Key resources table

REAGENT or RESOURCE	SOURCE	IDENTIFIER
Chemicals, peptides, and recombinant proteins		
Lysing Buffer	BD	555899
Gibico PBS, pH 7.2	Thermofisher	20012027
Gibico PBS, pH 7.2	Thermofisher	20012043
Formic Acid	Fisher Chemical	A117-50
Acetonitrile	Fisher Chemical	A955-4
Water	Fisher Chemical	W6-4
Methanol	Fisher Chemical	A456-4
Isopropanol (IPA)	Fisher Chemical	A464-4
Ammonium bicarbonate	Merck	5.33E+09
Metabolism Compound Library	Selleck	L3700
Dimethyl sulfoxide	MCE	HY-Y0320
Penicillin & Streptomycin solution (100×)	BasalMedia	S110JV
Phosphate buffered saline	BasalMedia	B320KJ
Critical Commercial Assays		
Software and Algorithms		
metID	https://github.com/jaspershen/metID	
metDNA	http://metdna.zhulab.cn/	
SERRF	https://github.com/linliliaabbcc1024/SERRFweb	
dplyr v1.1.4	https://cran.r-project.org/web/packages/dpl	

	yr/index.html	
MNet v0.1.0	https://github.com/tuantuangui/MNet	
ggplot2 v3.4.4	https://cran.r-project.org/web/packages/ggplot2/index.html	
ggcor v0.9.8.1	https://github.com/mj163163/ggcor-1	
tidyverse v2.0.0	https://cran.r-project.org/web/packages/tidyverse/index.html	
ggpubr v0.6.0	https://cran.r-project.org/web/packages/ggpubr/index.html	
ggsignif v0.6.4	https://cran.r-project.org/web/packages/ggsignif/index.html	
rstatix v0.7.2	https://cran.r-project.org/web/packages/rstatix/index.html	
matrixStats v1.2.0	https://cran.r-project.org/web/packages/matrixStats/index.html	
networkD3 v0.4	https://cran.r-project.org/web/packages/networkD3/index.html	
RColorBrewer v1.1-3	https://cran.r-project.org/web/packages/RColorBrewer/index.html	
webshot v0.5.5	https://cran.r-project.org/web/packages/webshot/index.html	
ComplexHeatmap v2.18.0	https://github.com/jokergoo/ComplexHeatmap	
devtools v2.4.5	https://cran.r-project.org/web/packages/devtools/index.html	
circlize v0.4.15	https://cran.r-project.org/web/packages/circlize/index.html	
Mfuzz v2.62.0	https://www.bioconductor.org/packages/release/bioc/html/Mfuzz.html	
factoextra v1.0.7	https://cran.r-project.org/web/packages/factoextra/index.html	
cluster v2.1.6	https://cran.r-project.org/web/packages/cluster/index.html	
stringr v1.5.1	https://cran.r-project.org/web/packages/stringr/index.html	
supraHex v1.40.0	https://bioconductor.org/packages/release/bioc/html/supraHex.html	Fang and Gough, PMID:24309102
reshape2 v1.4.4	https://cran.r-project.org/web/packages/reshape2/index.html	

limma v3.58.1	https://bioconductor.org/packages/release/bioc/html/limma.html
survminer v0.4.9	https://cran.r-project.org/web/packages/survminer/index.html
survival v3.5-7	https://cran.r-project.org/web/packages/survival/index.html
igraph v1.6.0	https://cran.r-project.org/web/packages/igraph/index.html
glmnet v4.1-8	https://cran.r-project.org/web/packages/glmnet/index.html
broom v1.0.5	https://cran.r-project.org/web/packages/broom/index.html
R Statistical Software version v4.3.2	https://www.r-project.org/

2

Inclusion Criteria

Each potential subject must satisfy all of the following criteria to be enrolled in the study:

1. Subjects 18-75 years of age.

2. Documented initial diagnosis of multiple myeloma according to IMWG diagnostic criteria.

3. Measurable disease at Screening as defined by any of the following:

Serum monoclonal paraprotein (M-protein) level ≥1.0 g/dL or urine M-protein level ≥200 mg/24 hours; or

Light chain multiple myeloma without measurable disease in the serum or the urine: Serum immunoglobulin free light chain ≥10 mg/dL and abnormal serum immunoglobulin kappa/lambda free light chain ratio.

