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Author Contributions
C.H., R.H. and S.L.G. contributed to the overall design and performed research; C.H., C.B. and S.L.G. analyzed the data and performed the statistical analyses; C.B., A.C., M.R., J.G. and S.C.Z. designed and performed *in vivo* CAR-T monitoring, C.H., E.B., P.B., C.T., T.G., T.L., K.B., D.B., G.C., J.O.B., D.B., M.T.R., M.M., F.L.B., O.C., S.G., C.C.L., O.H., E.G., S.C. and B.G. provided clinical care and collected data; all authors critically reviewed and approved the final version of the manuscript.

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Data sharing statement
Data supporting the findings of this study are available from the corresponding author on request by email.

Manuscript

Patients with mantle cell lymphoma (MCL) who discontinue the Bruton's tyrosine kinase inhibitor (BTKi) ibrutinib because of progressive disease or intolerance, have a reported median overall survival (OS) of 2.5 to 14.2 months.[1–3] ZUMA-2 is the pivotal trial of autologous anti-CD19 chimeric antigen receptor (CAR)-T cell therapy brexucabtagene autoleucel (brexu-cel or KTE-X19) in patients with heavily pretreated MCL that were refractory to or relapsing (R/R) after prior therapies, including a BTKi (ibrutinib or acalabrutinib). The primary efficacy analysis demonstrated a 93% overall response rate (ORR) by an independent radiologic review committee, including a 67% complete response (CR) rate.[4] In a standard-of-care setting, the response rates were consistent with those reported in the ZUMA-2 trial, but the duration of response (DOR) seemed shorter.[5–8] Of note, these results were reported with an analysis starting at the time of leukapheresis. Based on these results, the French health agency granted access to brexu-cel in its early access program[9] for patients with R/R MCL who failed after at least one line of chemoimmunotherapy and BTKi. The aim of the present study was to report the first intention-to-treat (ITT) results of brexu-cel use in R/R MCL from CAR-T cell therapy decision.

All patients in France with MCL for whom a treatment with brexu-cel was decided during the tumor board review (TBR) in the setting of the European Medicines Agency approval label (that is, who failed after at least one line of chemoimmunotherapy and one BTKi) were included in the DESCAR-T registry. As previously described[10], the protocol (NCT04328298) was approved by national ethics committees and the Data Protection Authority, and the study was undertaken in accordance with the Declaration of Helsinki. The

first patient was enrolled in December 20th 2019,[9] and data export from the DESCAR-T registry was set on 01 September 2023. ITT analyses were performed on all patients for whom a treatment with brexu-cel was decided during TBR, except those who had an ongoing manufacture at date of last cutoff (n=3). Survivals were defined from CAR-T decision at TBR (ITT) or from the date of CAR-T cell infusion (modified ITT = mITT). The "treated set" was defined as the patients who received brexu-cel infusion, and the "untreated set" as patients who did not receive it. Response was assessed according to the Lugano 2014 criteria, based on ^{18}fluorodeoxyglucose positron emission tomography (FDG-PET)[11]. CRS and ICANS were graded according to the consensus criteria from the American Society for Transplantation and Cellular Therapy (ASTCT)[12]. The blood expansion of CAR-T cells was monitored using multiparametric flow cytometry (MFC) on EDTA-anticoagulated fresh blood samples obtained from 21 patients at different time points following CAR-T cell infusion. Statistical analyses were performed using SAS software version 9.3.

A total of 181 patients from 24 French centers were registered, 71.8% of whom did not meet the ZUMA-2 eligibility criteria. The most common reasons for ineligibility included necessity of a bridge other than corticosteroids or BTKi (61.1%), performance status [PS] ≥2 (12%), and prior malignancy (8.3%). Three patients were excluded because of an ongoing manufacture at date of last cutoff, therefore, the "treated set" and the "untreated set" included 152 and 26 patients respectively (Figure 1A). Detailed patient characteristics for both sets are presented in Table 1. Among the 152 patients of the "treated set", 5 did not receive a BTKi before CAR-T therapy and 2 did not receive chemotherapy. The main reasons for patients not receiving brexu-cel were disease progression (n=15, including 7 patients who died before administration) and manufacturing failure (n=5). Of the 152 treated

patients, 3 needed a second attempt at lymphocyte collection. They were not included in the manufacturing failure population. In ITT (n=178), with a median follow-up of 14.2 months, the median OS was of 19.8 months (Figure 1B). As expected, the OS of the "untreated set" was poor with a median of 1.8 months, compared with the median OS of the "treated" patients that was not reached (55.6% at 24 months, Figure 1C). The median time between inclusion and leukapheresis was 20 days (interquartile range [IQR]: 11-31), and the median time between apheresis and infusion was 39 days (IQR: 33-53). In the "treated set", a total of 125 (82.2%) patients received bridging therapy, 61.1% of which included chemotherapy. Holding (treatment before leukapheresis) and bridging strategy, response and timing are detailed in Supplemental Data.

The median follow-up since first CAR-T cell administration (mITT) was 12.2 months (95% CI: 11.8-13.4). The best ORR for the 144 patients with at least one efficacy evaluation was 84.7%, including CR in 72.2%. Median PFS calculated from infusion was 9.5 months (95% CI [6.2, 15.1]), with an estimated PFS of 61.3% at 6 months (95% CI [52.2, 69.3]) and 45.6% at 12 months (95% CI [36.2, 54.5], Figure 2A). Median OS calculated from infusion was not reached (51.1% at 24 months, Figure 2B). Median duration of CR from infusion was 21.9 months (95% CI [10.7, not reached]). In patients with at least one safety evaluation (n=149), CRS was observed in 87.9% and ICANS in 55%. CRS or ICANS of grade ≥ 3 were seen in 12.1% (n=18) and 15.4% (n=23) of patients, respectively. The median time to CRS onset was 5 days (range, 0-10), and the median duration of CRS was 6 days (range, 1-28). The median time to ICANS onset was 7 days (range, 1-16), and the median duration of ICANS was 7 days (range, 1-174). Drugs used to manage CRS and/or ICANS included tocilizumab (74.8%), corticosteroids (64.9%), anakinra (11.5%), and siltuximab (5.3%, always in association with

