Submitted by:
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Date of request: August xx, 2020
NCCN Guidelines Panel: Breast Cancer

Dear NCCN Guidelines Breast Panel:

Please find references for your review regarding Perjeta® (pertuzumab) and Kadcyla® (ado-trastuzumab emtansine). This submission also references Herceptin® (trastuzumab).

Requests:

1. Consider the enclosed KAITLIN presentation of Perjeta + Kadcyla vs. Herceptin + Perjeta + taxanes in the first-line treatment of patients with metastatic breast cancer (MBC) for your drug information updating needs.
2. Consider applying footnote 'zz' on page BINV-15, which allows for concomitant radiation as part of adjuvant therapy after preoperative systemic therapy, to Kadcyla based on the KATHERINE protocol and subgroup analysis.

Key Takeaways: Perjeta + Kadcyla

- The Phase III KAITLIN study evaluated the efficacy and safety of Perjeta + Kadcyla (KP) versus Herceptin + Perjeta + taxanes (THP) after anthracyclines (AC) as adjuvant therapy in patients with high-risk HER2+ early breast cancer (eBC).[1] The study did not meet its co-primary endpoints of invasive disease-free survival in both node-positive and intent-to-treat populations. Grade ≥3 adverse events were 51.8% and 55.4% for AC-KP and AC-THP, respectively, with specific events reflecting the types and severities of the known safety profiles of each treatment.

Key Takeaways: Kadcyla

- KATHERINE is a Phase 3, randomized, open-label trial conducted to evaluate the efficacy and safety of adjuvant treatment with Kadcyla vs. Herceptin in patients with HER2-positive eBC who had residual invasive disease after neoadjuvant systemic therapy. The primary results were previously submitted.[2]
    - Please consider use of concomitant radiotherapy with Kadcyla because it was part of the KATHERINE protocol. Additionally, results from a post-hoc exploratory subgroup analysis of patients who received adjuvant radiotherapy (ART) provide additional clinical support.
    - In the KATHERINE trial, radiation was recommended to start within 60 days of surgery and given concurrently with study treatment. Otherwise radiotherapy was administered per institutional standards. Please see the protocol for further details.[2-4]
    - In a post-hoc exploratory subgroup analysis in patients who received adjuvant radiotherapy (ART), there was a consistent invasive disease-free survival benefit with Kadcyla regardless of ART and no new safety signals were reported with concomitant ART.[4]

FDA Clearance:

- Kadcyla is FDA-approved for use in the early and metastatic HER2-positive breast cancer. Please refer to the product prescribing information for the full FDA-approved indications and safety information, available at: https://www.gene.com/download/pdf/kadcyla_prescribing.pdf
- Perjeta is FDA-approved for use in the early and metastatic HER2-positive breast cancer. Please refer to the product prescribing information for the full FDA-approved indications and safety information, available at: https://www.gene.com/download/pdf/perjeta_prescribing.pdf
- Herceptin FDA-approved for use in the early and metastatic HER2-positive breast cancer. Please refer to the product prescribing information for the full FDA-approved indications and safety information, available at: https://www.gene.com/download/pdf/herceptin_prescribing.pdf

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Thank you for your consideration and I hope this information is helpful to you. If you have any questions, please contact us at the phone number and email provided above.

Respectfully submitted,
Ellen Yang, PharmD

References

1. Harbeck N, Im SA, Barrios C, et al. Primary analysis of KAITLIN: A phase 3 study of trastuzumab emtansine (T-DM1) + pertuzumab versus trastuzumab + pertuzumab + taxane, after anthracyclines as adjuvant therapy for high-risk HER2-positive early breast cancer. Oral presentation at the American Society of Clinical Oncology (ASCO) annual meeting; May 29–31 2020.
2. Von Minckwitz G, Huang CS, Mano MS, et al. Trastuzumab emtansine for residual invasive HER2-positive breast cancer [supplementary appendix appears online]. N Engl J Med. 2019 Feb 14;380(7):617-628. https://www.nejm.org/doi/full/10.1056/NEJMoa1814017
3. Protocol for KATHERINE: Trastuzumab emtansine for residual invasive HER2-positive breast cancer June 2012. Available at https://www.nejm.org/doi/suppl/10.1056/NEJMoa1814017/suppl_file/nejmoa1814017_protocol.pdf Accessed on July 31, 2020.
4. Loibl S, Huang CS, Mano MS, et al. Adjuvant trastuzumab emtansine (T-DM1) vs trastuzumab (T) in patients with residual invasive disease after neoadjuvant therapy for HER2-positive breast cancer: subgroup analysis from KATHERINE. Presented at the European Society for Medical Oncology Breast Cancer Virtual Meeting May 23–24, 2020. ESMO Oral Presentation.