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Submitted by:
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NCCN Guidelines Panel: Bladder Cancer

On behalf of Genentech, I respectfully request the NCCN Bladder Cancer Guideline Panel to consider the following enclosed Supplementary Appendix of the Phase II trial (IMvigor210) for Tecentriq™ (atezolizumab) in the treatment of patients with metastatic urothelial carcinoma (mUC).

- Rosenberg JE, Hoffman-Censits J, Powles T, et al. Atezolizumab in patients with locally advanced and metastatic urothelial carcinoma who have progressed following treatment with platinum-based chemotherapy: a single-arm, multicentre, Phase 2 trial [supplementary appendix appears online]. Lancet 2016;387:1909-20.

Specific Changes:
In addition to your recent inclusion of Tecentriq as an option for second-line locally advanced or mUC, please consider:

1. Tecentriq as a treatment option for patients with locally advanced or mUC who have progressed within 12 months of neoadjuvant or adjuvant platinum chemotherapy, which is consistent with the FDA-approved indication and the design of the Phase II IMvigor210 study.
2. Reconsider the statement "No standard therapy exists in this setting" for second-line systemic therapy.

FDA Clearance:
Tecentriq was recently approved by the FDA for the treatment of patients with locally advanced or mUC who:

- Have disease progression during or following platinum-containing chemotherapy
- Have disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy

Please refer to the Tecentriq prescribing information for the full FDA-approved indication and safety information.

- Full Tecentriq prescribing information available at: http://www.gene.com/download/pdf/tecentriq_prescribing.pdf

Rationale:
In the "Principles of Systemic Therapy" section (BL-H; 2 of 4) of the Bladder Guidelines, Tecentriq is not listed as a treatment option for first-line therapy in a subset of patients with locally advanced or metastatic disease. In the Phase II IMvigor210 trial, 18% (n=57) of patients in Cohort 2 (label-enabling) received previous neoadjuvant or adjuvant platinum chemotherapy with first progression within ≤12 months.[1] In a subgroup analysis with a median follow-up of 11.7 months, these patients demonstrated an overall response rate (ORR) of 23% per the RECIST v1.1 Independent Review and 26% using the Modified RECIST Investigator Assessed ORR.[2] Safety results were not reported for these patients. Based on a median follow-up of 14.4 months, the Tecentriq prescribing information (page 13) results are consistent with the published results (n=59; ORR: 22%; 95% CI: 12.3%-34.7%).[2] Furthermore, the FDA-approved

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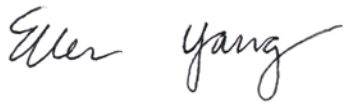
indication statement of the US prescribing information specifies that this patient population is eligible for Tecentriq.

In the section “Second-line systemic therapy for locally advanced or metastatic disease” (BL-H; 2 of 4), the statement “No standard therapy exists in this setting” is directly followed by a table that includes "Standard regimens". The similar phrases used sequentially appear to be in contradiction.

If you have any questions, please contact me directly at (440) 292-5535 or by email at yang.ellen@gene.com.

Respectfully submitted,



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References:

1. Rosenberg JE, Hoffman-Censits J, Powles T, et al. Atezolizumab in patients with locally advanced and metastatic urothelial carcinoma who have progressed following treatment with platinum-based chemotherapy: a single-arm, multicentre, Phase 2 trial [supplementary appendix appears online]. Lancet 2016;387:1909-20.
2. Tecentriq® [package insert]. South San Francisco, CA: Genentech, Inc; May 2016. http://www.gene.com.