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NCCN Guidelines Panel: Breast Cancer

Dear NCCN Breast Panel,

Please find a request for your review regarding Tecentriq® (atezolizumab).

Request(s):

1. Consider the recent Phase III IMpassion 130 publication on the use of Tecentriq + nab-paclitaxel in patients with first-line metastatic triple-negative breast cancer (TNBC) for inclusion into the guideline.
2. In the workup for Recurrent/Stage IV breast cancer on page BINV-18, please include determination of tumor PD-L1 status to ensure appropriate patient selection for treatment with Tecentriq.

Rationale:

The IMpassion 130 study met its co-primary endpoints of progression-free survival (PFS) in the intent-to-treat (ITT) and PD-L1-positive (PD-L1+) population for Tecentriq + nab-paclitaxel versus placebo + nab-paclitaxel. The safety profile was consistent with previously reported safety risks of the individual medicines.[1]

- Additional co-primary endpoints included overall survival (OS) in the ITT and PD-L1+ populations. The first interim OS in the ITT population was not statistically significant; however, an OS benefit was observed for the Tecentriq + nab-paclitaxel arm versus placebo + nab-paclitaxel arm in the PD-L1+ population. No formal testing was conducted for the PD-L1 positive population (statistical design details reported in the publication and Supplementary Appendix).[1]
- After a median of follow up of 12.9 months, ITT median OS was 21.3 months with Tecentriq + nab-paclitaxel and 17.6 months with placebo + nab-paclitaxel, while median OS was 25.0 and 15.5 months in PD-L1–positive patients, respectively (ITT OS HR was 0.84 [95% CI=0.69–1.02; p=0.08], and PD-L1+ OS HR was 0.62 [95% CI=0.45–0.86].[1]
- PD-L1 scoring evaluated PD-L1 expression on tumor-infiltrating immune cells (IC) from a representative tumor specimen (formalin-fixed paraffin-embedded archival or fresh pretreatment relapsed-disease tumor tissue) according to immunohistochemical testing. PD-L1 positive tumors were defined as PD-L1 expression ≥1%, and PD-L1 negative tumors were defined as expression <1%. PD-L1 scoring is reported in the Supplementary Appendix.[1]
- For patients treated with Tecentriq + nab-paclitaxel and placebo + nab-paclitaxel:
    - Serious adverse events occurred in 22.8% and 18.3%, respectively.[1]
    - Overall Grade 3 or 4 adverse events occurred in 48.7% and 42.2% while those of special interest occurred in 7.5% and 4.3%, respectively.[1]
- Please note that the dosing of Tecentriq used in the IMpassion 130 study is different than the FDA-approved dose for non-small cell lung cancer (NSCLC) and urothelial cancer (UC) listed in the U.S. Prescribing Information.
    - TNBC: 840mg administered intravenously on Day 1 and Day 15 of every 28-day cycle[1]
    - NSCLC and UC: 1200 mg administered intravenously on Day 1 and Day 21 of every 28-day cycle.[2]

Results from a Phase I study were previously reported on the use of Tecentriq + nab-paclitaxel in first-line metastatic TNBC (Arm F).[3,4] After a median efficacy follow-up of 24.4 months in all patients, the efficacy results for first-line patients were as follows: overall response rate (ORR) was 54% (95% CI: 25-81), PFS was 8.6 months (5.2-11.5), and OS was 24.2 months (11.5-not estimable). Clinical results by PD-L1

status were also reported. Grade 3-4 treatment-related adverse events occurred in 73% of patients. An additional study has been conducted to evaluate Tecentriq in triple-negative breast cancer.[5]

FDA Clearance:

- Tecentriq is not FDA-approved for triple-negative breast cancer. Please refer to the product prescribing information for the full FDA-approved indications and safety information of Tecentriq, available at:
    - https://www.gene.com/download/pdf/tecentriq_prescribing.pdf

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. Schmid P, Adams S, Rugo HS, et al. Atezolizumab and Nab-Paclitaxel in Advanced Triple-Negative Breast Cancer. N Engl J Med. E-pub Date: [published online ahead of print] October 2018. DOI # 10.1056/NEJMoa1809615.
2. Tecentriq® [package insert]. Genentech; South San Francisco, CA. 2018.
3. Adams S, Diamond JR, Hamilton EP, et al. Phase Ib trial of atezolizumab in combination with nab-paclitaxel in patients with metastatic triple-negative breast cancer (mTNBC). Presented at the American Society of Clinical Oncology 2016 Annual Meeting in Chicago, IL; June 3–7, 2016. ASCO Poster #114.
4. Pohlmann PR, Diamond JR, Hamilton E, et al. Atezolizumab + nab-paclitaxel in metastatic triple-negative breast cancer: 2-year update from a Phase Ib trial. Presented at the American Association for Cancer Research Annual Meeting in Chicago, IL; April 14–18, 2018. AACR Poster.
5. Emens LA, Cruz C, Eder JP, et al. Long-term Clinical Outcomes and Biomarker Analyses of Atezolizumab Therapy for Patients With Metastatic Triple-Negative Breast Cancer: A Phase 1 Study. JAMA Oncol. 2018. DOI# 10.1001/jamaoncol.2018.4224 [Epub ahead of print]