tocilizumab). Persistent cytopenias of any grade were observed in 19.7% (n=24) of evaluable patients at month 3, with grade ≥3 neutropenia and thrombocytopenia in 13 and 1 patients respectively. Infections of grade ≥3 were seen from infusion to day 10 in 25.5% of patients (n=38) and were mostly bacterial (n=25, 16.8%). Overall, transfer to intensive care unit (ICU) was needed in 34.3% of patients (n=46), with a median duration of hospitalization of 6 days. The main reasons for admission were CRS (n=44: 26 cases of grade 2 and 18 cases of grade 3 or more) and/or ICANS (n=36: 13 cases of grade 2 and 23 cases of grade 3 or more). Except for the 2 grade 5 CRS, all patients successfully recovered from their ICU admission. Among the 152 patients infused, 46 died, with a non-relapse mortality of 11.2%. The first cause of death was progressive disease (n=29), followed by infectious events (n=11: 7 bacterial sepsis, 3 COVID and 1 cerebral toxoplasmosis) CRS (n=2), myelodysplastic syndrome (n=2) and 2 deaths of unknow cause. A total of 9 infused patients received allogeneic stem cell transplant prior to inclusion in the present work, none of them developed graft versus host disease (GVHD).

We performed several preplanned exploratory analyses. The need of a bridging therapy and the response after it was significantly associated with OS from infusion. The OS rate at 12 months was 58% for patients who received a bridge and did not respond, versus 79.9% for patients who responded, and 84.3% for whom a bridge was not necessary (Figure 2C). At first infusion, CRP levels > 30mg/l and ferritin above the ULN were significantly associated with shorter OS (p=0.004 and 0.04, respectively, Figure 2D and E). We observed no difference in OS or PFS according to bridge timing, age or LDH levels at infusion. Cellular kinetics parameters were measured in 21 patients, including area under the curve (AUC), maximal expansion post infusion (C_{MAX}) and the time to maximal expansion (T_{MAX}). Regarding

safety prediction, both C_{MAX} and AUC were significantly higher for patients experiencing CRS or ICANS of any grade (Supplemental Data). Regarding efficacy prediction, with the ad-hoc threshold of 60 cells/µl and/or 500 AU (arbitrary units) for C_{MAX} and AUC, respectively, both parameters were predictors of PFS. The difference was not significant for OS. Finally, T_{MAX} was not a discriminator in our study.

We acknowledge that our study has significant limitations, primarily retrospective data collection and substantial amount of missing data. However, this is the first intention-to-treat analysis from local panel decision (TBR) of brexu-cel use, in R/R MCL standard of care practice. The main reasons for not receiving brexu-cel were disease progression and manufacturing failure. The response rate of brexu-cel observed in our study (mITT) was consistent with those reported in the ZUMA-2 trial[4] or other standard of care studies[5–8]. However, the PFS seemed shorter and the rate of grade ≥3 ICANS seemed lower. In addition to more aggressive diseases and patients with more comorbidities, we can hypothesize that T cell fitness could be lower in our study because of more heavily pretreated patients and a substantial number receiving holding therapy.[13,14] Overall, this "real-life" study experience supports the use of brexu-cel in R/R MCL patients who progressed after BTKi, especially when disease control before infusion is possible. We also demonstrate that *in vivo* CAR-T cell monitoring is feasible in the standard of care practice.

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	Treated set n=152	Untreated set n=26
Sex Male	131 (86.2%)	18 (69.2%)
Age (years)		
Median (min ; max)	68.0 (39 ; 83)	66.5 (47 ; 77)
Age >= 65 years	99 (65.1%)	16 (61.5%)
Age > 75 years	19 (12.5%)	3 (11.5%)
ECOG Performance Status		
0-1	125 (88.0%)	14 (60.9%)
>=2	17 (12.0%)	9 (39.1%)
Missing	10	3
MIPI risk group		
Low risk (< 5.7)	27 (19.9%)	3 (15.0%)
Intermediate risk ([5.7 - 6.2])	54 (39.7%)	5 (25.0%)
High risk (>= 6.2)	55 (40.4%)	12 (60.0%)
Missing	16	6
Ki-67 >= 30%		
< 30%	22 (20.6%)	3 (21.4%)
>= 30%	85 (79.4%)	11 (78.6%)
Missing	45	12
TP53 mutation		
Yes	29 (30.2%)	6 (42.9%)
No	67 (69.8%)	8 (57.1%)
Missing	56	12
Blastoid variant		
Yes	41 (31.1%)	3 (16.7%)
No	91 (68.9%)	15 (83.3%)
Missing	20	8
Prior lines of therapy		
Median (min ; max)	3.0 (1 ; 9)	3.0 (2 ; 9)
Prior transplant		
Autograft	60 (39.5%)	9 (34.6%)
Allograft	9 (5.9%)	0 (0%)
Bridging therapy	126 (82.9%)	15 (57.7%)

Table

Table 1: Main baseline characteristics of patients. The "untreated" and "treated" sets are presented separately. Age, ECOG (Eastern Cooperative Oncology Group), MIPI (Mantle Cell Lymphoma International Prognostic Index), Ki-67, TP53 mutation and blastoid morphology are given at the time of inclusion (local panel decision of brexu-cel treatment).

