Request for New ICD-10-PCS Codes for the Inpatient Administration of KTE-X19, an Anti-CD19 Chimeric Antigen Receptor (CAR) T-cell Therapy

ICD-10 Coordination and Maintenance Committee Meeting

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Request for ICD-10-PCS Codes in Support of KTE-X19 New Technology Add-on Payment (NTAP) Application Under Review

KTE-X19*, A DISTINCT AUTOLOGOUS CELLULAR PRODUCT:	Generated by a unique manufacturing process for B-cell malignancies with a high circulating tumor cell burden
PROPOSED INDICATION:	Treatment of adult patients with relapsed/refractory (r/r) mantle cell lymphoma (MCL) • KTE-X19 would be the first FDA-approved CAR T-cell therapy for the treatment of adult patients with r/r MCL
REGULATORY STATUS:	BLA submitted December 11, 2019 with a request for Priority Review **FDA Breakthrough Therapy and Orphan Drug Designation**

**Proposed technology name and tradename, not yet determined; referred to by investigational name, KTE-X19*

KTE-X19 Will Meet a Substantial Unmet Treatment Need in Patients with r/r MCL Who Have Not Responded to Currently Available Therapies

- r/r MCL is a rare, aggressive subtype of non-Hodgkin lymphoma (NHL) and remains incurable[1,2]
  - Median age of diagnosis is 68 years (range: 20 to > 80 years)[3]
  - Often diagnosed at advanced stage (Stage III/IV), characterized by aggressive clinical course
  - Has one of the poorest prognoses of all lymphomas[2-4]
- Most patients eventually relapse after frontline therapy[5-7]
- There is neither a single established standard of care nor a defined sequence of treatment for patients with r/r MCL
- Efficacy outcomes generally decline with each additional line of therapy

Meta-analysis of Salvage Therapy after BTKi Failure Confirms Dismal Outcomes[8-13]

- Pooled Objective Response Rate (ORR): 28% (95% CI: 24%, 34%)
- Complete Response (CR) Rate: 7% to 22%
- Median Overall Survival (OS) with salvage therapy: 2.5 to 9 months

BTKi, Bruton's tyrosine kinase inhibitor

1. Fakhri B Ther Adv Hematol 2017; 2. NCCN 2018; 3. Fu S Oncotarget 2017; 4. Smith A Br J Cancer 2015; 5. Flinn IW J Clin Oncol 2019; 6. LaCasce AS Blood 2012; 7. Lenz G J Clin Oncol 2005; 8. Cheah CY Ann Oncol 2015; 9. Martin P Blood 2016; 10. Dreyling M Lancet 2016; 11. Epperla N Hematological Oncology 2017; 12. Wang M J Hematol Oncol 2017; 613 Jain P Br J Haematol 2018

MCL is a Unique Subtype of B-cell NHL and Differs Substantially from Diffuse Large B-cell Lymphoma (DLBCL)

- DLBCL is the disease treated by the currently available CAR T-cell therapies, YESCARTA and KYMRIAH
- Both were approved under a single NTAP effective October 1, 2018 (FY2019)

Mantle Cell Lymphoma (MCL)[1,2,3]	Diffuse Large B-cell Lymphoma (DLBCL)[4,5,6,7]
Results from a malignant transformation of a B lymphocyte in the outer edge of a lymph node follicle - the mantle zone.	*Defined as a neoplasm of large B-cells arranged in diffuse pattern. The lymphoma cells are typically larger than the nuclei of benign histocytes in the biopsy.*
• **Comprises 3 to 6% of all NHL in the US** and is conventionally an aggressive lymphoma with a heterogeneous disease profile	• Represents approximately **24% of new cases of NHL each year in the US**, the most common type of NHL
• **Blastoid MCL noted in 25 to 30% of patients** is an aggressive variant where cells resemble lymphoblasts with dispersed chomatin and a high mitotic rate	• **Double-hit DLBCL with MYC and BCL2 rearrangements constitute approximately 10% of DLBCL** and have a more aggressive course
• **Extranodal involvement is common and > 90% of patients have gastrointestinal involvement**	• **40% of patients present with extranodal disease**

1. Cheah CY J Clin Oncol 2016; 2. Shrestha R Leuk Lymph 2015; 3. Salar A Am J Surg Path, 2006; 4.Sehn LH and Gascoyne RD Blood 2015; 5. Liu Y and Barta S Am J Hematol 2019; 6. Jacobson CA The Hematologist 2019; 7. Moller MB Br J Haematol 2004.

