Submitted by:
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NCCN Guidelines Panel: Head and Neck Cancers

Dear NCCN Guidelines Panel,

On behalf of Genentech, Inc., please find data from the MyPathway study enclosed for your review. The enclosed publication provides efficacy and safety results in patients with advanced salivary gland cancer (SGC) who were treated with targeted therapies based on tumor molecular characteristics.

- R. Kurzrock, D.W. Bowles, H. Kang, F. et al. Targeted therapy for advanced salivary gland carcinoma based on molecular profiling: results from MyPathway, a phase IIa multiple basket study. Annals of Oncology, Volume 31: 412-421.[1]

Request:

Consider the inclusion of Herceptin® (trastuzumab) and Perjeta® (pertuzumab) as a treatment option in the Treatment for Recurrence section of the guideline (SALI-4, SYST-A) for patients with HER2-amplified and/or overexpressing SGC.

Rationale:

Systemic treatment options for patients with advanced SGC remain limited, especially in patients who are unable to tolerate chemotherapy. Recent evidence has suggested a role for targeted treatment of HER2-amplified and/or overexpressing SGC.[2,3,4]

Efficacy and safety results from MyPathway in a subgroup of patients with advanced SGC are presented below[1]:

- In 15 patients with advanced SGC characterized by HER2 amplification and/or overexpression and treated with Herceptin and Perjeta, an ORR of 60% (9 of 15 patients comprised of 1 complete response and 8 partial responses, 95% CI: 32-84). An overall CBR of 67% was observed with one additional patient having SD (n=10).
- Median PFS was 8.6 months (95% CI: 2.3-NE) and median OS was 20.4 months (95% CI: 8.2-NE). Median duration of follow-up was 10.6 months. Estimated median response duration in patients with an objective response was 9.2 months (range 1.4+ to 19.7+ months).
- The most common drug-related AEs in patients treated with Herceptin and Perjeta were diarrhea (8/16), pruritus (5/16), and chills (4/16). One patient had Grade 3 peripheral neuropathy considered related to the study drugs.
- No new safety signals were observed for Herceptin and Perjeta and the safety profiles were consistent with the product labels.

Data from MyPathway demonstrate that the combination of Herceptin and Perjeta are a promising systemic treatment option in patients with HER2-amplified and/or overexpressing advanced SGC.

FDA Clearance:

- Herceptin is not FDA-approved for use in the treatment of salivary gland 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

- Perjeta is not FDA-approved for use in the treatment of salivary gland 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

Thank you for your consideration.

Respectfully submitted,
Patrice Esser, PharmD, MPH

References:

1. R. Kurzrock, D.W. Bowles, H. Kang, F. et al. Targeted therapy for advanced salivary gland carcinoma based on molecular profiling: results from MyPathway, a phase IIa multiple basket study. Annals of Oncology, Volume 31: 412-421. https://doi.org/10.1016/j.annonc.2019.11.018.
2. Takahashi H, Tada Y, Saotome T et al. Phase II trial of trastuzumab and docetaxel in patients with human epidermal growth factor receptor 2-positive salivary duct carcinoma. *J Clin Oncol* 2019; 37: 125–134.
3. Falchook GS, Lippman SM, Bastida CC, Kurzrock R. Human epidermal receptor 2-amplified salivary duct carcinoma: regression with dual human epidermal receptor 2 inhibition and anti-vascular endothelial growth factor combination treatment. *Head Neck* 2014; 36: E25–E27.
4. Corrêa TS, Matos GDR, Segura M, Dos Anjos CH. Second-line treatment of HER2-positive salivary gland tumor: ado-trastuzumab emtansine (T-DM1) after progression on trastuzumab. *Case Rep Oncol* 2018; 11: 252–257.