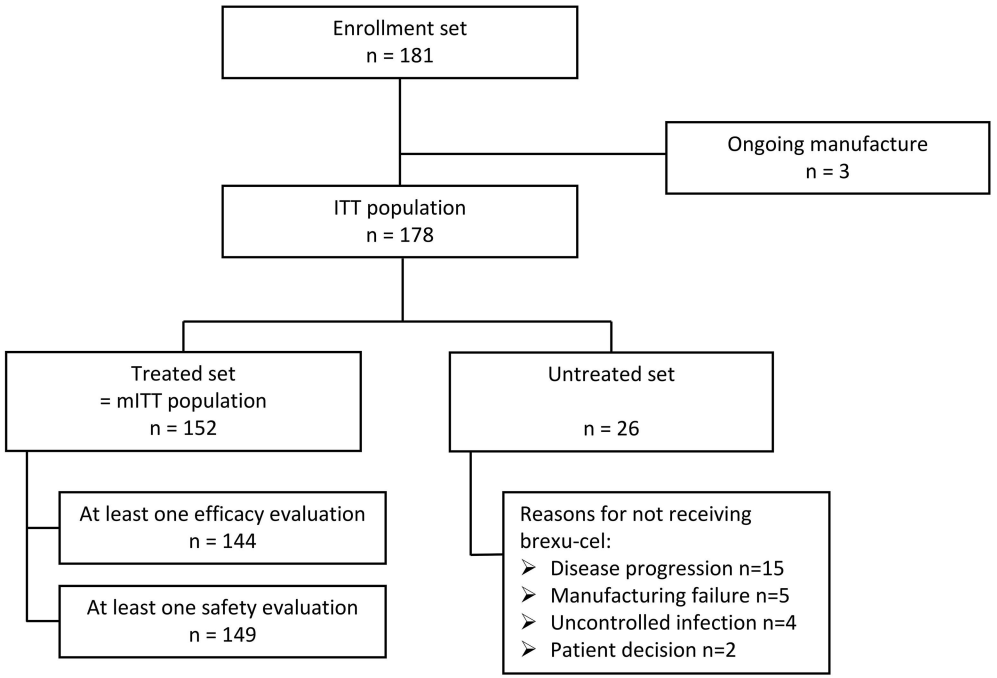
Figure legends

Figure 1: Characteristics of the intention-to-treat population. A/ Description of the different sets of patients. ITT: intention to treat. B/ OS since inclusion in the DESCAR-T cohort in ITT. C/ OS since inclusion in the DESCAR-T cohort according to treatment set.

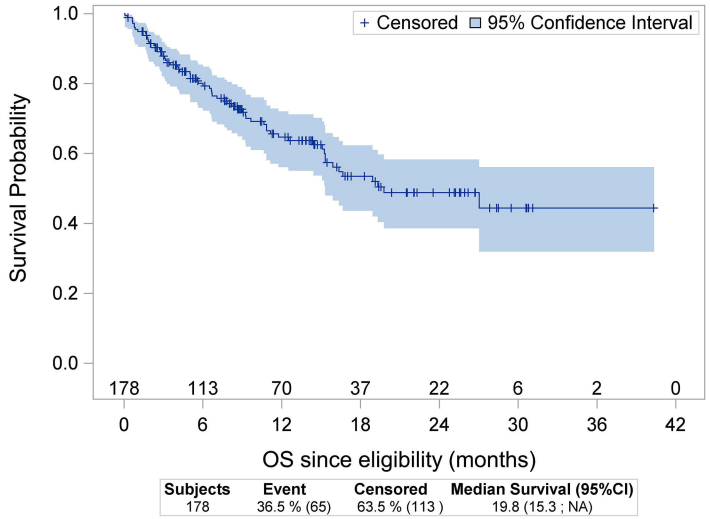
Figure 2: Efficacy description of all patients who received brexu-cel. A and B/ Outcome of patients in the treated set, progression free survival (PFS) and overall survival (OS), respectively. C/ OS according to response after bridging strategy, responders are defined as patients achieving partial or complete response. D/ OS according to CRP level the day of brexu-cel infusion. E/ OS according to ferritin level the day of brexu-cel infusion.

Figure 1

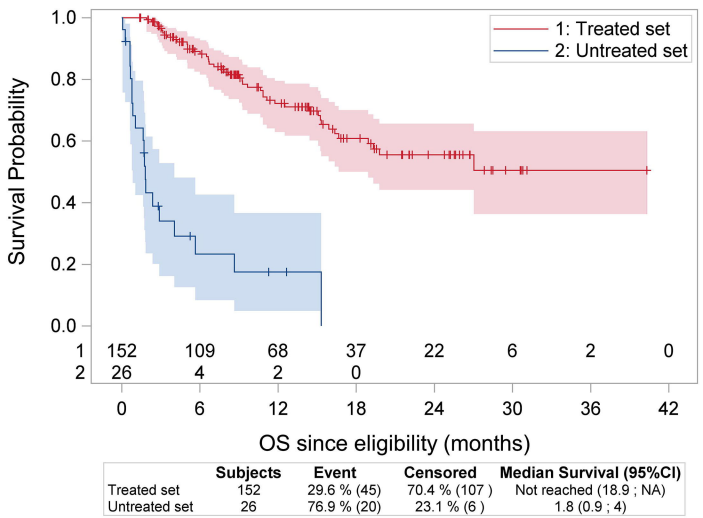
A


Enrollment set
n = 181
Ongoing manufacture
n = 3
ITT population
n = 178
Treated set
= mITT population
n = 152
Untreated set
n = 26
At least one efficacy evaluation
n = 144
At least one safety evaluation
n = 149
Reasons for not receiving brexu-cel:
Disease progression n=15
Manufacturing failure n=5
Uncontrolled infection n=4
Patient decision n=2

