Exhibit 436

Report of Walter Stadler, M.D., FACP

Howard v. United States, 7:23-cv-00490 (E.D.N.C.)

Walter Stadler

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Walter Stadler, M.D., FACP

April 8, 2025

Contents

I. Expert Background and Qualifications

I am a genitourinary oncologist focused on care and treatment of patients with kidney, bladder, prostate, and testicular cancer. Full details of my academic and clinical qualification are detailed in my CV. Briefly, I received my MD from the Yale University School of Medicine in 1988, followed by an internship/residency at the University of Chicago affiliate Michael Reese Hospital and then a fellowship in Hematology/Oncology at the University of Chicago that I completed in 1994. I have been a faculty member at the University of Chicago for most of my career but have recently taken a position as Chief Clinical Officer for City of Hope, Chicago where I will continue my clinical role as genitourinary oncologist as well as my academic role conducting and leading genitourinary cancer clinical trials. I will also take on administrative responsibilities for clinical operations. I have held a number of additional administrative roles including Section Chief for Hematology/Oncology, Deputy Director for the University of Chicago Comprehensive Cancer Center and Associate Dean for Clinical Science Research, Clinical Trials.

I have conducted research on novel treatments and management of patients with genitourinary cancer and have authored over 250 peer-reviewed original manuscripts and over 120 reviews, chapters, and commentaries in this field (see CV, Attachment A). I have specifically contributed to the development of gemcitabine in bladder cancer, vascular endothelial growth factor receptor (VEGFR) inhibitors in renal cancer, and hormonal therapies in prostate cancer. I routinely give presentations at national and international meetings regarding these malignancies.

From a clinical perspective, I continue to consult and manage patients with these diseases for approximately 30% of my time generating greater than the 65th percentile in prorated relative value units (RVU's) for my specialty (i.e. corrected for a full-time clinician, my clinical activity is equal to or greater than 65% of American oncologists). I have been recognized as a clinical expert through Castle Connolly Top Doctors every year since 2007.

I have testified as an expert witness at trial or deposition in the past four years only in support of Sandoz and other generic companies in their effort to invalidate Sanofi cabazitaxel patents (*Sanofi-Aventis U.S. LLC v. Sandoz Inc.*, Civ. No. 20-804-RGA, D. Del.). My hourly rate for my work here is $750/hr.

II. Basis of Opinions

My opinions are based on my extensive experience, standard guidelines from the National Comprehensive Cancer Network (NCCN), as well as generally accepted medical literature. For much of the latter, and unless referenced otherwise, I used information summarized in available textbooks including UpToDate, which is the most widely referenced source for practicing clinicians and for which I have acted as an Editor, and Holland-Frei Cancer Medicine, 10th edition, one of the major textbooks of oncology for which I also contributed a chapter. Other specific literature references are in the detailed report below and listed under References.

I have reviewed case and medical records provided by counsel including military service records, medical provider notes, and the deposition of plaintiff (2/16/24), his daughter (5/7/24), his former law enforcement partner (5/7/24), as well as the depositions of Drs. Kelly Miller (5/29/24), Ahmad Shabsigh (5/31/24), and Saba Qureshi (7/29/24). I have also reviewed and rely upon the United States's general causation reports (Goodman Report; Shields Report, Lipscomb report), the United States's exposure

report (LaKind Report), and the United States's risk assessment report (Bailey Report). Finally, I have reviewed the expert depositions of Drs. Bove and Savitz.

A complete list of the facts and data I considered are listed in Attachment B, which will be provided separately.

I reserve the right to supplement the opinions offered here as appropriate, including if new information is made available to me.

III. Summary of Opinion

It is my opinion that Mr. Howard's renal cancer is most likely idiopathic in origin and unlikely related to any Camp Lejeune exposures. It is furthermore my opinion that Mr. Howard is most likely cured of his renal cancer and the consequences of treatment are minimal. More specifically, the nephrectomy has not led to any significant impacts on his kidney function, nor has it materially impacted the risk of future renal dysfunction. Furthermore, his renal cancer has had and will likely have no impact on Mr. Howard's survival and its treatment is unrelated to his subsequent hypothyroidism or non-Hodgkin's lymphoma and overall health status.

