the number of hospitalizations during historical period were similar between cohorts (age: p-value 0.675; gender: p-value >0.999, hospitalizations: p-value 0.545).

Five patients of the Kymriah cohort not matched any of the Yescarta patients and were excluded from the analysis. The average age of these patients was superior to the average age observed for all Kymriah cohort and had more hospital stay during the period previous the CAR-T hospital stay.

Primary and Secondary Outcome Result(s)

DLBCL cohort: Effectiveness indicators

N (%)	Adult R/R DLBCL cohort	
	KYMRIAH® N= 77	YESCARTA® N= 162
Overall survival: number of events	20 (26%)	33 (21%)
TTNT analysis: number of events	27 (35%)	61 (37%)
TTNT or death analysis: number of events	35 (44%)	75 (33%)
Follow-up time (days)*		
Mean (SD)	137.30 (120.21)	139.27 (101.45)
Median [Q1, Q3]	87 [46, 203]	127.50 [55, 189]
Min-Max	9 - 520	0** - 434

* Follow-up is the time between the CAR-T injection (index date) and the last hospital stay observed.

**Two patients died at the time or just after the injection, on the same day.

Based on the information available in PMSI, patients were followed-up in average for 137 days for Kymriah patients and 139 days for Yescarta patients. During this period, 20 deaths were observed during a hospital stays in the Kymriah cohort (26%) and 33 deaths in the Yescarta cohort (21%). Furthermore, 27 patients were identified with a TTNT event in the Kymriah cohort (35%) and 61 patients in the Yescarta cohort (37%).

Effectiveness indicators	ALL pediatric and young adult cohort
	KYMRIAH® N= 34
Overall survival: number of events N (%)	8 (24%)
TTNT analysis: number of events N (%)	10 (29%)
TTNT or death analysis: number of events N (%)	12 (35%)
Follow-up time (days)*	
Mean (SD)	201.41 (123.92)
Median [Q1, Q3]	187 [88.75, 280.25]
Min-Max	6, 466

Based on the information available in PMSI, patients were followed-up in average of 201 days for Kymriah patients. During this period, 8 deaths were observed during a CAR-T hospital stays in the Kymriah cohort (24%). Furthermore, 10 patients were identified with a TTNT event in the Kymriah cohort (29%).

CAR-T hospitalization details of costs - R/R DLBCL Results

	Adult R/R DLBCL cohort	
	KYMRIAH® N= 77	YESCARTA® N= 162
Overall cost for CAR-T hospitalization (€)		
Mean (SD)	342 275 € (6 373)	373 208 € (9 267)
Median [Q1, Q3]	341 588 € [340 146, 343 563]	371 844 € [369 785, 374 909]
Min-Max	327 151 €, 367 842 €	357 102 €, 435 035 €
On top of DRG CAR-T cost (€)	303 916 €	333 867 €
On top of DRG drug cost (CAR-T cost included)		
Mean (SD)	304 707 € (2 282)	335 055 € (2 468)
Median [Q1, Q3]	303 916 € [303 916, 304 682]	333 867 € [333 867, 335 155]
Min-Max	303 916 €, 320 479 €	333 867 €, 349 446 €
DRG base cost (GHS) (€)		
Mean (SD)	13 427 € (2 019)	13 726 € (1 627)
Median [Q1, Q3]	14 206 € [14 182, 14 206]	14 206 € [14 206, 14 206]
Min-Max	8 235 €, 14 206 €	8 235 €, 14 206 €
DRG cost updated with TSE (€)		
Mean (SD)	13 288 € (2 152)	13 984 € (2 514)
Median [Q1, Q3]	14 206 € [14 182, 14 206]	14 206 € [14 206, 14206]
Min-Max	8 235 €, 17 960 €	8 235 €, 28 385 €
Medical unit supplement cost (€)		
Mean (SD)	9 279 € (3 995)	9 167 € (6 378)
Median [Q1, Q3]	8 466 € [7 660, 9 676]	8 465 € [6 450, 10 885]
Min-Max	0.00 €, 27 840 €	0.00 €, 44 706 €
CART extra fee (ATIH guidelines)	15 000 €	15 000 €

The total cost of CAR-T hospital stay for Kymriah cohort was €342,275 of which 89% (€304,707) is represented by the CAR-T cost and others extra drugs cost, 4% (€13,288) by the DRG cost updated with TSE, 3% (€9,279) for the medical unit medical unit supplement cost and 4.4% (€15,000) for the CAR-T extra fee. The total cost of CAR-T hospital stay for Yescarta cohort was €373,208 of which 89% (€335,055) is represented by the CAR-T cost and others extra drugs cost, 4% (€13,984) by the DRG cost, 2% (€9,167) for the medical unit medical unit supplement cost and 4% (€15,000) for the CAR-T extra fee.

CAR-T hospitalization details of costs - R/R ALL Results

ALL pediatric and young adult cohort	
KYMRIAH®	
N = 34	
Overall cost for CAR-T hospitalization (€)	
Mean (SD)	368 867 € (29 134)
Median [Q1, Q3]	363 526 € [351 607, 375 593]
Min-Max	338 550 €, 462 362 €
On top of DRG CAR-T cost (€)	
303 916 €	
On top of DRG drug cost (CAR-T cost included)	
Mean (SD)	311 105 € (13 572)
Median [Q1, Q3]	306 187 € [304 725, 309 486]
Min-Max	303 916 €, 369 329 €
DRG base cost (GHS) (€)	
Mean (SD)	24 688 € (7 729)
Median [Q1, Q3]	24 628 € [24 600, 32 205]
Min-Max	11 961 €, 34 768 €
DRG cost updated with TSE (€)	
Mean (SD)	24 981 € (7 913)
Median [Q1, Q3]	24 628 € [24 600, 34 690]
Min-Max	11 961 €, 34 768 €
Medical unit supplement cost (€)	
Mean (SD)	17 781 € (14 851)
Median [Q1, Q3]	13 290 € [9 071, 19 654]
Min-Max	7 662 €, 85 409 €
CART extra fee (ATIH guidelines)	
15 000 €	

The total cost of CAR-T hospital stay for Kymriah population was €368,867 of which 82% (€311,105) of the total cost is represented by CAR-T and others extra drug costs, 7% (€24,981) by the DRG cost updated with TSE, 5% (€17,781) for the medical unit supplement cost and 4% (€15,000) for the CAR-T extra fee.

Safety Results

Not reported

Other Relevant Findings

None

Conclusion

This study has provided description of patient's characteristics, care pathways and associated costs of French patients treated with CAR-T cells from January 2017 to December 2019 in the indications for R/R ALL for patients ≤ 25 years refractory, in relapse after transplantation or in second or more relapses, and for R/R DLBCL for adults after at least two lines of systemic treatment.

For effectiveness analysis, nonsignificant difference of effectiveness outcomes (TTNT or death; OS) between Kymriah matched patients and Yescarta matched patients were observed. The median time to event (TTNT or death) was 4.3 months [3.2- not reached] for Kymriah and 3.8 months [3.3- not reached] for Yescarta. Median OS were not reached for both cohorts. Furthermore, longitudinal health care costs at 6 months and 12 months of follow up showed that Kymriah patients were less expensive than Yescarta patients, between €5,000 and €10,000 by patient. The results of this study provided first insights about the hospital care pathway for patients treated with CAR-T.

Date of Clinical Study Report

31 August 2021