

# Exhibit 358

# **Rebuttal Expert Report**

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I have received a copy of the expert reports of Max Kates, M.D., regarding Mark Cagiano and Jimmy Laramore. Dr. Kates concludes that Mr. Cagiano's upper tract urothelial carcinoma was most likely caused by idiopathy and, to a lesser extent, his body-mass index, and not his exposure to the water at Camp Lejeune. Dr. Kates concludes that Mr. Laramore's bladder cancer diagnosis was most likely caused by his smoking history and, to a limited degree, his occupational exposure from trucking<sup>1</sup>, but could not rule out idiopathy as a possibility.

I disagree with Dr. Kates' identification of idiopathy as a potential risk factor for Mr. Cagiano and Mr. Laramore, and I disagree with his methodology of incorporating idiopathic causes despite known risk factors, including the exposure to the water at Camp Lejeune. Finally, I agree that Mr. Cagiano's BMI is unlikely to have caused his upper tract urothelial carcinoma.

### **I. Bladder Cancer is Rarely Idiopathic**

The National Cancer Institute defines idiopathic to mean "a disease of unknown cause."<sup>2</sup> Here, it is important to stress that an unknown cause does not mean there is no cause; an unknown cause just means that we do not know of the cause.<sup>3</sup>

Dr. Kates opined that 40% of bladder cancer cases cannot be attributed to a known risk factor and are thus idiopathic because the causes either are spontaneous or not yet known. Dr. Kates' sole citation for his claim that 40% of bladder cancer cases are idiopathic is to *Burger et al*, Epidemiology and Risk Factors of Urothelial Bladder Cancer. Eur Urol. 2013 Feb 1;63(2):234–41. I have reviewed this publication, and it does not address idiopathic urothelial carcinoma or upper tract urothelial carcinoma. Instead, *Burger et al* state that "most bladder tumors are associated with an acquired carcinogen exposure[.]" Without specific scientific support for his claim, Dr. Kates may be relying on anecdotal estimation of the patients he sees in his practice, and while such anecdotal evidence may be informative, it is ill-suited to elevate idiopathy alongside established risk factors in a differential diagnosis.

Furthermore, other reliable studies have suggested that the percentages of idiopathic bladder cancer are far lower than what Dr. Kates suggests. For example, Al-Zalabani et al<sup>4</sup> (2016) found that 81.8% of bladder cancer diagnoses were attributable to modifiable risk factors and 7% attributable to genetic factors. Further, as Al-Zalabani notes, modifiable and genetic risk factors do not include medical conditions, which would include chronic bladder infections or other medical conditions. This means that at

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<sup>1</sup> I address this risk factor in my February 7, 2025 report and reiterate my position on Mr. Laramore's potential trucking occupational exposure.

<sup>2</sup> <https://www.cancer.gov/publications/dictionaries/cancer-terms/def/idiopathic> (last visited May 12, 2025)

<sup>3</sup> Dr. Kates defines "idiopathy" to include both unknown causes and spontaneous causes; however, Dr. Kates does not suggest that Mr. Laramore or Mr. Cagiano's diagnoses were spontaneous, or that bladder cancer is ever spontaneous.

<sup>4</sup> Abdulmohsen H. Al-Zalabani et al. Modifiable risk factors for the prevention of bladder cancer: a systematic review of meta-analyses. Eur J. Epidemiol 2016 31:811-851 doi: 10.1007/s10654-016-0138-6. Epub 2016 Mar 21.

most (but probably less) 11.2% of bladder cancer diagnoses would be from potentially unknown risk factors.

While Dr. Kates dismisses toxic exposures as an "oversimplification of the disease", urothelial carcinoma (the predominant type of bladder cancer) "is highly associated with chemical exposure..." Saginala et al (2020); see also Halaseh et al (2022)<sup>5</sup> ("The urothelial cells that line the bladder and urinary tract are always exposed to environmental chemicals that could cause mutations...Most bladder cancers may be dated directly to exposure to environmental and occupational toxins..."). Similarly, upper tract urothelial carcinoma shares the same types of cells as those that line the bladder – urothelial cells – that would be subjected to carcinogens. Even as Dr. Kates identifies a genetic component in some bladder cancer diagnoses, one of the studies he cites – Kiemeny (2008) – notes the role of exogenous carcinogens in the development of bladder cancer. In the case of Mr. Cagiano and Mr. Laramore they both had exposures to contaminated water in Camp Lejeune and thus have exposure that is linked to their urothelial carcinoma diagnosis and thus idiopathic urothelial carcinoma is not an appropriate conclusion in their cases.

**II. It is Methodologically Unsound to Rule In Unknown Causes of Bladder Cancer when an Individual has Known Risk Factors**

I respectfully disagree with Dr. Kates' inclusion of idiopathy as part of the differential etiology prior to analyzing known risk factors. While it is certainly true that an individual's bladder cancer diagnosis may be unknown, I disagree with Dr. Kates insofar as he would include an unknown potential cause alongside known potential causes for an individual's bladder cancer diagnosis. For bladder cancer in particular, when the vast majority of causes are attributable to a known risk factor, elevating an unknown cause alongside known causes dilutes the differential etiology and produces false results. Only when all the risk factors for a disease have been reasonably ruled out then the cause of development of the disease is labeled "idiopathic", but such a label is not achieved until after the application of known risk factors. In my clinical work, it makes little sense to include an unknown cause as an explanation to a given disease while there are other risk factors that can plausibly explain its etiology. Thus, it is important to make sure that a thorough history is performed in helping to develop the underlying cause of disease; of course, the failure to obtain a full and complete history or the patient's own limited understanding of potential exposures serve as limits to identifying risk factors. In that sense, reaching a conclusion that an individual's bladder cancer is attributable to an unknown cause depends somewhat on the ability to identify and elicit correct information from the individual. Here, both Mr. Cagiano and Mr. Laramore were exposed to the water at Camp Lejeune that contained carcinogens associated with bladder cancer and thus it is inappropriate to conclude that their diagnoses are idiopathic.

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<sup>5</sup> Halaseh SA, Halaseh S, Alali Y, Ashour ME, Alharayzah MJ. A Review of the Etiology and Epidemiology of Bladder Cancer: All You Need To Know. Cureus. 2022 Jul 27;14(7):e27330. doi: 10.7759/cureus.27330. PMID: 36042998; PMCID: PMC9411696.

**III. Mr. Cagiano's BMI is Unlikely a Cause of his Upper Tract Urothelial Carcinoma**

Dr. Kates opined that obesity played a "lessor role" in contributing to Mr. Cagiano's upper tract urothelial carcinoma than idiopathy, but he could not rule it out. I agree that there is a lack of clear and coherent data regarding the association between BMI and upper tract urothelial carcinoma and thus it would not constitute a significant risk factor.

**IV. Conclusions regarding etiology of diagnosis**

After review of Mr. Cagiano's and Mr. Laramore's records, evaluation of their previous chemical exposures at Camp Lejeune and their other risk factors, it is my opinion that Mr. Cagiano's and Mr. Laramore's diagnoses were at least as likely as not to be caused by their exposure to the water at Camp Lejeune and not from idiopathic origin or, in Mr. Cagiano's case, from increased BMI.