Supplementary File

Adverse Event	Patient Distribution (%)	Source	Resource consumption	Source	Average duration (days)	Source
CRS: Grade I	42.00	(22)	Therapy: hydration or tocilizumab[A] Diagnostic resources for monitoring [B]	(19)	9.10	(10)
CRS: Grade II						
CRS: Grade III-IV	2.00		ICU			
Neutropenia	27.00		Ward hospitalization	DRG: 574 (coded from ICD-9 288.03)	10.00	(21)
Hypophosphatemia	17.00			DRG: 299 (coded from ICD-9 275.9)	5.50	
Hyperglycemia	8.00			DRG: 297 (coded from ICD-9 790.29)	6.10	
Anemia	8.00			DRG: 395 (coded from ICD-9 285.22)	8.60	

Table S 1 – Adverse Events, Mosunetuzumab: AE incidence, healthcare resources needed and specific average duration per event

Notes: A, 92.00% and 8.00% of patients receive hydration and tocilizumab, respectively *(22)*, these resources are not applied to hospitalized patients (CRS grade III+), as the cost of ICU already covers these expenses *(20)*; B, frequencies of use are based on Neelapu et al., 2018 *(19)*; CRS, Cytokine Release Syndrome.

Drug	Pack size (mg)	Price (€)	Discount	Source	Notes
Hydration	-	0	-	-	Assumption = 0
Tocilizumab	200	320.80	-	(18)	ROACTEMRA, Roche S.p.A. 20 mg/ml; EV 1 fl. 10 ml.
CRS Diagnostics Costs	271.07			(19,21)	
ICU	1,256.81			(20)	Adjusted, 2022.
Ward hospitalization	911.78			(35)	Adjusted, 2022.

Table S 2 – Adverse Events Costs, Mosunetuzumab

Tisagencleucel Therapy Phases	Patient Distribution (%)	Source
Apheresis	100	(13)
Bridging Therapy	44.90	
Rituximab	*22.00*	
Gemcitabine	*10.00*	
Oxaliplatin	*7.00*	

Etoposide	*6.00*	
Ciclophosphamide	*5.00*	
Vincristine	*5.00*	
Conditioning	100	
Infusion	99.00	
Monitoring	99.00	

Table S 3 – Patient Distribution across Phases, Tisagenlecleucel

Phase	Activity	Personnel	Time spent (minutes)	Source	Notes
Drug preparation PRE-INFUSION	*Drug preparation*	Pharmacist	3.40	(33)	DPA tasks[A]
Drug administration PRE-INFUSION	*Patient preparation*	CSN	11.20		Bringing Rituximab Bag to Patient Bed/Chair + Install Venous Catheter/Line Flushing + Pre-medication Administration
	Consumables preparation		15.10		DPA tasks/Patient Monitoring During Infusion.
	Non-specified	Patient	26.30	Sum of the time spent by the CSN for preparing the patient and the instruments/consumable resources for the infusion.	
		Caregiver	26.30		
Drug administration INFUSION	*Drug administration*	CSN	2.12% of the infusion time	(33)	Infusion Initiation Administration + Patient Monitoring During Infusion[B]
		Patient	Infusion time	SPC	Infusion time as reported in the SPC of each drug (i.e. rituximab, gemcitabine, …) of bridging therapy.
		Caregiver			
Drug administration POST-INFUSION	*Post-infusion activities*	CSN	3.40	(33)	DPA tasks[A]
		Patient	3.40		
		Caregiver	3.40		
	Clearing and tidying the operational site	CSN	6.50		Disconnect Infusion/Flush Line/Dispose of materials
	Active monitoring	CSN	5.70		Patient Monitoring Post-Infusion
		Patient	5.70		
		Caregiver	5.70		

Table S 4 –Resource Use Synopsys (Bridging Therapy), Tisagenlecleucel

Notes: A, the drug preparation time (pharmacist) was assumed to be half of the time defined as "DPA tasks" in de Cock et al., 2016. Since there was no precise indication on the distribution of such DPA tasks in literature, the other half of the "DPA tasks" time was applied to post-infusion operations (33). B, is the proportion of time needed to perform "Infusion Initiation + Patient Monitoring During Infusion" for rituximab, which corresponds to 10.8 minutes over the total infusion time of the drug as per its Summary of Product Characteristics. It represents 2.12% of the total infusion time, intended as active observation time during the infusion. This percentage was used to proportionally adjust the active observation times during infusions of other IV-administered drugs; SPC: Summary of Product Characteristics.