KTE-X19 is a Distinct Cellular Product Developed Specifically For Hematologic Malignancies With Circulating Blasts

- Due to unique aspects of MCL, including circulating tumor cells seen in 26 to 34% of patients and peripheral mobilization of tumor cells induced by BTK inhibitor therapy, **patients with r/r MCL often present with high levels of circulating tumor blasts**

- Therefore, **functional autologous cellular therapy for the treatment of r/r MCL requires a customized product distinct from other currently available CAR T-cell therapy products**, namely YESCARTA (axicabtagene ciloleucel) and KYMRIAH (tisagenleceucel)

- **Kite developed KTE-X19, which is manufactured by a unique, proprietary process**, as a novel, investigational adoptive cellular immunotherapy

- The **FDA determined that KTE-X19 required a new BLA based on differences in the manufacturing process** between KTE-X19 and YESCARTA that may result in differences in potency and cellular composition of the final product

ZUMA-2: KTE-X19 Investigated for the Treatment of r/r MCL

A heavily pre-treated r/r MCL population

Key Inclusion Criteria

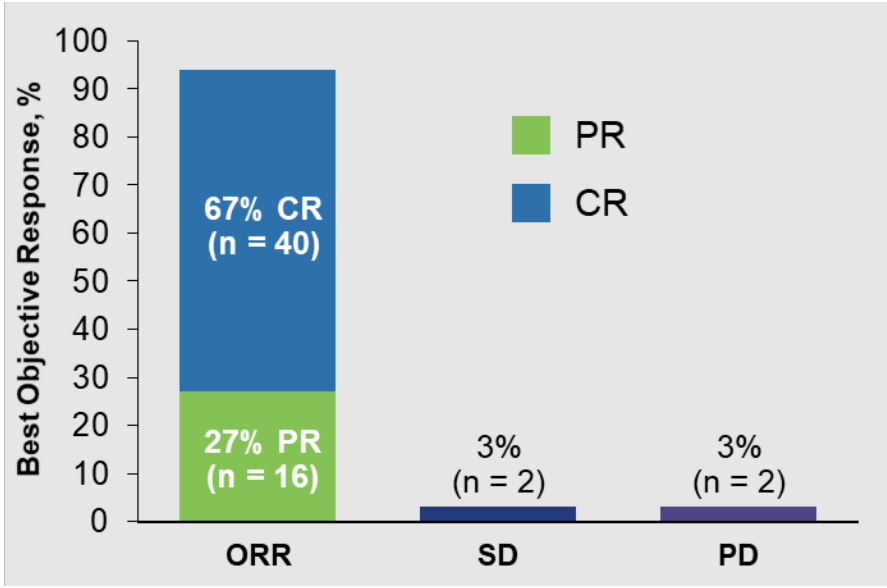
- r/r MCL defined as:
  - Disease progression after last regimen or
  - Failure to exhibit a CR or PR to the last regimen
- 1 – 5 Prior therapies that must have included
  - An anthracycline- or bendamustine-containing chemotherapy and
  - Anti-CD20 monoclonal antibody therapy and
  - Ibrutinib or acalabrutinib
- ≥ 1 Measurable lesion
- Age ≥ 18 years
- ECOG of 0 or 1
- Adequate bone marrow, renal, hepatic, pulmonary, and cardiac function
- ALC ≥ 100/μL

ALC, absolute lymphocyte count; BTK, Bruton's tyrosine kinase; CR, complete response; ECOG, Eastern Cooperative Oncology Group; PR, partial response

- N=68, safety analysis set; N=60, efficacy analysis
- Median age: 65 years (range: 38-79)
  - 57% ≥ 65 years
- Stage IV disease: 58 (85%)
- 81% had ≥ 3 prior therapies
  - Anthracycline or bendamustine (99%)
  - Anti-CD20 mAb (100%)
  - BTK inhibitors (100%)
- Relapsed/refractory status
  - Relapsed after autoSCT: 29 (43%)
  - Refractory to ibrutinib: 38 (56%)
  - Refractory to acalabrutinib: 8 (12%)