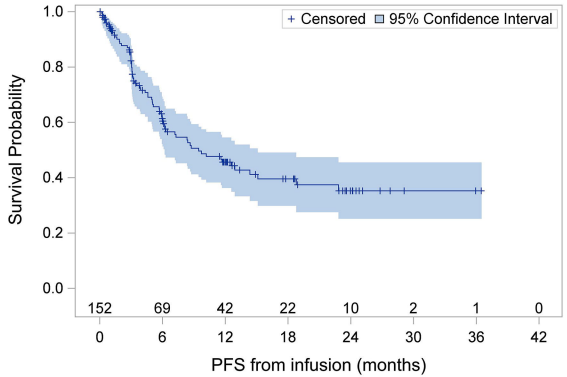
B


Censored
95% Confidence Interval
Survival Probability
1.0
0.8
0.6
0.4
0.2
0.0
178 113 70 37 22 6 2 0
0 6 12 18 24 30 36 42
OS since eligibility (months)
Subjects Event Censored Median Survival (95%CI)
178 36.5 % (65) 63.5 % (113) 19.8 (15.3 ; NA)

C

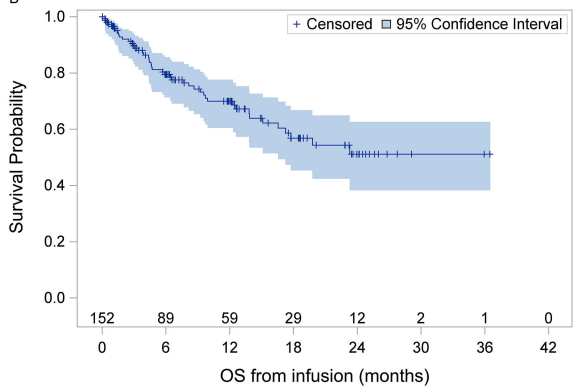

1: Treated set
2: Untreated set
Survival Probability
1.0
0.8
0.6
0.4
0.2
0.0
1 152 109 68 37 22 6 2 0
2 26 4 2 0
0 6 12 18 24 30 36 42
OS since eligibility (months)
Subjects Event Censored Median Survival (95%CI)
Treated set 152 29.6 % (45) 70.4 % (107) Not reached (18.9 ; NA)
Untreated set 26 76.9 % (20) 23.1 % (6) 1.8 (0.9 ; 4)

A



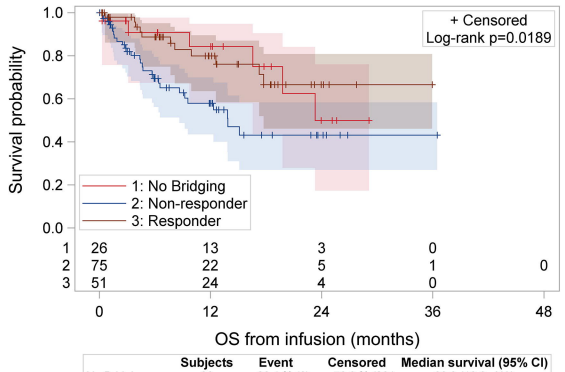
Subjects	Event	Censored	Median Survival (95%CI)
152	46.7 % (71)	53.3 % (81)	9.5 (6.2 ; 15.1)

B



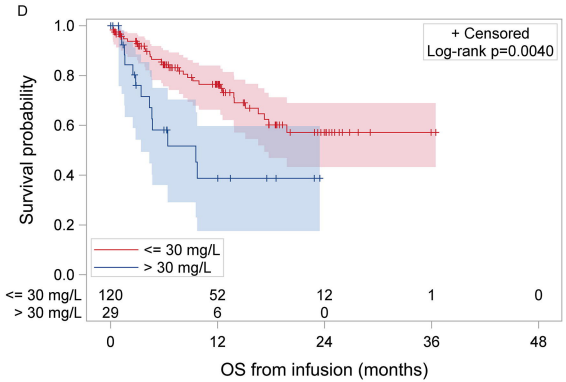
Subjects	Event	Censored	Median Survival (95%CI)
152	29.6 % (45)	70.4 % (107)	Not reached (16.6 ; NA)

C



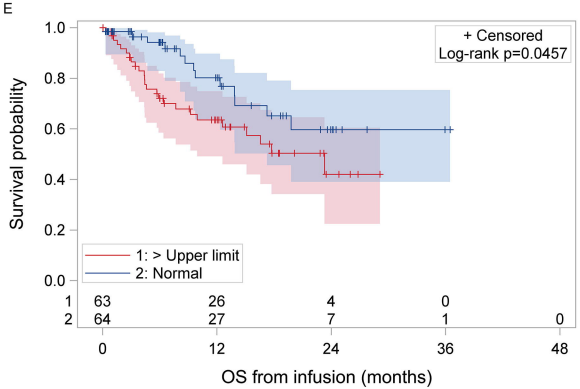
	Subjects	Event	Censored	Median survival (95% CI)
No Bridging	26	23.1 % (6)	76.9 % (20)	23.3 (16.6 ; NA)
Non-responder	75	37.3 % (28)	62.7 % (47)	13.9 (8.6 ; NA)
Responder	51	21.6 % (11)	78.4 % (40)	Not reached (17.7 ; NA)

D



	Subjects	Event	Censored	Median survival (95% CI)
<= 30 mg/L	120	25.8 % (31)	74.2 % (89)	Not reached (17.2 ; NA)
> 30 mg/L	29	44.8 % (13)	55.2 % (16)	9.6 (3.4 ; NA)

E



	Subjects	Event	Censored	Median survival (95% CI)
> Upper limit	63	39.7 % (25)	60.3 % (38)	23.3 (9.9 ; NA)
Normal	64	20.3 % (13)	79.7 % (51)	Not reached (17.2 ; NA)