Resource	Tariff (€)	Source	Frequency, first 100 days post-infusion	Frequency, rest of the year	Source
Complete blood count (CBC)	5.78	Tariff 91.49.2 (Venous Blood Collection) + 90.62.2 (Complete Blood Count)	10	9	(15,21)
Biochemical analysis	37.23	Tariff 90.40.4 (Sodium) + 90.37.4 (Potassium) + 90.13.3 (Chloride) + 90.24.5 (Phosphorus) + 90.05.1 (Albumin) + 90.44.1 (Urea) + 90.72.3 (C-Reactive Protein) + 90.10.1 (Beta2 Microglobulin) + 90.69.2 (Immunofixation)	10	9	
Protein electrophoresis	4.23	Tariff 90.38.4 (Protein Electrophoresis)	3	9	
Immunoglobulins	14.97	Tariff 90.69.4 (Immunoglobulins IgA, IgG, or IgM)	3	9	
Urine test	18.33	Tariff 90.39.1 (Urinary Protein Electrophoresis) + 91.39.4 (Cytological Examination of Urine for Neoplastic Cells)	3	9	
Renal function tests	2.73	Tariff 90.16.3 (Creatinine) + 90.16.4 (Creatinine Clearance)	3	9	
Monitoring of arterial saturation	9.30	Tariff 89.65.5 (Non-invasive Monitoring of	10	9	

		Arterial Saturation)			
Calcium levels	1.13	Tariff 90.11.4 (Total Calcium)	10	9	
Biopsy	48.86	Tariff 41.31 (Bone Marrow Biopsy)	1	0	

Table S 5 – Resource Consumption for Post-Infusion Monitoring, Tisagenlecleucel

Adverse Event	Patient Distribution (%)	Source	Resource consumption	Source	Average duration (days)	Source
CRS: Grade I	27.80	(24)	Hydration	(25)	8.30	(24)
CRS: Grade II	20.60		Tocilizumab			
CRS: Grade III-IV	0[A]	(13)	ICU[A]			
CRS: All Grades	48.40	(24)	Diagnostic resources for monitoring			
ICANS: Grade I	3.10[B]		Lorazepam[B]		20.20[C]	(25)
			Aloperidol[B]			
ICANS: Grade II			Dexamethasone[B]			
			Methylprednisolone[B]			
ICANS: Grade III-IV	1.00		ICU			
Neutropenia	32.00		Ward hospitalization	DRG: 574 (coded from ICD-9 288.03)	10.00	(21)
Febrile Neutropenia	10.30			DRG: 574 (coded from ICD-9 288.03)	10.00	
Anemia	13.40			DRG: 395 (coded from ICD-9 285.22)	8.60	
Reduced White Blood Cell Count	12.40			DRG: 399 (coded from ICD-9 288.59)	6.20	
Thrombocytopenia	9.30			DRG: 397 (coded from ICD-9 287.5)	7.60	
Reduced Platelet Count	3.10			DRG: 397 (coded from ICD-9 287.1)	7.60	

Reduced Neutrophil Count	15.50			DRG: 574 (coded from ICD-9 288.03)	10.00	
Leucopenia	4.10			DRG: 574 (coded from ICD-9 288.03)	10.00	
Reduced White Blood Cell Count	5.20			DRG: 574 (coded from ICD-9 288.03)	10.00	
Infections	5.20			DRG: 423 (coded from ICD-9 418.9)	10.70	
Neurological Events	3.10			DRG: 019 (coded from ICD-9 357.89)	7.60	
Headache	1.00			DRG: 564 (coded from ICD-9 346.20)	5.20	
Gastrointestinal Events	4.10			DRG: 183 (coded from ICD-9 535.40)	5.50	
Diarrhea	1.00			DRG: 183 (coded from ICD-9 535.40)	5.50	
Nausea	2.10			DRG: 183 (coded from ICD-9 535.40)	5.50	
Abdominal Pain	1.00			DRG: 183 (coded from ICD-9 535.40)	5.50	

General Symptoms	4.10			DRG: 464 (coded from ICD-9 780.99)	5.30	
Fatigue	3.10			DRG: 464 (coded from ICD-9 780.79)	5.30	
Fever	1.00			DRG: 420 (coded from ICD-9 780.6)	6.30	
Metabolic or Nutrition Events	4.10			DRG: 297 (coded from ICD-9 783.9)	6.10	
Hypophosphatemia	3.10			DRG: 299 (coded from ICD-9 275.3)	5.50	
Musculoskeletal or Connective Tissue Events	1.00			DRG: 256 (coded from ICD-9 756.89)	4.70	
Vascular Events	1.00			DRG: 145 (coded from ICD-9 999.2)	6.00	

Table S 6 – Adverse Events, Tisagenlecleucel

Notes: A, even though the number of patients that experienced CRS Grade III+ was N=0, but 8.5% of patients was reported as hospitalized in ICU *(24)*. This percentage of patients was used to adjust CRS-related costs, scaling the % of patients with CRS Grade I-II; B, it was assumed an even distribution of patients with CRES grade I-II, thus, the 25% of patients receive lorazepam, aloperidol, dexamethasone or methylprednisolone; C, average duration, calculated with the exponential function of the median (14 days) *(25)*; CRS, Cytokine Release Syndrome; ICANS, Immune Effector Cell-Associated Neurotoxicity Syndrome.

