KTE-C19-104 (ZUMA-4)

A Phase 1/2 Multi-Center Study Evaluating the Safety and Efficacy of KTE-X19 in Pediatric and Adolescent Subjects with Relapsed/Refractory B-precursor Acute Lymphoblastic Leukemia or Relapsed/Refractory B-Cell Non-Hodgkin Lymphoma (ZUMA-4)

Study Design

- ZUMA-4 is a Phase 1/2, multicenter, open-label study evaluating the safety and efficacy of KTE-X19 in pediatric and adolescent subjects with r/r B-precursor ALL or r/r B-cell NHL.
- relapsed or refractory is defined as 1 of the following: primary refractory, relapsed or refractory after second-line or higher therapy, relapsed or refractory after SCT (allogeneic SCT for ALL and either allogeneic or autologous SCT for NHL) provided the transplant occurred ≥ 100 days prior to enrollment and that no immunosuppressive medications were taken ≤ 4 weeks prior to enrollment.
- Approximately 100 subjects with ALL may be enrolled and treated.
- Approximately 16 subjects with NHL may be enrolled and treated.

Treatment

- Bridging chemotherapy is recommended for all subjects, particularly for those subjects with ALL/NHL high disease burden at screening: ALL cohort: M3 marrow (> 25% leukemic blasts) or ≥ 1000 blasts/mm3 in the peripheral circulation
  NHL cohort: bulky disease or rapidly progressing disease
- If prescribed, bridging chemotherapy must be administered after leukapheresis and completed at least 7 days or 5 half-lives, whichever is shorter, prior to initiating conditioning chemotherapy.
- All subjects with ALL, and subjects with NHL who have central nervous system (CNS)-2 disease without neurological symptoms, will receive CSF prophylaxis consisting of an intrathecal regimen according to institutional or national guidelines
- The KTE-X19 target doses explored in Phase 1 were 1 x 106 anti-CD19 CAR T cells/kg and 2 x 106 anti-CD19 CAR T cells/kg (The day of KTE-X19 infusion is considered Day 0)
- In Phase 2, KTE-X19 infusion will be administered at the Recommended Phase 2 Dose (RP2D) target dose of 1 x 106 anti--CD19 CAR T cells/kg
- All subjects will be hospitalized to receive treatment with KTE-X19 and for a minimum of 7 days after infusion for observation unless otherwise required by country regulatory agencies

Subject eligibility

Basic Inclusion Criteria for the ALL cohort

Relapsed or refractory Ph-precursor ALL defined as at least 1 of the following:

- Primary refractory disease
- Any relapse within 18 months after first diagnosis
- Relapsed or refractory disease after 2 or more lines of systemic therapy ≥
- Relapsed or refractory disease after allogeneic transplant; provided subject is at least 100 days from stem cell transplant at the time of enrollment and off of immunosuppressive medications for at least 4 weeks prior to enrollment

Disease burden defined as at least 1 of the following:

- Morphological disease in the bone marrow (> 5% blasts)
- MRD positive (threshold 10-4 by flow or PCR)
- Subjects with Ph+ disease are eligible if they are intolerant to TKI therapy or if they have r/r disease despite treatment with at least 2 different TKIs.
- Age ≤ 21 years and weight ≥ 6 kg
- Lansky (age < 16 years at the time of assent/consent) or Karnofsky (age ≥ 16 years at the time of assent/consent) performance status ≥ 80 at screening

Subject eligibility
Basic Inclusion Criteria for the NHL cohort

Histologically confirmed aggressive B cell NHL:

- Primary mediastinal large B-cell lymphoma (including Mediastinal gray zone lymphoma)
- Burkitt lymphoma, Burkitt-like lymphoma and Unclassified B-cell lymphoma intermediate between DLBCL and Burkitt lymphoma
- DLBCL not otherwise specified

Relapsed or refractory disease defined as 1 or more of the following:

- Primary refractory disease
- Relapsed or refractory disease after 2 or more lines of systemic therapy
- Relapsed or refractory disease after autologous /allogeneic SCT provided subject is at least 100 days from SCT at the time of enrollment and off of immunosuppressive medications for at least 4 weeks prior to enrollment

Subjects must have received adequate prior therapy including at a minimum all of the following:

- Anti-CD20 monoclonal antibody, unless the investigator determines that the tumor is CD20 negative
- An anthracycline-containing chemotherapy regimen
- At least 1 measurable lesion according to the revised International Pediatric Non-Hodgkin Lymphoma Staging System {Rosolen 2015}. Lesions that have been previously irradiated will be considered measurable only if progression has been documented following completion of radiation therapy.
- Age <18 years old and weight ≥ 6kg.
- Lansky (age < 16 years at the time of assent/consent) or Karnofsky (age ≥ 16 years at the time of assent/consent) performance status ≥ 80 at screening