High Objective Response Rate (ORR) after Single Dose of KTE-X19 in Heavily Pretreated r/r MCL

KTE-X19 ORR, CR and PR Rates



- ORR: 93% (95% CI: 84-98)
  - 94%, ≥ 65 years of age (n=30)
  - 93%, < 65 years of age (n=26)
- Significantly higher than prespecified historical control rate of 25%[1,2] and pooled meta-analysis rate of 28%[1-6]

- Complete response (CR) rate: 67% (95% CI: 53-78)
  - 55% of those achieving CR were ≥ 65 years of age (n=22)
- Significantly higher than meta-analysis rates (7% to 22%)[1,2,5,6]

Investigator-assessed ORR in N = 60 was 88% (CR rate 70%), with 95% and 90% concordance between IRRC- and investigator-assessed ORR and CR rate, respectively. IRRC-assessed ORR in ITT (N = 74) was 85% (CR Rate 59%).

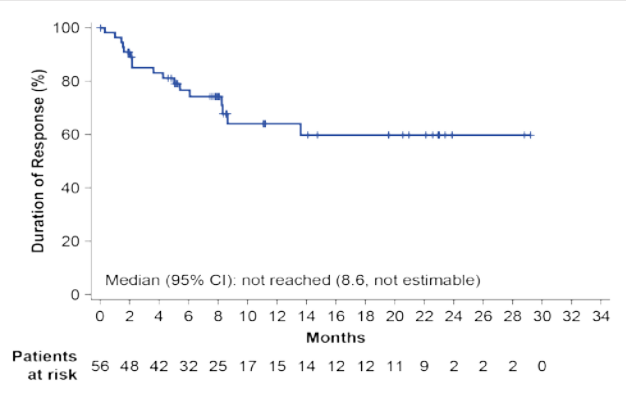
CR, complete response; IRRC, Independent Radiology Review Committee; ORR, objective response rate; PD, progressive disease; PR, partial response; SD, stable disease

1. Cheah CY *Ann Oncol* 2015; 2. Martin P Blood 2016; 3. Dreyling M *Lancet* 2016; 4. Epperla N *Hematological Oncology* 2017; 5. Wang M *J Hematol Oncol* 2017; 6. Jain P *Br J Haematol* 2018

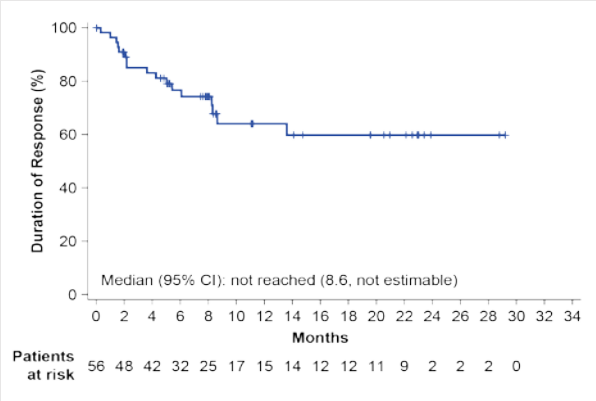
Median Duration of Response (DOR) and Overall Survival (OS) Were Not Reached After Median Follow-up of 12.3 Months

- 57% of all patients and 78% of patients with a CR remain in remission
- The first 28 patients treated had a median follow-up of 27.0 months (range, 25.3 to 32.3); 43% remained in response without additional therapy
- KTE-X19 OS rate estimates at 6 months and 12 months were 86.7% and 83.2%
- Currently available therapies have a median OS that ranges from 2.5 months to 9 months[1-4]

KTE-X19 Duration of Response



KTE-X19 Overall Survival



1. Cheah CY *Ann Oncol* 2015; 2. Martin P *Blood* 2016; 3. Epperla N *Hematological Oncology* 2017; 4. Jain P *Br J Haematol* 2018