Drug	**Package size (mg)**	**Price (€)**	**Discount (%)**	**Source**	**Notes**
Hydration	-	0	-	-	Assumption = 0
Tocilizumab	200	320.80	-	(18)	ROACTEMRA, Roche S.p.A. 20 mg/ml; EV 1 fl. 10 ml.
CRS Diagnostics Costs	271.07			(19,21)	Calc.

ICANS Diagnostics Costs	491.06			(19,21)	Calc.
Lorazepam	-	0	-	-	Assumption = 0
Haloperidol	-	0	-	-	Assumption = 0
Dexamethasone	24	2.90	-	(18)	DECADRON, Istituto Biochimico Nazionale Savio S.r.l. 4 mg/ml injectable solution 6 vials 1 ml.
Methylprednisolone	1000	155.03	-	(18)	METILPREDNISOLONE, Hikma Pharmaceutica S.A. 1000 mg, 10 vials.
ICU	1,256.81			(20)	Adjusted, 2022.
Ward hospitalization	911.78			(35)	Adjusted, 2022.

Table S 7 – Adverse Events Costs, Tisagencleucel

Category	Cost (€/h)	Source
Pharmacist	39.66	(29,31)
CSN	18.31	
Patient	6.30	(29,30)
Caregiver (informal/formal)	3.54[A]	

Table S 8 – Cost per Time Unit, HCWs, Patient and Caregiver

Notes: *; HCW costs were adjusted for the estimated indirect overhead cost, which is assumed to be 25%; A, unit cost per second of the caregiver was adjusted by its distribution of use (80,00%) in the Italian population (36). It is assumed that 91,00% of patients is accompanied by a family member; CNS, Clinical Nurse Specialist; HCW, Health Care Worker.

Category	Unit cost (€)	Source
Pre-cleaning of LAF	0.24	(34)
Post-cleaning of LAF	0.24	
IV preparation consumables	10.54	
IV set-up consumables	3.42	
IV administration consumables	10.75	

Table S 9 – Non-Drug Consumables Costs

Notes: *, overall structure costs were adjusted for the estimated indirect overhead cost, which is assumed to be 25% *(34)*; LAF: laminal air flow, filtered hood.

Transport Category	Use distribution (%)	Source	Cost (€/h)	Source	Average commuting time (minutes)	Average commuting cost (€/minute)
Public transport	11.10	Data on file	7.20[A]*	Assumption	30.00	0.21
Taxi	2.00		56.50[B]	(43)		
Private car	86.90		12.50[B]	(37)		

Table S 10 – Commuting Costs

Notes: A, the estimated cost of public transportation was based on the average price of a bus ticket, which is €2.00; B, the average cost of a taxi or private car was calculated based on the average cost per kilometre, assuming an average car speed of 25 kilometres per hour; *, public transportation costs are adjusted by 80% for formal caregivers' availability (36).

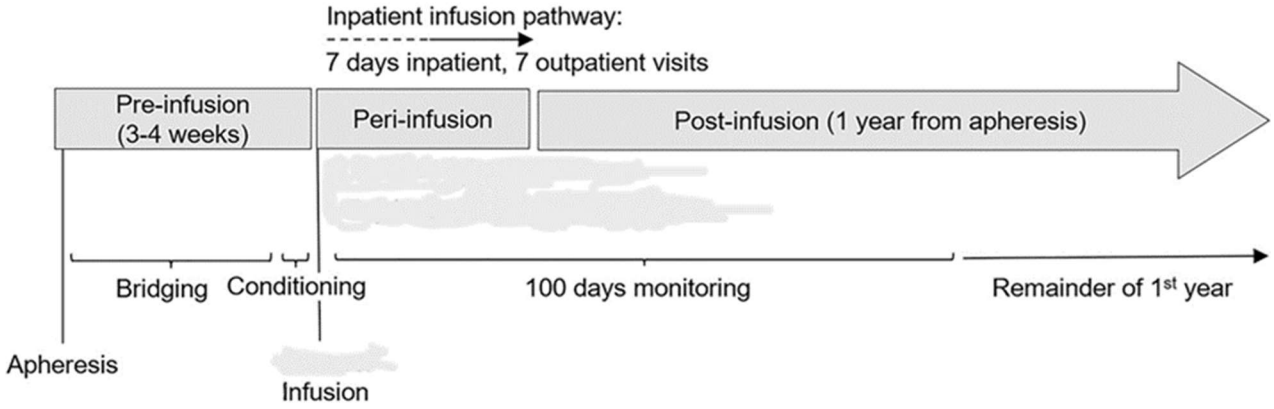
Accommodation Category	Use distribution (%)	Source	Cost (€/day)	Source	Average relocation period (days)	Source
Rent	85.00	Assumption	19.14*	(44)	130.00	(15)
Hotel room	15.00		154.24*	Assumption		