	Patient without bridge or holding N=27		Patients with bridge only N=63		Patients with holding then bridge N=62	
Sex Male	22	(81.5%)	56	(88.9%)	53	(85.5%)
Age at inclusion (years)						
Median (min ; max)	70.0 (39 ; 78)		67.0 (40 ; 83)		68.5 (39 ; 79)	
Age (TBR) > = 65 years	13	(48.1%)	36	(57.1%)	31	(50.0%)
Age (TBR) > 75 years	5	(18.5%)	6	(9.5%)	8	(12.9%)
ECOG at inclusion						
0-1	20	(80.0%)	52	(89.7%)	53	(89.8%)
>=2	5	(20.0%)	6	(10.3%)	6	(10.2%)
Missing	2		5		3	
MIPI risk group at inclusion						
Low risk (< 5.7)	5	(21.7%)	11	(19.0%)	11	(20.0%)
Intermediate risk ([5.7 - 6.2[)	10	(43.5%)	24	(41.4%)	20	(36.4%)
High risk (>= 6.2)	8	(34.8%)	23	(39.7%)	24	(43.6%)
Missing	4		5		7	
Ki-67 > = 30% at inclusion						
< 30%	4	(26.7%)	13	(27.7%)	5	(11.1%)
>= 30%	11	(73.3%)	34	(72.3%)	40	(88.9%)
Missing	12		16		17	
LDH (TBR) > Normal*						
No	14	(51.9%)	23	(36.5%)	25	(40.3%)
Yes	10	(37.0%)	40	(63.5%)	35	(56.5%)
Missing	3	(11.1%)	0	(0.0%)	2	(3.2%)
Bulky disease (>5cm) at Lymphodepletion*						
No	23	(85.2%)	40	(63.5%)	49	(79.0%)
Yes	3	(11.1%)	21	(33.3%)	12	(19.4%)
Missing	1	(3.7%)	2	(3.2%)	1	(1.6%)
Number or prior lines of therapy**						
Median (min ; max)	3.0 (2 ; 8)		3.0 (2 ; 9)		3.0 (1 ; 6)	
Prior autologous transplant	8	(29.6%)	23	(36.5%)	29	(46.8%)
Previous BTK inhibitor therapy						
IBRUTINIB	25	(92.6%)	61	(96.8%)	54	(87.1%)
ACALABRUTINIB	2	(7.4%)	2	(3.2%)	0	(0.0%)
ZANUBRUTINIB	0	(0.0%)	0	(0.0%)	0	(0.0%)
Bridging therapy	0	(0.0%)	63	(100.0%)	62	(100.0%)
Type of treatment***						
Monoclonal antibody	0	-	45	(71.4%)	37	(59.7%)
Other immunotherapy	0	-	0	(0.0%)	0	(0.0%)
Chemotherapy	0	-	43	(68.3%)	34	(54.8%)
Radiotherapy	0	-	6	(9.5%)	4	(6.5%)
IMiD	0	-	5	(7.9%)	5	(8.1%)
Epigenetic modifiers agents	0	-	0	(0.0%)	0	(0.0%)
Kinase inhibitor	0	-	12	(19.0%)	24	(38.7%)
Corticosteroids	0	-	8	(12.7%)	5	(8.1%)
Other anti-cancer therapy	0	-	14	(22.2%)	21	(33.9%)
Disease status before CAR-T infusion						
Complete Response	0	-	6	(9.5%)	9	(14.5%)
Partial Response	0	-	15	(23.8%)	21	(33.9%)
Stable Disease	0	-	9	(14.3%)	8	(12.9%)
Progressive Disease	0	-	29	(46.0%)	19	(30.6%)
Not Evaluated	0	-	4	(6.3%)	4	(6.5%)
Missing	0	-	0	(0.0%)	1	(1.6%)

* Patients with missing Data are included in Denominator
** Up to 10 treatment lines may be collected in the register
*** Several treatments possible

Supplemental Table 1: Main characteristics of patients according to bridging subgroup. TBR: tumor board review, MIPI: mantle cell lymphoma international prognostic index.

Patient	Bridging strategy	Regroupement (Holding + Bridging)	Response after treatment (Bridging)	Started the same day as leukapheresis?
1	Patients with bridge only	RITUXIMAB - CHOP	Progressive Disease	No
2	Patients with holding then bridge	IBRUTINIB	Progressive Disease	No
3	Patients with holding then bridge	IBRUTINIB	Complete Response	No
4	Patients with bridge only	OBINUTUZUMAB - BENDAMUSTINE - BORTEZOMIB	Partial Response	No
5	Patients with bridge only	RADIOTHERAPY	Partial Response	No
6	Patients with bridge only	VENETOCLAX	Progressive Disease	No
7	Patients with holding then bridge	RITUXIMAB - LENALIDOMIDE - IBRUTINIB - DEXAMETHASONE	Not Evaluated	No
8	Patients with holding then bridge	IBRUTINIB	Stable Disease	No
9	Patients with bridge only	RITUXIMAB - BENDAMUSTINE - IBRUTINIB	Progressive Disease	No
10	Patients with bridge only	RITUXIMAB - BENDAMUSTINE	Not Evaluated	No
11	Patients with holding then bridge	VENETOCLAX	Stable Disease	No
12	Patients with bridge only	RITUXIMAB - DHAOX	Not Evaluated	No
13	Patients with holding then bridge	RITUXIMAB - IBRUTINIB - CYTARABINE - METHOTREXATE	Not Evaluated	Yes
14	Patients with bridge only	RADIOTHERAPY	Progressive Disease	Yes
15	Patients with holding then bridge	Corticosteroids	Partial Response	No
16	Patients with holding then bridge	RADIOTHERAPY - LENALIDOMIDE - IBRUTINIB	Stable Disease	No
17	Patients with bridge only	RADIOTHERAPY	Stable Disease	No
18	Patients with bridge only	CHOP - PREDNISONE	Progressive Disease	Yes
19	Patients with bridge only	RITUXIMAB - CHOP	Partial Response	Yes
20	Patient without bridge or holding		.	No
21	Patients with holding then bridge	RITUXIMAB - CHOP - RITUXIMAB - VENETOCLAX	Progressive Disease	No
22	Patients with holding then bridge	RITUXIMAB - CYTARABINE	Partial Response	No
23	Patients with bridge only	RITUXIMAB - BENDAMUSTINE - HOLOXAN-VP16	Not Evaluated	Yes
24	Patient without bridge or holding		.	No
25	Patients with holding then bridge	RITUXIMAB - DHAOX	Complete Response	No
26	Patients with bridge only	RITUXIMAB - CYCLOPHOSPHAMIDE - DOXORUBICINE - VINCRISTINE	Stable Disease	No