4. Received at least 3 prior lines of treatment for multiple myeloma.

Underwent at least 1 complete cycle of treatment for each line, unless PD (Progressive Disease) was documented by IMWG criteria as the best response to the regimen.

5. Received a PI (Proteasome Inhibitor) and/or an IMiD (Immunomodulatory Drug).

6. Documented disease progression during, or within 12 months of, most recent anti-myeloma therapy.

7. ECOG Performance Status grade of 0-2.

8. Clinical laboratory values meeting the following criteria during the Screening Phase:

Hemoglobin ≥6.0 g/dL (without prior red blood cell [RBC] transfusion within 7 days before the laboratory test; recombinant human erythropoietin use is permitted).

Platelets ≥50×10^9/L (must be without transfusion support in the 7 days prior to the laboratory test).

Absolute Neutrophil Count (ANC) ≥1.0×10^9/L (prior growth factor support is permitted).

AST and ALT ≤2.5×upper limit of normal (ULN).

Creatinine clearance ≥30 mL/min/1.73 m^2 based upon Modified Diet in Renal Disease formula calculation or a 24-hour urine collection.

Total bilirubin ≤1.5×ULN; except in subjects with congenital bilirubinemia, such as

Gilbert syndrome (in which case direct bilirubin ≤1.5×ULN is required).

Corrected serum calcium ≤14.0 mg/dL (≤3.5 mmol/L) or free ionized calcium ≤6.5 mg/dL (≤1.6 mmol/L).

9. Women of childbearing potential must have a negative pregnancy test at screening and prior to the first dose of cyclophosphamide with or without fludarabine using a highly sensitive serum pregnancy test (β human chorionic gonadotropin).

10. Women of childbearing potential must agree to practice a highly effective method of contraception (failure rate of <1% per year when used consistently and correctly) and agree to remain on a highly effective method of contraception from the time of signing the informed consent form (ICF) until at least 100 days after receiving an LCAR-B38M CAR-T cell infusion.

11. Subject must sign an ICF indicating that he or she understands the purpose of and procedures required for the study and is willing to participate in the study. Consent is to be obtained prior to the initiation of any study-related tests or procedures that are not part of standard-of-care for the subject's disease.

12. Willing and able to adhere to the prohibitions and restrictions specified in this protocol.

Exclusion Criteria

Any potential subject who meets any of the following criteria will be excluded from participating in the study:

1. The following cardiac conditions:

New York Heart Association (NYHA) Class III or IV congestive heart failure.

Myocardial infarction or coronary artery bypass graft (CABG) ≤6 months prior to enrollment.

History of clinically significant ventricular arrhythmia or unexplained syncope, not believed to be vasovagal in nature or due to dehydration.

History of severe non-ischemic cardiomyopathy.

Impaired cardiac function (LVEF <45%) as assessed by echocardiogram or multiple-gated acquisition (MUGA) scan (performed ≤8 weeks prior to apheresis).

2. Systemic corticosteroid therapy of greater than 5 mg/day of prednisone (or equivalent dose of another corticosteroid) within 2 weeks prior to apheresis.

3. Received either of the following:

An allogeneic stem cell transplant for multiple myeloma.

An autologous stem cell transplant ≤12 weeks before apheresis.

4. Seropositive for human immunodeficiency virus (HIV).

5. Active or chronic Hepatitis B infection as defined according to the American Society of Clinical Oncology (ASCO) guidelines. In the event the infection status is unclear, quantitative levels are necessary to determine the infection status.

6. Hepatitis C (anti-hepatitis C virus [HCV] antibody positive or HCV-RNA quantitation positive) or known to have a history of hepatitis C.

7. Serious underlying medical condition, such as:

Evidence of serious active viral, bacterial, or uncontrolled systemic fungal infection.

Active autoimmune disease or a history of autoimmune disease within 3 years.

Overt clinical evidence of dementia or altered mental status.

8. Known life-threatening allergies, hypersensitivity, or intolerance to LCAR-B38M CAR-T cells or its excipients, including DMSO (refer to Investigator's Brochure).

9. Pregnant or breast-feeding, or planning to become pregnant while enrolled in this study or within 100 days after receiving study treatment.

10. Any uncontrolled diseases, other than multiple myeloma, that may lead to premature death.

11. Other cases excluded by the Investigators.