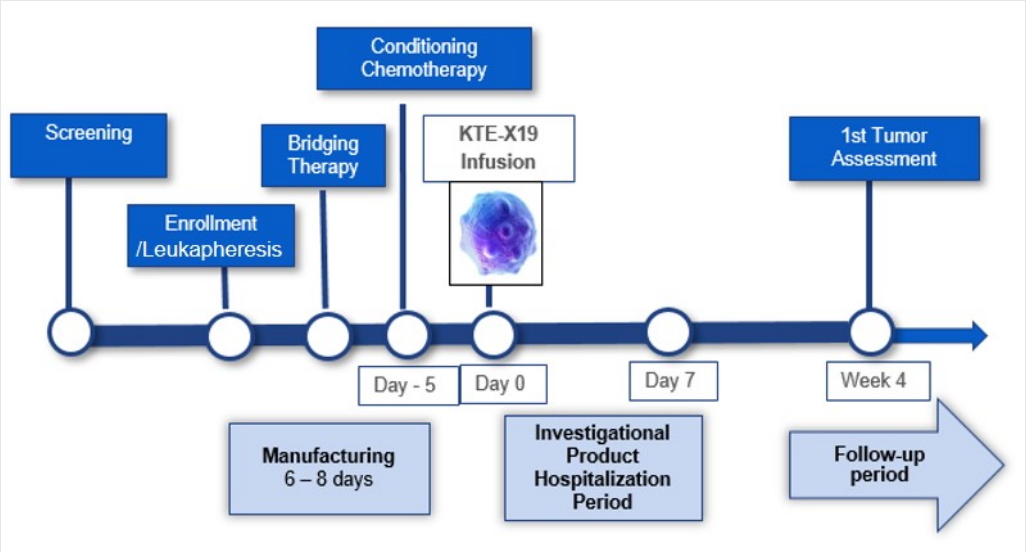
Efficacy and Safety Data Demonstrate a Positive Benefit-Risk of KTE-X19; A Meaningful Advantage Over Currently Available Therapies

ZUMA-2 primary analysis data have demonstrated a positive benefit-risk profile for KTE-X19 as an innovative and effective treatment for r/r MCL that represents a substantial improvement over currently approved and available therapies

Patients with r/r MCL are faced with dismal outcomes that can be substantially improved upon by KTE-X19 therapy

- **Substantial improvements were observed in ORR, CR rate, DOR, and OS** as compared to available therapies
- **Most Grade 3 or higher adverse events (AEs)**, including cytokine release syndrome (CRS) and neurologic events, **were generally self-limiting and reversible** under study AE management guidance
- 16 of 68 (24%) had died at data cutoff; 14 due to disease progression and 2 related to AEs. **No patient died from CRS or neurologic event**
- **Consistent promising results were observed across age groups (≥ 65 and < 65 years of age)** with 93% ORR in elderly patients and generally manageable cytokine release syndrome and neurologic events in older patients under study AE management guidance
- The **median DOR and OS had not been reached**
- Importantly, current ZUMA-2 results have shown the **potential for durable remissions** after a single infusion of KTE-X19

ICD-10-PCS Codes Are Needed to Identify the Inpatient Infusion of KTE-X19



Investigational Product Hospitalization Period:

At least 7 days hospitalization, discharge once all KTE-X19-related non-hematological toxicities return to Grade ≤ 1 or baseline

Follow-up Period:

Tumor assessments with PET-CT at Wk 4, Mo 3, then every 3 months through Mo 18, and then per standard of care. BM biopsy at screening and if positive, need one to confirm CR

KTE-X19 will be supplied as autologous cell suspension for infusion in a single-use, patient-specific infusion bag (infused by gravity or a peristaltic pump over 30 minutes) consisting of 2.0 x 106 anti-CD19 CAR T cells/kg of body weight (± 20%), with a maximum dose of 2 x 108 anti-CD19 CAR T cells (for subjects ≥ 100 kg)

No ICD-10-PCS Code Identifies KTE-X19 or its Administration

- Currently, CMS has created ICD-10-PCS codes for the introduction of Engineered Autologous Chimeric Antigen Receptor T-cell Immunotherapy into Peripheral and Central Vein: XW033C3 and XW043C3; mapped to YESCARTA and KYMRIAH
- Because KTE-X19 is a distinct cellular product and, if approved by the FDA, will be indicated to treat a different patient population than the currently available CAR T therapies, it will be necessary for CMS to establish specific ICD-10-PCS codes to identify the administration of KTE-X19 if our NTAP application is approved

Kite Pharma strongly recommends CMS to follow its precedents in establishing a new ICD-10 PCS code in order to accurately report and track administration of KTE-X19 in the inpatient setting