		DEXAMETHASONE - BORTEZOMIB - METHOTREXATE		
27	Patient without bridge or holding		.	No
28	Patients with bridge only	RITUXIMAB - BAC	Partial Response	Yes
29	Patient without bridge or holding		.	No
30	Patient without bridge or holding		.	No
31	Patients with bridge only	RITUXIMAB - CHOP	Stable Disease	Yes
32	Patients with holding then bridge	RADIOTHERAPY - IBRUTINIB - VENETOCLAX	Partial Response	No
33	Patients with holding then bridge	RITUXIMAB - DHA - BORTEZOMIB	Partial Response	No
34	Patient without bridge or holding		.	No
35	Patients with bridge only	RITUXIMAB - CYTARABINE - DEXAMETHASONE - RITUXIMAB - IBRUTINIB - VENETOCLAX	Progressive Disease	No
36	Patients with bridge only	RITUXIMAB - CYTARABINE - DEXAMETHASONE	Partial Response	No
37	Patients with bridge only	RITUXIMAB - CHOP	Progressive Disease	No
38	Patients with bridge only	RITUXIMAB - IBRUTINIB	Partial Response	No
39	Patients with holding then bridge	METHOTREXATE - IBRUTINIB - VENETOCLAX	Progressive Disease	No
40	Patients with holding then bridge	IBRUTINIB - VENETOCLAX	Progressive Disease	No
41	Patients with holding then bridge	IBRUTINIB	Progressive Disease	No
42	Patients with bridge only	RITUXIMAB - DHAC - IBRUTINIB	Progressive Disease	No
43	Patients with holding then bridge	VENETOCLAX	Progressive Disease	No
44	Patients with holding then bridge	RITUXIMAB - VCAP - OBINUTUZUMAB - BENDAMUSTINE	Partial Response	No
45	Patients with holding then bridge	RITUXIMAB - CYTARABINE - BENDAMUSTINE - OTHER TK INHIBITOR	Progressive Disease	No
46	Patients with holding then bridge	RITUXIMAB - BENDAMUSTINE	Stable Disease	No
47	Patients with holding then bridge	RADIOTHERAPY - DEXAMETHASONE	Partial Response	No
48	Patients with bridge only	RITUXIMAB - BENDAMUSTINE - BVD - BORTEZOMIB	Progressive Disease	No
49	Patients with bridge only	OBINUTUZUMAB - BENDAMUSTINE - BENDAMUSTINE - BORTEZOMIB	Progressive Disease	No
50	Patients with holding then bridge	IBRUTINIB	Partial Response	No
51	Patient without bridge or holding		.	No
52	Patients with holding then bridge	RITUXIMAB - IFOSFAMIDE - ETOPOSIDE	Progressive Disease	No

