Dear NCCN Guidelines® B-Cell Lymphomas Panel,

On behalf of Kite, I respectfully request the NCCN B-Cell Lymphomas Guideline Panel to review the enclosed data for inclusion of TECARTUS™ (brexucabtagene autoleucel or brexu-cel, formerly referred to as KTE-X19) for the treatment of adult patients with relapsed or refractory mantle cell lymphoma (MCL).

Specific Changes

Please consider the addition of brexucabtagene autoleucel as a second line therapy for relapsed or refractory MCL (MANT-A 2 OF 4)

FDA Clearance

TECARTUS™ (brexucabtagene autoleucel) is a novel CD19-directed genetically modified autologous T-cell immunotherapy that was granted priority review designation by the FDA on February 10, 2020.1 TECARTUS™ was approved by the FDA on July 24, 2020 for the treatment of adult patients with relapsed or refractory MCL.2 This indication is approved under accelerated approval based on the overall response rate and durability of response with continued approval being contingent upon verification and description of clinical benefit in a confirmatory trial.

Rationale

Patients with relapsed or refractory MCL remain difficult to treat with declining complete remission (CR) rates of 45% or less with second and subsequent lines of therapy.3,4 Based on the results from the ZUMA-2 study, brexucel became the first chimeric antigen receptor (CAR) T-cell therapy approved by the FDA for adult patients with relapsed or refractory MCL.2 Results from this study demonstrated 87% of patients responding with 62% achieving a CR.2 Grade ≥3 Cytokine Release Syndrome (CRS) and Neurologic Events (NE) was experienced in 18% and 37% patients respectively. Additional details from the ZUMA-2 study are described below:

ZUMA-2 is a Phase 2, single-arm, open-label, multicenter study evaluating the safety and efficacy of brexucel in patients with MCL who relapsed after or were refractory to 2 to 5 prior therapies.2,5 Eligible patients underwent leukapheresis to obtain peripheral blood mononuclear cells for brexucel production. The manufacture of brexucel includes a T-cell enrichment step that may reduce the likelihood of circulating CD19-expressing tumor cells in the leukapheresis material driving the activation, expansion, and exhaustion of the anti-CD19 CAR T cells during the ex vivo manufacturing process.2 Per protocol, patients were to receive lymphodepleting chemotherapy regimen consisting of 30 mg/m² fludarabine IV and 500 mg/m² cyclophosphamide IV on Days −5, −4, and −3 followed by a single IV infusion of brexucel at a target dose of 2 × 10⁶ CAR T-cells/kg.5 The primary endpoint was the objective response rate (ORR) as assessed by an independent radiology review committee (IRRC) per the Lugano classification.2,5

Of 74 patients enrolled and leukapheresed, brexucel was successfully manufactured for 71 (96%) and administered to 68 (92%).2 Sixty of these patients were followed for at least 6 months after their week 4 disease assessment and were considered efficacy evaluable. For these 60 patients, the median age was 65 years (range:
38 to 79 years) with 83% having Stage IV disease and 23% having blastoid MCL. The median number of prior therapies was 3 (range: 2-5). Twenty-six (43%) patients had relapsed after or were refractory to autologous hematopoietic stem cell transplant (HSCT). Twenty-one (35%) had relapsed after their last therapy for MCL, while 36 (60%) were refractory to their last therapy for MCL. Twenty-one (35%) patients received bridging therapy post-apheresis with a BTK inhibitor and/or corticosteroids. The primary efficacy analysis, conducted on the 60 efficacy evaluable patients, demonstrated an ORR of 87% (95% CI, 75 – 94), with a 62% rate of complete remission (CR; 95% CI, 48 – 74).² With median follow-up of 8.6 months, the median duration of response (DOR) was not reached.

The safety of brexu-cel was evaluated in 82 patients from the ZUMA-2 study and included all patients who received a single dose of viable anti-CD19 CAR T-cells/kg (2 × 10⁶ or 0.5 × 10⁶ anti-CD19 CAR T cells/kg) that was weight based.² Grade ≥3 CRS occurred in 18% patients and Grade ≥3 NE occurred in 37% patients. The most common adverse reactions (incidence ≥ 20%) were pyrexia, CRS, hypotension, encephalopathy, fatigue, tachycardia, arrhythmia, infection – pathogen unspecified, chills, hypoxia, cough, tremor, musculoskeletal pain, headache, nausea, edema, motor dysfunction, constipation, diaphoresis, decreased appetite, dyspnea, rash, insomnia, pleural effusion, and aphasia. Serious adverse reactions occurred in 66% of patients. The most common serious adverse reactions (> 2%) were encephalopathy, pyrexia, infection – pathogen unspecified, CRS, hypoxia, aphasia, renal insufficiency, pleural effusion, respiratory failure, bacterial infections, dyspnea, fatigue, arrhythmia, tachycardia and viral infections.

Because of the risk of CRS and neurologic toxicities, TECARTUS™ is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the YESCARTA and TECARTUS REMS Program.² Additional information regarding the REMS program can be found at www.YescartaTecartusREMS.com.

We appreciate the opportunity to submit this information for consideration by the NCCN Guidelines® B-Cell Lymphomas Panel. If you have any questions or require additional information, please do not hesitate to contact us via phone 1-844-454-5483 or email medinfo@kitepharma.com

Sincerely,
Neil Sheth, Pharm.D, Hon BSc
Senior Manager, Medical Information
Kite, A Gilead Company

Enclosures
TECARTUS™ Prescribing Information² and referenced primary literature³-⁵

References