Fitness-for-Use Assessment across Four Data Sources for Real-World Safety and Effectiveness Studies of CAR-T cell therapies

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Study Ongoing

Administrative details

EU PAS number

EUPAS1000000955

Study ID

1000000955

DARWIN EU® study

No

Study countries

France

United Kingdom

United States

Study description

Chimeric antigen receptor T-cell (CAR-T) therapy has emerged as an important cancer treatment, with six treatments approved by the EMA since 2018. Non-interventional studies play an important role for supporting regulatory decisions especially when randomised controlled trials are unfeasible or unethical, which was often the case in the CAR-T cell area whose effectiveness and safety evidence mostly rely on single arm trials.

This assessment evaluates the fitness-for-use of the National Cancer Registration and Analysis Service (NCRAS) & Hospital Episode Statistics (HES), US Flatiron Health Research Database, Système National des Données de Santé (SNDS [French national health system main database]), and Dispositif d'Enregistrement et Suivi des patients traités par CAR-T cells (DESCAR T) for conducting research into CAR-T cell therapy. The study assesses whether each data source contains the necessary data elements, completeness, structure, and quality to support future regulatory relevant non interventional studies on CAR T cell therapies. The assessment involved the simulation of the following 3 theoretical scenarios.

1. To estimate the incidence rates of five safety outcomes (neurotoxicity, CRS, neutropenia, infections, second primary malignancies) among patients treated with CAR-T cell therapy
2. To develop an external control arm for CARTITUDE-1, a single-arm phase 1b/2 trial (NCT03548207) to assess the effectiveness of cilta-cel among adult patients with RRMM
3. To emulate the CARTITUDE-4 (NCT04181827) clinical trial to compare the effectiveness of cilta-cel to standard of care among adult patients with lenalidomide-refractory MM who had received 1-3 prior LOT

A retrospective, observational cohort design was used as a template for each theoretical scenario, to simulate how such studies would be implemented using

the available data. Upon creation of the study cohorts, data quality metrics were assessed and the fitness-for-use assessment was undertaken.

Study status

Ongoing

Research institutions and networks

Institutions

Evidence and Access/Analytica Laser, Certara

France

United Kingdom (Northern Ireland)

First published: 24/05/2021

Last updated: 06/03/2024

Institution **Non-Pharmaceutical company** **ENCePP partner**

1. Dispositif d'Enregistrement et Suivi des patients traités par CAR-T cells (DESCAR-T)

2. Flatiron Health

Contact details

Study institution contact

Nadia Quignot nadia.quignot@certara.com

Study contact

nadia.quignot@certara.com

Primary lead investigator

Artak Khachatryan 0000-0003-3888-2347

Primary lead investigator

ORCID number:

0000-0003-3888-2347

Study timelines

Date when funding contract was signed

Actual: 08/12/2024

Study start date

Actual: 27/11/2025

Data analysis start date

Actual: 27/11/2025

Date of final study report

Planned: 15/07/2026

Sources of funding

- EMA

Study protocol

20250805_FWC_EMA_2020_46_TDA_L5.07_SC01 protocol objective 3_v1.0.pdf
(1.43 MB)

Regulatory

Was the study required by a regulatory body?

No

Is the study required by a Risk Management Plan (RMP)?

Not applicable

Methodological aspects

Study type

Study type list

Study topic:

Human medicinal product

Study type:

Not applicable

Scope of the study:

Feasibility analysis

Data collection methods:

Secondary use of data

Study design:

This is a fitness-for-use assessment to test the feasibility of implementing the three theoretical scenarios in NCRAS & HES, US Flatiron Health Research Database, SNDS and DESCAR-T data sources. A retrospective, observational cohort design was used as a template for each theoretical scenario.

Main study objective:

To evaluate the fitness-for-purpose of NCRAS & HES, US Flatiron Health Research Database and Dispositif d'Enregistrement et Suivi des patients traités par CAR-T cells (DESCAR-T) data sources to address the following regulatory-relevant theoretical scenarios:

1. To estimate the incidence rates of five safety outcomes (neurotoxicity, CRS, neutropenia, infections, second primary malignancies) among patients treated with CAR-T cell therapy
2. To develop an external control arm for CARTITUDE-1, a single-arm phase 1b/2 trial (NCT03548207) to assess the effectiveness of cilta-cel among adult patients with relapsed-refractory MM
3. To emulate the CARTITUDE-4 (NCT04181827) clinical trial to compare the effectiveness of cilta-cel to standard of care among adult patients with lenalidomide-refractory MM who had received 1-3 prior LOT (CARTITUDE-4 clinical trial emulation).

Study drug and medical condition

Medicinal product name

ABECMA

BREYANZI

CARVYKTI

KYMRIAH

TECARTUS

YESCARTA

Anatomical Therapeutic Chemical (ATC) code

(L01XL07) idecabtagene vicleucel

idecabtagene vicleucel

(L01XL08) lisocabtagene maraleucel

lisocabtagene maraleucel

(L01XL05) ciltacabtagene autoleucel

ciltacabtagene autoleucel

(L01XL04) tisagenlecleucel

tisagenlecleucel

(L01XL06) brexucabtagene autoleucel

brexucabtagene autoleucel

(L01XL03) axicabtagene ciloleucel

axicabtagene ciloleucel

Population studied

Short description of the study population

For each theoretical scenario, a series of inclusion and exclusion criteria were specified and the extent to which these eligibility criteria might be implemented in each data source was evaluated as part of the fitness-for-purpose

assessment. The inclusion and exclusion criteria have been formulated to align with the CARTITUDE-1 and CARTITUDE-4 trials, where applicable. A brief illustrative overview of the eligibility criteria for each theoretical scenario is provided below.