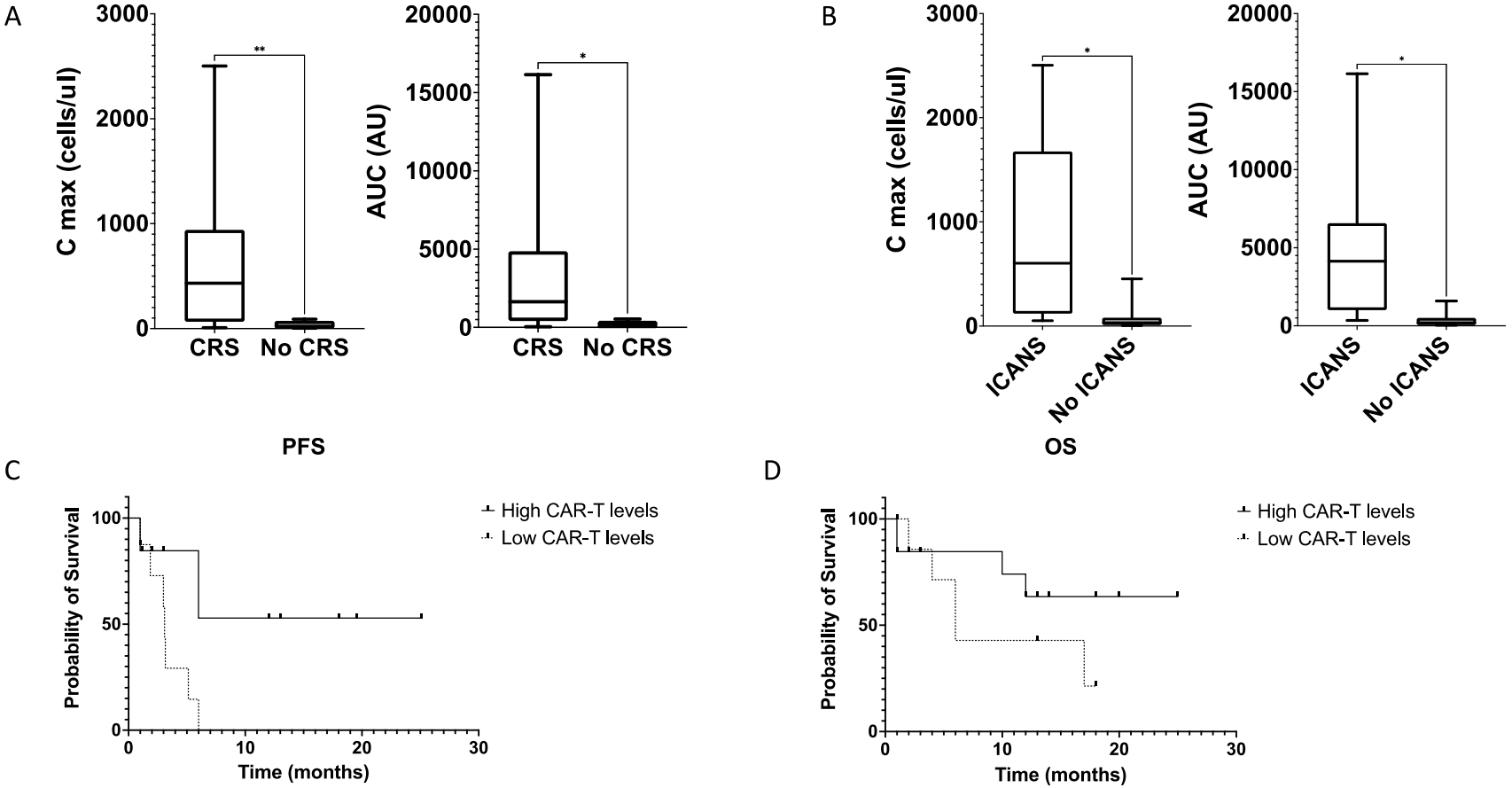
53	Patients with holding then bridge	OBINUTUZUMAB - LENALIDOMIDE - PREDNISONE	Progressive Disease	Yes
54	Patients with bridge only	IBRUTINIB - VENETOCLAX	Complete Response	No
55	Patients with holding then bridge	RITUXIMAB - DHAOX	Stable Disease	No
56	Patients with holding then bridge	RITUXIMAB - BVD - CYTARABINE - DEXAMETHASONE	Progressive Disease	No
57	Patient without bridge or holding		.	No
58	Patients with bridge only	RITUXIMAB - BENDAMUSTINE	Partial Response	No
59	Patients with bridge only	IBRUTINIB	Progressive Disease	Yes
60	Patients with holding then bridge	RITUXIMAB - BVD - GEMOX - LENALIDOMIDE	Partial Response	No
61	Patients with bridge only	IBRUTINIB	Progressive Disease	No
62	Patient without bridge or holding		.	No
63	Patients with holding then bridge	RITUXIMAB - DHAOX - IBRUTINIB	Partial Response	No
64	Patients with bridge only	RITUXIMAB - HOLOXAN-VP16	Complete Response	Yes
65	Patients with holding then bridge	RITUXIMAB - CHOP - VIM - IBRUTINIB	Progressive Disease	No
66	Patients with holding then bridge	IBRUTINIB - RITUXIMAB - MINI DHAOX - DHAOX - VENETOCLAX - BENDAMUSTINE	Progressive Disease	No
67	Patients with holding then bridge	IBRUTINIB - RITUXIMAB	Not Evaluated	No
68	Patients with holding then bridge	LENALIDOMIDE - RITUXIMAB - CHOP	Progressive Disease	No
69	Patients with holding then bridge	RITUXIMAB - CHVP - OBINUTUZUMAB - IBRUTINIB - VENETOCLAX	Partial Response	No
70	Patients with bridge only	MINI CHOP - IBRUTINIB	Progressive Disease	No
71	Patients with holding then bridge	IBRUTINIB - VENETOCLAX	Partial Response	No
72	Patients with bridge only	RITUXIMAB - CHOP - LENALIDOMIDE	Progressive Disease	No
73	Patients with bridge only	RITUXIMAB - CYTARABINE - DEXAMETHASONE	Partial Response	No
74	Patient without bridge or holding		.	No
75	Patient without bridge or holding		.	No
76	Patients with bridge only	CAELYX - CEP	Progressive Disease	No
77	Patients with holding then bridge	IBRUTINIB	Partial Response	No
78	Patients with bridge only	IBRUTINIB - VENETOCLAX	Progressive Disease	Yes
79	Patients with bridge only	VENETOCLAX	Progressive Disease	No

80	Patient without bridge or holding		.	No
81	Patients with holding then bridge	RITUXIMAB - HOLOXAN-VP16 - GVD - LENALIDOMIDE	Progressive Disease	No
82	Patients with bridge only	RITUXIMAB - LENALIDOMIDE	Progressive Disease	No
83	Patients with holding then bridge	RITUXIMAB - DHAC	Partial Response	No
84	Patient without bridge or holding		.	No
85	Patient without bridge or holding		.	No
86	Patients with bridge only	RITUXIMAB - CYTARABINE - LENALIDOMIDE	Progressive Disease	No
87	Patient without bridge or holding		.	No
88	Patients with holding then bridge	RITUXIMAB - CHOP	Progressive Disease	No
89	Patients with bridge only	OBINUTUZUMAB - CYTARABINE	Complete Response	No
90	Patients with holding then bridge	RITUXIMAB - GEMOX	Progressive Disease	No
91	Patients with holding then bridge	IBRUTINIB - VENETOCLAX	Stable Disease	No
92	Patients with holding then bridge	RITUXIMAB - IBRUTINIB - BENDAMUSTINE	Progressive Disease	No
93	Patients with holding then bridge	IBRUTINIB - VENETOCLAX	Complete Response	No
94	Patient without bridge or holding		.	No
95	Patients with bridge only	IBRUTINIB	Progressive Disease	No
96	Patients with bridge only	BENDAMUSTINE - RITUXIMAB - TEC	Progressive Disease	No
97	Patients with bridge only	RITUXIMAB - TEC	Progressive Disease	No
98	Patient without bridge or holding		.	No
99	Patients with bridge only	RITUXIMAB - CHOP - VENETOCLAX	Complete Response	No
100	Patients with holding then bridge	RITUXIMAB - CAP - BORTEZOMIB	Partial Response	No
101	Patients with bridge only	RITUXIMAB - MINI CHOP	Partial Response	No
102	Patients with holding then bridge	OBINUTUZUMAB - IBRUTINIB - VENETOCLAX	Complete Response	No
103	Patients with holding then bridge	RITUXIMAB - CHOP - IBRUTINIB - PREDNISONE - VENETOCLAX - BVD	Complete Response	No
104	Patients with bridge only	RITUXIMAB	Stable Disease	No
105	Patients with bridge only	RITUXIMAB - DHAOX	Partial Response	No
106	Patients with holding then bridge	RITUXIMAB - CHOP - VENETOCLAX	Stable Disease	No

