Rebuttal: CON Position

Should Microalbuminuria Ever Be Considered as a Renal Endpoint in Any Clinical Trial?

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A correlate does not a surrogate make' [1] is a very apt quotation for this debate. The data analyzed by Lambers Heerspink and De Zeeuw in the accompanying debate primarily show a correlation between the development of overt nephropathy (in type 2 diabetes) and/or a decline in GFR with persistence of microalbuminuria (MA; in type 2 diabetes, hypertension with CKD in African Americans and essential hypertension). None of the studies was specifically designed to evaluate prospectively the effect of altering MA on more clinically relevant renal endpoints such as advanced CKD or ESRD. Each of the studies analyzed has the potential of confounding, particularly in relation to concomitant changes in systolic blood pressure. Thus, the third criterion of the International Conference of Harmonization dealing with surrogates has not been unequivocally fulfilled. We have learned that surrogate biochemical/hematological endpoints do not always meet their desired utility in renal diseases (such as treating anemia in CKD or lowering cholesterol in ESRD). If I were given a choice, I would prefer a decline in blood pressure to a decline in MA as a surrogate mea-

sure. This is based on currently available data in renal disease (including diabetes mellitus). The use of MA as a surrogate renal endpoint in intervention trials should come with the label – 'use with caution'.

Disclosure Statement

R.J. Glassock is a consultant for Vifor Pharmaceuticals, Fibro-Gen, Novartis, Genentech: Quest Diagnostics/Nichols Institute, Science Partners, QuestCor, Gilead Sciences, Wyeth, Bio-Marin, Bristol-Myers-Squibb, Lighthouse Learning. He has ownership interests in La Jolla Pharmaceuticals, Inc. (400 shares of common stock – values <USD 500) and Reata, Inc. (limited partnership). He is also a member on the Board of Directors/Advisory Boards of the University Kidney Research Organization (UKRO) and Los Angeles Biomedical Institute.

Reference

- 1 Fleming TR, DeMets DL: Surrogate endpoints in clinical trials: are we being misled? *Ann Intern Med* 1996;125:605–613.