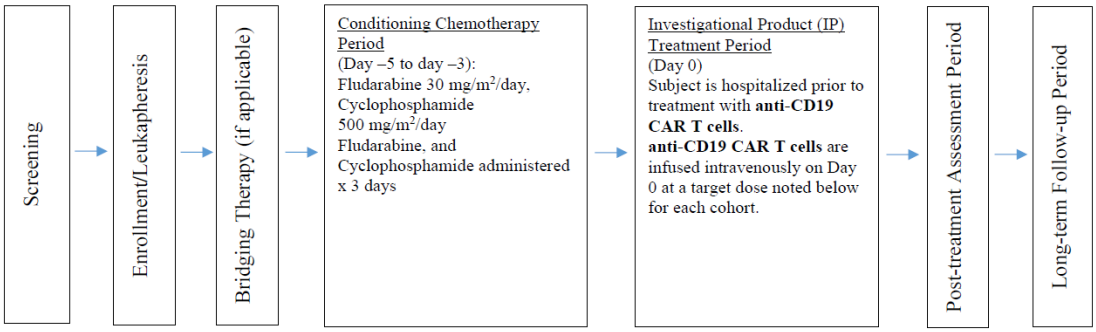
SAMENVATTING ZUMA-2

TITEL A Phase 2 Multicenter Study Evaluating the Efficacy of KTE-C19 in Subjects with Relapsed/Refractory Mantle Cell Lymphoma (ZUMA-2)

INDICATIE The treatment of adult subjects with relapsed/refractory mantle cell lymphoma (r/r MCL)

SCHEMA



Study KTE-C19-**102** is a Phase 2, multicenter, open-label study evaluating the efficacy of KTE-C19 in subjects with r/r MCL.

Up to approximately 130 subjects with r/r MCL will be enrolled into 2 separate cohorts designated as Cohort 1 and Cohort 2.

- Cohort 1 will enroll and treat **90** subjects at a target dose of 2 x 10^6 anti-CD19 CAR T cells/kg, **including 10 axicabtagene ciloleucel subjects and approximately 80 KTE-C19 subjects**.
- Cohort 2 will enroll and treat **up to** approximately 40 **KTE-C19** subjects at a target dose of 0.5 x 10^6 anti-CD19 CAR T cells/kg.

INCLUSIE CRITERIA

1. Pathologically confirmed MCL, with documentation of either overexpression of cyclin D1 or presence of t(11;14)

2. Up to 5 prior regimens for MCL. Prior therapy must have included:

   - Anthracycline or bendamustine-containing chemotherapy, and
   - Anti-CD20 monoclonal antibody therapy, and
   - Ibrutinib or acalabrutinib

3. Relapsed or refractory disease, defined by the following:

   - Disease progression after last regimen, or

- Refractory disease is defined failure to achieve a partial response (PR) or CR to the last regimen

4. At least 1 measurable lesion. Lesions that have been previously irradiated will be considered measurable only if progression has been documented following completion of radiation therapy

    - If the only measurable disease is lymph node disease, at least 1 lymph node should be ≥ 2 cm

5. Magnetic resonance imaging (MRI) of the brain showing no evidence of central nervous system (CNS) lymphoma

6. At least 2 weeks or 5 half-lives, whichever is shorter, must have elapsed since any prior systemic therapy or **BTKi (ibrutinib or acalabrutinib)** at the time the subject is planned for leukapheresis, except for systemic inhibitory/stimulatory immune checkpoint therapy. At least 3 half-lives must have elapsed from any prior systemic inhibitory/stimulatory immune checkpoint molecule therapy at the time the subject is planned for leukapheresis (eg, ipilimumab, nivolumab, pembrolizumab, atezolizumab, OX40 agonists, 4-1BB agonists).