Theoretical Scenario 1

The study population included patients who received at least one dose of a CAR-T cell therapy during the indexing period (23 August 2018 to 31 December 2024) and who had 12 months data source history. Patients were excluded if they had evidence of any of the safety outcomes of interest or were enroled in a clinical trial in the 12 months prior to index date.

Theoretical Scenario 2

The study population included adults with multiple myeloma (MM), with an Eastern Cooperative Oncology Group (ECOG) performance status score of 0 or 1, who received 3 or more previous LOT or were double refractory to a proteasome inhibitor (PI) and an immunomodulatory drug (IMiD), and had received a PI, IMiD, and an anti-CD38 antibody. Patients who met the above criteria and initiated a standard of care MM treatment during the indexing period (01 January 2018 to 31 December 2023) were included. Patients were excluded if they received CAR-T cell therapy or an agent targeting B-cell maturation antigen prior to index date.

Theoretical Scenario 3

The study population was adults with MM, with an ECOG performance status score of 0 or 1, who were lenalidomide-refractory and who had received one to three LOT including a PI or an IMiD and who initiated treatment with cilta-cel (treatment arm) or pomalidomide, bortezomib and dexamethasone (PVd) or daratumumab, pomalidomide and dexamethasone (comparison arm) during the

indexing period (28 February 2022 to 31 December 2023). Patients were excluded if they received CAR-T cell therapy or an agent targeting BCMA prior to index date.

Age groups

- **Paediatric Population (< 18 years)**
  - Neonate
    - Preterm newborn infants (0 – 27 days)
    - Term newborn infants (0 – 27 days)
  - Infants and toddlers (28 days – 23 months)
  - Children (2 to < 12 years)
  - Adolescents (12 to < 18 years)
- **Adult and elderly population (≥18 years)**
  - Adults (18 to < 65 years)
    - Adults (18 to < 46 years)
    - Adults (46 to < 65 years)
  - Elderly (≥ 65 years)
    - Adults (65 to < 75 years)
    - Adults (75 to < 85 years)
    - Adults (85 years and over)

Study design details

Setting

The study is conducted within four real-world data sources, NCRAS & HES in England, US Flatiron Health Research Database in the United States, and SNDS and DESCAR-T in France, each capturing oncology patients from 2018 onwards,

when CAR-T therapies became available.

Interventions

This project does not involve any patient level intervention and is neither a clinical trial nor a non interventional study; rather, it is a non interventional methodological assessment conducted solely to evaluate the fitness for purpose of selected real world data sources for potential future regulatory studies on CAR T cell therapies.

Outcomes

The study assessed whether each data source could accurately capture key safety (e.g., cytokine release syndrome, secondary malignancies) and effectiveness (e.g., progression, response, overall survival) endpoints.

Data analysis plan

Aligning with the approach recommended in the European Medicine Agency (EMA) “Data Quality Framework for European Union (EU) medicines: Application to Real-World data”, a series of research question-specific metrics for each dimension of data quality (extensiveness, coherence, reliability, relevance and timeliness) were evaluated as part of the fitness-for-purpose assessment of each data source for each theoretical scenario.

Data management

ENCePP Seal

The use of the ENCePP Seal has been discontinued since February 2025. The ENCePP Seal fields are retained in the display mode for transparency

but are no longer maintained.

Data sources

Data source(s)

Système National des Données de Santé (French national health system main database)

Cancer Analysis System

Data source(s), other

1. US Flatiron Health Research Database

2. Dispositif d’Enregistrement et Suivi des patients traités par CAR-T cells (DESCAR-T)

Data sources (types)

Administrative healthcare records (e.g., claims)

Cancer registry

Disease registry

Drug registry

Electronic healthcare records (EHR)

Use of a Common Data Model (CDM)

CDM mapping

No

Data quality specifications

Check conformance

Yes

Check completeness

Yes

Check stability

No

Check logical consistency

Yes

Data characterisation

Data characterisation conducted

Yes

Data characterisation moment

after data extraction

after creation of study variables

Data characterisation details

Data characterisation involved assessing whether NCRAS & HES, US Flatiron Health Research Database, SNDS and DESCAR T contained the necessary variables to support the three theoretical CAR T study scenarios. Following data extraction, key fields such as exposures, outcomes, covariates and dates were examined for completeness, precision and availability. Logical consistency checks were performed to identify implausible or duplicate records and verify alignment between related data elements. Additional checks were conducted

after constructing study specific variables to confirm the feasibility of implementing inclusion and exclusion criteria for each scenario. The process focused on evaluating data suitability rather than generating any clinical outcomes or estimates.

Data characterisation details

20250805_FWC_EMA_2020_46_TDA_L5.07_SC01 protocol objective 3_v1.0.pdf

English (1.43 MB - PDF)

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Procedures

Procedure of data extraction

20250805_FWC_EMA_2020_46_TDA_L5.07_SC01 protocol objective 3_v1.0.pdf

English (1.43 MB - PDF)

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Procedure of results generation

20250805_FWC_EMA_2020_46_TDA_L5.07_SC01 protocol objective 3_v1.0.pdf

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