

Sixth Circuit Confirms Experts Cannot Infer Causation from Association Based on Single Study to Exclusion of Contrary Studies Without Explanation

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“[The] sin was methodological inconsistency[.]” The Sixth Circuit recently affirmed an MDL court’s exclusion of the plaintiffs’ only general causation expert and subsequent grant of summary judgment in *In re Onglyza (Saxagliptin) & Kombiglyze (Saxagliptin & Metformin) Products Liability Litigation*, No. 22-6078, ---F. 4th---, 2024 WL 577372, at *1 (6th Cir. Feb. 13, 2024). Among other issues, the court found that the expert’s reliance on a single, un-replicated epidemiological study to infer causation, to the exclusion of all other contrary studies involving human data, without adequate explanation, rendered his testimony unreliable.

The litigation involved claims that type 2 diabetes drugs containing saxagliptin caused heart failure. The genesis of the claims goes back to 2008 when the FDA urged additional clinical studies examining diabetes drugs and cardiovascular risks. *Id.* That resulted in a randomized controlled trial called the SAVOR study (Saxagliptin Assessment of Vascular Outcomes Recorded in Patients with Diabetes Mellitus). *Id.*

The SAVOR study found no statistically significant difference between saxagliptin and a placebo on either the primary or secondary endpoints for heart failure. *Id.* It did show a statistically significant result, however, on *hospitalizations* for heart failure. *See id.* at *2. The study concluded that the association was “unexpected” and warned that the results could be a “false positive” and “a class effect should not be presumed.” *Id.* Even so, the *Onglyza & Kombiglyze* MDL followed.

After a general causation *Daubert* hearing, the district court excluded the plaintiffs’ expert as unreliable.

Significantly, the court rejected the expert’s sole reliance on the SAVOR study to the exclusion of all other human clinical studies, including four observational studies conducted *after* SAVOR that found no association between saxagliptin and heart failure. The expert dismissed the four observational studies as “generally limited due to issues related to confounding” but, as the court explained, the expert pinpointed no specific issues or confounders. *Id.* at *4. The court explained that neglecting “to adequately account for contrary evidence is not reliable or scientifically sound.” *Id.* (internal citations omitted). The court also found problematic that the expert failed to adequately explain how he inferred a causal relationship from a study that drew a conclusion about association but not causation. *Id.* at *5. By doing so, the court explained, the expert “drew ‘unauthorized conclusions from limited data—conclusions the authors of the study d[id] not make,’ betraying a ‘lack of scientific rigor.’” *Id.* at *4 (internal citations omitted). The court also found the expert’s opinion unreliable because of his unqualified interpretation of animal studies, cherry-picking

data linked to a different kind of second-line diabetes medication, and inconsistent application of the Bradford Hill criteria.^[1] *Id.* at *6.

The Sixth Circuit affirmed the district court’s decision, finding that the court did not abuse its discretion by concluding that the expert’s “methodological inconsistency” left his testimony unreliable under Federal Rule of Evidence 702. *Id.* at *5.

This decision reinforces the importance of comprehensive and rigorous analysis of epidemiological evidence to support a reliable methodology. If an expert improperly disregards contrary studies or interprets data well beyond a study’s conclusions to support a finding of general causation, their testimony may be excluded.

Law clerk Junda He also contributed to this blog post.

^[1] For additional discussion of the Bradford Hill criteria as it relates to expert methodologies, please see Winston’s previous analyses [here](#), [here](#) and [here](#).

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