7. Toxicities due to prior therapy must be stable and recovered to ≤ Grade 1 (except for clinically non-significant toxicities such as alopecia)

8. Age 18 years or older

9. Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1

10. Absolute neutrophil count (ANC) ≥ 1 000/uL

11. Platelet count ≥ 75 000/uL

12. Absolute lymphocyte count ≥ 100/uL

13. Adequate renal, hepatic, pulmonary, and cardiac function defined as: – Creatinine clearance (as estimated by Cockcroft Gault) ≥ 60 cc/min

    - Serum alanine aminotransferase/aspartate aminotransferase ≤ 2.5 upper limit of normal (ULN)

    - Total bilirubin ≤ 1.5 mg/dl, except in subjects with Gilbert's syndrome

    - Cardiac ejection fraction ≥ 50%, no evidence of pericardial effusion as determined by an echocardiogram (ECHO), and no clinically significant electrocardiogram (ECG) findings

    - No clinical significant pleural effusion

    - Baseline oxygen saturation > 92% on room air

14. Females of childbearing potential must have a negative serum or urine pregnancy test. Females who have undergone surgical sterilization or who have been postmenopausal for at least 2 years are not considered to be of childbearing potential.

EXCLUSIE CRITERIA

1. History of malignancy other than nonmelanomatous skin cancer or carcinoma in situ (eg, cervix, bladder, breast) unless disease-free for at least 3 years
2. AutoSCT within 6 weeks of planned KTE-C19 infusion
3. History of allogeneic stem cell transplantation
4. Prior CD19 targeted therapy with the exception of subjects who received KTE-C19 in this study and are eligible for re-treatment
5. Prior CAR therapy or other genetically modified T-cell therapy
6. History of severe, immediate hypersensitivity reaction attributed to aminoglycosides
7. Presence of fungal, bacterial, viral, or other infection that is uncontrolled or requiring intravenous (IV) antimicrobials for management. Simple urinary tract infection (UTI) and uncomplicated bacterial pharyngitis are permitted if responding to active treatment and after consultation with the Kite medical monitor
8. History of human immunodeficiency virus (HIV) infection or acute or chronic active hepatitis B or C infection. Subjects with a history of hepatitis infection must have cleared their infection as determined by standard serological and genetic testing.
9. Presence of any in-dwelling line or drain (eg, percutaneous nephrostomy tube, in-dwelling Foley catheter, biliary drain, or pleural/peritoneal/pericardial catheter). Ommaya reservoirs and dedicated central venous access catheters, such as a Port-a-Cath or Hickman catheter, are permitted.
10. Subjects with detectable cerebrospinal fluid malignant cells or brain metastases or with a history of CNS lymphoma, cerebrospinal fluid malignant cells, or brain metastases
11. History or presence of CNS disorder, such as seizure disorder, cerebrovascular ischemia/hemorrhage, dementia, cerebellar disease, cerebral edema, posterior reversible encephalopathy syndrome, or any autoimmune disease with CNS involvement
12. History of myocardial infarction, cardiac angioplasty or stenting, unstable angina, or other clinically significant cardiac disease within 12 months of enrollment
13. Subjects with cardiac atrial or cardiac ventricular lymphoma involvement
14. History of symptomatic deep vein thrombosis or pulmonary embolism within the last 6 months of enrollment
15. Possible requirement for urgent therapy due to ongoing or impending oncologic emergency (eg, tumor mass effect, tumor lysis syndrome)
16. Primary immunodeficiency
17. Any medical condition likely to interfere with assessment of safety or efficacy of study treatment
18. History of severe immediate hypersensitivity reaction to any of the agents used in this study

19. Live vaccine ≤ 6 weeks prior to planned start of conditioning regimen

20. Women of childbearing potential who are pregnant or breastfeeding because of the potentially dangerous effects of the preparative chemotherapy on the fetus or infant

21. Subjects of both genders who are not willing to practice birth control from the time of consent through 6 months after the completion of KTE-C19

22. In the investigator's judgment, the subject is unlikely to complete all protocol-required study visits or procedures, including follow-up visits, or comply with the study requirements for participation.

23. History of autoimmune disease (eg Crohn's disease, rheumatoid arthritis, systemic lupus) resulting in end organ injury or requiring systemic immunosuppression/systemic disease modifying agents within the last 2 years