107	Patients with bridge only	CHOP - LENALIDOMIDE - DEXAMETHASONE	Progressive Disease	No
108	Patients with holding then bridge	IBRUTINIB - CHOP	Progressive Disease	No
109	Patients with holding then bridge	VENETOCLAX	Progressive Disease	No
110	Patients with bridge only	RITUXIMAB - CYTARABINE - DEXAMETHASONE - BORTEZOMIB	Complete Response	No
111	Patients with bridge only	RITUXIMAB - CHOP	Not Evaluated	Yes
112	Patients with bridge only	RADIOTHERAPY	Progressive Disease	No
113	Patient without bridge or holding		.	No
114	Patients with holding then bridge	RITUXIMAB - CYTARABINE - ETOPOSIDE - METHOTREXATE - IBRUTINIB	Progressive Disease	No
115	Patients with bridge only	RITUXIMAB - DHA	Complete Response	No
116	Patients with bridge only	OBINUTUZUMAB - IBRUTINIB - VENETOCLAX	Partial Response	No
117	Patients with holding then bridge	RITUXIMAB - LENALIDOMIDE	Complete Response	No
118	Patients with bridge only	RITUXIMAB - CYTARABINE - MINI CHOP	Partial Response	No
119	Patients with holding then bridge	RITUXIMAB - CHOP - LENALIDOMIDE	Not Evaluated	No
120	Patients with bridge only	RITUXIMAB - CHOP	Progressive Disease	No
121	Patients with holding then bridge	IBRUTINIB - VENETOCLAX	Partial Response	No
122	Patients with bridge only	RITUXIMAB - BVD	Progressive Disease	No
123	Patient without bridge or holding		.	No
124	Patients with bridge only	RITUXIMAB - BENDAMUSTINE	Partial Response	Yes
125	Patient without bridge or holding		.	No
126	Patients with bridge only	RADIOTHERAPY	Progressive Disease	No
127	Patients with bridge only	RITUXIMAB - LENALIDOMIDE	Stable Disease	No
128	Patient without bridge or holding		.	No
129	Patient without bridge or holding		.	No
130	Patients with bridge only	IBRUTINIB	Stable Disease	No
131	Patient without bridge or holding		.	No
132	Patients with bridge only	RITUXIMAB - BVD	Stable Disease	No
133	Patients with holding then bridge	RITUXIMAB - IBRUTINIB - CHOP	Partial Response	No

134	Patient without bridge or holding		.	No
135	Patient without bridge or holding		.	No
136	Patients with holding then bridge	RITUXIMAB - DHAOX	Complete Response	No
137	Patients with holding then bridge	IBRUTINIB - VENETOCLAX	Progressive Disease	No
138	Patients with holding then bridge	RITUXIMAB - CHOP - VENETOCLAX	Partial Response	No
139	Patient without bridge or holding		.	No
140	Patients with holding then bridge	RITUXIMAB - CHOP - IBRUTINIB	Partial Response	No
141	Patients with holding then bridge	RITUXIMAB - BORTEZOMIB - CAP	Partial Response	No
142	Patients with bridge only	RITUXIMAB - HOLOXAN-VP16	Progressive Disease	No
143	Patients with holding then bridge	IBRUTINIB	Complete Response	No
144	Patients with bridge only	RITUXIMAB - DHA	Partial Response	No
145	Patients with holding then bridge	RITUXIMAB - IBRUTINIB - BVD - METHOTREXATE	Partial Response	No
146	Patients with bridge only	RITUXIMAB - HOLOXAN-VP16	Progressive Disease	Yes
147	Patients with bridge only	RADIOTHERAPY - VENETOCLAX	Progressive Disease	No
148	Patient without bridge or holding		.	No
149	Patients with bridge only	RITUXIMAB - IBRUTINIB	Progressive Disease	No
150	Patients with holding then bridge	OBINUTUZUMAB - RADIOTHERAPY - IBRUTINIB - VENETOCLAX	Progressive Disease	Yes
151	Patients with holding then bridge	IBRUTINIB - VENETOCLAX	Stable Disease	No
152	Patients with bridge only	RITUXIMAB -DHAC	Progressive Disease	No

Supplemental Table 2: Individual type of bridging strategy, response to this procedure (when applicable).


A
C max (cells/ul)
3000
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CRS
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AUC (AU)
20000
15000
10000
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CRS
No CRS
B
C max (cells/ul)
3000
2000
1000
0
*
ICANS
No ICANS
AUC (AU)
20000
15000
10000
5000
0
*
ICANS
No ICANS
PFS
OS
C
Probability of Survival
100
50
0
0
10
20
30
Time (months)
High CAR-T levels
Low CAR-T levels
D
Probability of Survival
100
50
0
0
10
20
30
Time (months)
High CAR-T levels
Low CAR-T levels

Supplemental Figure 1: CAR-T cell kinetics impact on efficacy and safety, statistical significance ($p<0.05$) was calculated using an unpaired t-test with Welch's correction as it could not be assumed that standard deviations were equal. A/ Maximal expansion post infusion (C_{MAX}) and area under the curve (AUC, representing the exposure from day 0 to day 28) are shown for patients who developed a Cytokine Release Syndrome (CRS), and for those who did not. * = $p \leq 0.05$ and ** = $p \leq 0.01$ B/ C_{MAX} and AUC for patients who developed an immune effector cell–associated neurotoxicity syndrome (ICANS), and for those who did not. C/ PFS for patients who received brexu-cel and for whom cellular kinetics parameters were evaluated. High and low CAR-T cell levels are defined with the ad-hoc threshold of 60 cells/µl and/or 500 AU (arbitrary unit) for C_{MAX} and AUC respectively. These thresholds were chosen because they correctly separate patient profiles with low and high expansions. They are intended to serve as a proof of concept in this real-life setting. D/ OS in the same population.