Submitted by:
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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 YESCARTA® (axicabtagene ciloleucel) for the treatment of adult patients with relapsed or refractory B-cell indolent Non-Hodgkin's Lymphoma (iNHL) of Follicular Lymphoma (FL) and Marginal Zone Lymphoma (MZL) histological subtypes.

Specific Changes

Please consider the addition of axicabtagene ciloleucel under second-line and subsequent therapy for follicular lymphoma (FOLL-B 2 OF 4) and second-line or subsequent therapy for marginal zone lymphomas (MZL-A 2 OF 3).

Rationale

Patients with multiple relapses in iNHL, including double R/R FL have suboptimal outcomes; a recent systematic literature review demonstrated this unmet need with CR rates ranging from 1.2% to 14% in R/R FL studies where patients were treated with ≥2 prior lines of therapy.[1] This submission is an update to our previous request dated September 18, 2020. We would like to take this opportunity and provide you with updated results from primary analysis of ZUMA-5 study that was recently presented at the 2020 American Society of Hematology (ASH) Annual Meeting and attached for reference.[2]

The primary analysis of ZUMA-5 involved 151 patients that were enrolled and leukapheresed.[2] Axicabtagene ciloleucel was successfully manufactured for all enrolled patients with 146 patients eventually receiving the product (FL= 124, MZL= 22). Efficacy analysis was conducted on 104 patients (FL=84, MZL=20) as of March 12, 2020 data cut-off, with a median follow-up of 17.5 months (range: 1.4-31.6). Safety analysis was conducted on all 146 patients who received axicabtagene ciloleucel with median follow-up of 15.1 months (range: 0.5-31.6). Key highlights from these analyses for all iNHL patients include:

- ORR = 92% (95%CI: 85-97) and CR = 76% (95%CI: 67-84) as assessed by IRRC (central read)
- Median DOR = Not Reached (95% CI: 20.8-NE), 12-month DOR rate= 71.7% (95%CI: 60.7-80.1);
  Median PFS = Not Reached (95%CI: 23.5-NE), 12 month PFS rate =73.7% (95%CI: 63.3-81.6);
  Median OS = Not Reached (95%CI: NE-NE), 12 month OS rate = 92.9% (95%CI: 85.6-96.5)
- Subgroup analysis showed IRRC-assessed ORR to be consistent among patients with high risk characteristics such as POD24, high tumor burden (GELF criteria), refractory disease and high FLIPI scores
- Grade≥3 AEs occurred in 126 (86%) patients with most common grade≥3 AEs being cytopenia (70%) and infections (16%)
- Any grade CRS events were experienced in 119 (82%) patients with 10 (7%) experiencing grade ≥3 CRS. One patient had Grade 5 multi-organ system failure related to axicabtagene ciloleucel in the context of CRS.
- Any grade neurologic events were experienced in 87 (60%) patients with 28 (19%) experiencing grade ≥3 neurologic event. No grade 5 neurologic events were reported.

FDA Status

YESCARTA® is not FDA approved for treatment of adult patients with relapsed or refractory B-cell indolent Non-Hodgkin's Lymphoma (iNHL) of Follicular Lymphoma (FL) and Marginal Zone Lymphoma (MZL) histological subtypes.[3] Kite, a Gilead company, recently submitted a supplemental biologics license application (BLA) to the U.S. Food and Drug Administration (FDA) for Yescarta® for the treatment of relapsed or refractory follicular FL and MZL after two or more prior lines of systemic therapy.[4] Yescarta was previously granted Breakthrough Therapy Designation by the FDA for these indications.

Please see enclosed YESCARTA prescribing information for approved indications and limitations of use.[3]

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

Abbreviations AE – Adverse Event, CI – Confidence Interval, CR – Complete Response, CRS – Cytokine Release Syndrome, DOR – Duration of Response, FLIPI- Follicular Lymphoma International Prognostic Index, GELF- Groupe d'Etude des Lymphomes Folliculaires, IRRC- Independent Radiology Review Committee, NE – Not Estimable, ORR – Overall Response Rate, OS – Overall Survival, PFS – Progression-Free Survival, POD24 – Progression of disease <24 months from first antiCD20 containing immunochemotherapy,

Enclosures YESCARTA® Prescribing Information[3] and referenced presentation[2]

References

1. Kahl BD, Patel AR, Zaidi O, et al. Efficacy Outcomes of Treatments for Double Relapsed/Refractory Follicular Lymphoma (R/R FL): A Systematic Literature Review. *Blood* (2020) 136 (Supplement 1): 42–43. Available at https://doi.org/10.1182/blood-2020-136228. Accessed November 23, 2020.
2. Jacobson CA, Chavez, JC, Sehgal AR, et al. Primary analysis of ZUMA-5: a phase 2 study of axicabtagene ciloleucel (AxiCel) in patients with relapsed/refractory (R/R) indolent non-Hodgkin lymphoma (iNHL). Presented at: 62nd ASH Annual Meeting and Exposition; December 07, 2020; Virtual Meeting.
3. YESCARTA® (axicabtagene ciloleucel) Prescribing Information, Kite Pharma, Inc. Santa Monica, CA. 2019.
4. Gilead Sciences, Inc., 2020. Kite submits supplemental Biologics License Application to U.S. Food and Drug Administration for YESCARTA® in relapsed or refractory indolent Non-Hodgkin Lymphomas. Available at https://www.gilead.com/news-and-press/press-room/press-releases/2020/9/kite-submits-supplemental-biologics-license-application-to-us-food-and-drug-administration-for-yescarta-in-relapsed-or-refractory-indolent-nonhodg. Accessed September 5, 2020.