Transport Category	Use distribution (%)	Source	Cost (€/km)	Source	Average distance (km)	Source
Private car	100A	Assumption	0.50	(37)	214.00	Data on file
Flight + Taxi (airport)	100B		0.27 + 65.50[C]*	(38) (39–42)	523.00	

Table S 11 – Relocation Costs

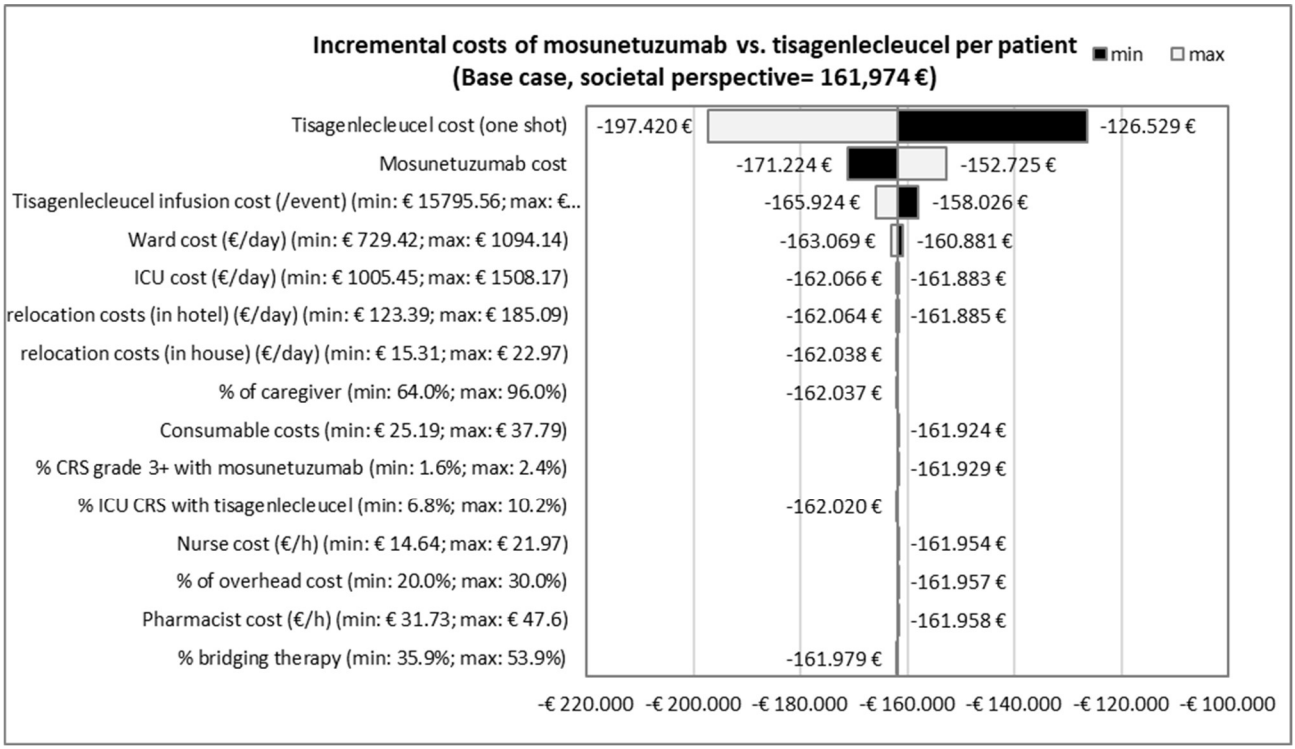
Note: A, mid-case scenario; B, worst case scenario; C, the cost for the usage of an airport transfer (€65.50) is added to the average air transportation cost per kilometre (€0.15) (37–41); * adjusted by 80% for formal caregivers availability (36).

Figure S 1 – CAR-T therapy outline, patient pathway



Notes: Elaborated from Jagannath et al. (15)

Figure S 2 – Univariate/One-way Sensitivity Analysis



Notes: Tornado Diagram, where the input variables in the vertical axis were varied by ±20%. The horizontal central axis presents the base-case cost difference amongst mosunetuzumab and tisagenlecleucel's patient pathways (-€ 161,974).