Corrected Net Health Benefit Calculations for Enzalutamide Using ASCO Value Framework Guidelines and NCCN Evidence Blocks

We write this letter to bring attention to potential errors in net health benefit (NHB) calculations presented by Shah-Manek et al. in their article “Value Frameworks for the Patient-Provider Interaction: A Comparison of the ASCO Value Framework Versus NCCN Evidence Blocks in Determining Value in Oncology” from the June 2017 supplement to the *Journal of Managed Care and Specialty Pharmacy (JMCP)*.¹

The authors assessed the revised ASCO Value Framework 2.0 (AVF) and NCCN Evidence Blocks (NEB) for enzalutamide (vs. placebo) in settings before and after chemotherapy for metastatic castration-resistant prostate cancer (mCRPC).^{2,3}

From the prechemotherapy pivotal study, the toxicity score for enzalutamide was reported as -4.2; however, Grade 1-2 adverse events (AEs) from the PREVAIL trial were not included in the published calculation.^{1,2} AVF guidance indicates that the toxicity calculation should include all AEs.⁴ Based on AEs reported in at least 10% of enzalutamide patients, at a rate that was $\geq 2\%$ compared with the placebo arm, we inferred “Grade 1-2” AEs as the difference between “All Grades” and “Grade ≥ 3 .” Our calculation produced a revised toxicity score of -2.78 for enzalutamide.

The authors also reported zero bonus points for enzalutamide in the tail-of-the-curve score. AVF guidance states: “Bonus points are awarded if the test regimen results in at least a 50% relative improvement in percentage of patients alive at a time point that is at twice the median overall survival or progression-free survival (PFS) point for the control regimen and if at least 20% of patients receiving the control regimen are alive at this time.”⁴ In the PREVAIL trial, enzalutamide achieved $>50\%$ relative improvement in radiographic PFS (rPFS) at 7.8 months, and trial results demonstrated twice the median rPFS of the placebo cohort (83% vs. 35%).² Therefore, enzalutamide should be awarded 16 bonus points for demonstrating long-term disease control in mCRPC. These toxicity and bonus point corrections would revise the prechemotherapy NHB score from 44.8 to 62.2 for enzalutamide.

Finally, the authors present new economic calculations derived from NHB scores. A “cost per unit of NHB” and “percentage of NHB score” were reported “to normalize results for comparisons.”¹ This approach is not consistent with AVF guidance and does not take into account the limitations of the NHB as an effectiveness measure of health benefit. Scoring errors in the reported NHB calculations are also carried into these unvalidated economic measures, potentially misleading

decision makers in understanding the relative value of alternative mCRPC therapies.

In conclusion, we appreciate the attempt made by Shah-Manek et al. to compare AVF and NEB, but we believe that the NHB score for enzalutamide in the mCRPC setting before chemotherapy should be revised to 62.2. *JMCP* is an important source of contemporary information for practice, policy, and research in managed care pharmacy, and we believe it is important to prominently update the previously published article in light of this information.

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DISCLOSURES

This research was funded by Astellas Pharma and Medivation, which was acquired by Pfizer in 2016. Astellas Pharma and Medivation are the co-developers of enzalutamide. Flanders, Brown, Massoudi, and Schultz are employees of Astellas Pharma. Ramaswamy is an employee of Pfizer and holds stock in Johnson & Johnson. Flanders holds stock in Johnson & Johnson, AbbVie, and Abbott Labs.

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