Genentech
A Member of the Roche Group

IMPORTANT PRESCRIBING INFORMATION

June 2018

Subject: Revision of TECENTRIQ® (atezolizumab) indication for the treatment of locally advanced or metastatic urothelial carcinoma in adults who are not eligible for cisplatin-containing chemotherapy

Dear Healthcare Provider,

Genentech, Inc., in agreement with the Food and Drug Administration (FDA) would like to inform you of a change in the prescribing information for TECENTRIQ® (atezolizumab) based on preliminary data from an ongoing clinical trial (IMvigor130) that showed reduced survival with TECENTRIQ monotherapy compared to platinum-based chemotherapy when used as first-line treatment for locally advanced or metastatic urothelial carcinoma (UC) patients whose tumors have low expression of PD-L1 (less than 5% of immune cells staining positive for PD-L1).

As a result, TECENTRIQ's first-line indication for urothelial carcinoma as monotherapy is being revised as follows (new text is bolded and italicized):

> TECENTRIQ® (atezolizumab) is indicated for the treatment of patients with locally advanced or metastatic urothelial carcinoma who:
>
> - are not eligible for cisplatin-containing chemotherapy, ***and whose tumors express PD-L1 (PD-L1 stained tumor-infiltrating immune cells [IC] covering ≥ 5% of the tumor area), or***
> - ***are not eligible for any platinum-containing chemotherapy regardless of level of tumor PD-L1 expression,*** or
> - have disease progression during or following any platinum-containing chemotherapy, or within 12 months of neoadjuvant or adjuvant chemotherapy

The use of TECENTRIQ after prior platinum-containing chemotherapy remains unchanged.

In patients already receiving TECENTRIQ who are responding to treatment and are cisplatin-ineligible, based on the treating physician's medical judgment, continuation of treatment could be considered, regardless of PD-L1 status.[1]

Patients taking TECENTRIQ for other approved uses should continue to take their medication as directed by their health care professional.

Background on the Efficacy Concern

IMvigor130 is an ongoing phase III, multicenter, randomized, placebo-controlled study comparing platinum-based chemotherapy with atezolizumab administered as monotherapy or atezolizumab in combination with platinum-based chemotherapy in patients with untreated locally advanced or metastatic urothelial

[1] See FDA Alert to Health Care Professionals and Oncology Clinical Investigators dated June 20, 2018: https://www.fda.gov/Drugs/DrugSafety/ucm608075.htm

carcinoma. IMvigor130 is enrolling patients in the first line setting who are both cisplatin eligible and cisplatin ineligible. The treatment arms are as follows:

- Arm A (atezolizumab combined with cisplatin or carboplatin and gemcitabine)
- Arm B (atezolizumab monotherapy)
- Arm C (placebo combined with gemcitabine and either cisplatin or carboplatin)

Preliminary data showed a reduced survival with Tecentriq monotherapy compared to platinum-based chemotherapy in patients with metastatic urothelial cancer (mUC) who have not received prior therapy and whose tumors have low expression of the protein programmed death ligand 1 (PD-L1) (less than 5% of immune cells staining positive for PD-L1). On 19 March 2018, the independent Data Monitoring Committee (iDMC) recommended that no new patients whose tumors have low PD-L1 expression should be recruited in Arm B. Patients already recruited in this arm were recommended to continue in the trial without treatment modification. Patients with tumors having high PD-L1 expression (greater than or equal to 5% of immune cells staining positive for PD-L1) were recommended to continue to be recruited in Arm B. Other arms of the trial (A and C) will continue as planned.

The iDMC has not noted any concerns with the adverse event profile of TECENTRIQ® in IMvigor130.

These recommendations were accepted and implemented by Genentech, Inc., and were also communicated to the FDA and EMA. Both the FDA and the EMA issued Alerts to Health Care Professionals and Oncology Clinical Investigators about this issue:

- https://www.fda.gov/Drugs/DrugSafety/ucm608075.htm
- http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/news/2018/05/news_detail_002964.jsp&mid=WC0b01ac058004d5c1

Reporting Adverse Events

Healthcare providers and patients are encouraged to report adverse events in patients taking TECENTRIQ® to Genentech at 1-888-835-2555. You are encouraged to report negative side effects of prescription drugs to FDA.

Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

Company Contact

If you have any questions or concerns about the information contained in this letter or the safe and effective use of TECENTRIQ®, you may contact the Genentech Medical Communications Department at 1-800-821-8590.

This letter is not intended as a complete description of the indications, benefits, and risks associated with the use of TECENTRIQ®. Please refer to the full prescribing information, including the Medication Guide. These can be found online at https://www.gene.com/download/pdf/tecentriq_prescribing.pdf.

Yours sincerely,

Lance Baldo, M.D.
Head of U.S. Medical Affairs