IV. Clinical Background

A. Oncogenesis

Generally, cancer is a disease that arises from a series of genetic errors, also known as mutations, within normal tissue. Most normal tissue typically regenerates through division and replication of normal cells. While this almost always occurs faithfully, amongst the billions of base pairs making up the DNA of a human cell and the trillions of cells in the human body, errors do occur. While the vast majority of these genetic mutations are corrected or eliminated, occasionally a cell with such mutations persists and can then go on to develop additional genetic mutations, which leads to ongoing replication and division without appropriate controls. Additional mutations and alterations can then give the cells the ability to move (or metastasize) to other areas of the body. Notably, there are a number of biological processes, including the immune system, that can eliminate these mutated cells. The complex interplay between accumulation of mutations and failure to eliminate mutated cells is scientifically known as oncogenesis and in patients is the disease known as cancer (see for example (Hanahan and Weinberg)).

It follows that anything that increases the frequency of mutations or inhibits the corrective mechanisms increases the risk for cancer. The single most common factor is age. Errors in cell replication are rare and generally must accumulate to cause cancer in a patient and this simply takes time. Additionally, error correction mechanisms and the immune system become less robust as we grow older.

Exposure to certain environmental toxins known as carcinogens, the most relevant being exposure to tobacco smoke, can also increase the risk of cancer. Toxin exposure can increase the rate of genetic mutations and thus the risk of developing a cancer. Importantly, it is both the amount of toxin exposure (typically known as "dose") and the duration of exposure that determines both the odds of developing cancer causing mutations and the development of cancer (Hofseth, Weston, and Harris). The science of toxin exposure and subsequent risk of developing cancer is generally conducted by epidemiologists and toxicologists.

While toxin exposure can increase the risk of cancer, it is important to specify that this simply increases the odds of developing this disease; not all exposed individuals will develop cancer and most individuals with cancer will not have a known exposure history (see Goodman report for further details).

Some patients are born with, or inherit, certain genetic abnormalities that make them more likely to develop a cancer. These genetic abnormalities, known as germ-line mutations, are typically tumor suppressor genes whose deletion is mechanistically related to oncogenesis. More importantly, these inherited predisposition syndromes make it much more likely that a mutated cell can accumulate the additional necessary mutations to become a clinical cancer. For example, patients that inherit a mutation of the Von-Hippel-Lindau (VHL) gene have up to a 45% risk of developing renal cancer in their lifetime (Binderup et al. 2022) as opposed to a 1.4% – 2.3% risk in the general American population (Siegel, Giaquinto, and Jemal 2024). Of note these predisposition syndromes are typically organ specific insomuch as patients with these inborn errors are more susceptible to some, but not necessarily all cancers. For example, patients born with a mutation in the VHL gene are at a higher risk of developing renal cancer, hemangioblastomas, pheochromocytomas, and pancreatic neuroendocrine tumors, but not other cancers such as upper tract urothelial cancer. Patients with such predisposition syndromes often develop multiple cancers in the same organ, with a classic example once again being the multiple independent clear cell renal cancers in patients with germ-line VHL mutations.

Finally, there are multiple families with specific cancers in multiple family members, without any common environmental exposure, but in whom a germline mutation has not been discovered. Therefore, there are almost certainly undiscovered and undescribed genetic predisposition mutations or syndromes and discovery of new cancer predisposing genes is an active area of scientific research (see for example (Roberts et al. 2016).

Chronic infection or inflammation has also been consistently linked to a number of different cancers. The scientific explanation for this is a bit more obscure, but two explanations have been offered (Zhao et al. 2021). First, the immune system produces a number of molecules designed to kill invading organisms and these substances can damage or mutate normal cells as well. As with toxin exposure the duration of the inflammation is critical. Second, the presence of chronic inflammation within a tissue or organ paradoxically leads to an immunosuppressive microenvironment, or in other words an environment in which the immune system is unable to function normally. This is critical because there is increasing evidence that the immune system is largely responsible for eliminating mutated cells that are destined to form a cancer. Thus, in a chronically inflamed tissue not only is the aforementioned rate and risk of developing cancer-causing mutations increased, the body's ability to eliminate such cells is compromised.

The above discussion emphasizes that development of cancer in any one individual is a random event that can occur in anyone. Certain clinical conditions or exposures can increase the odds of this random event (i.e. "cancer") occurring, but no one individual is absolutely protected or predestined to develop a cancer. Additionally, the increased odds for developing a cancer from any one condition can be low, modest or very high. Importantly, the difference between increased odds and absolute risk must be recognized. For example, if the odds of developing a specific cancer are 1/1000, even a doubling of risk means that the odds now are 2/1000 (see also Goodman report). Further, the studies determining these risks generally apply to a population and do not necessarily reflect the increased risk in an individual

patient, and more importantly do not necessarily reflect whether that factor (like a toxic exposure) is causative in that specific patient.

Finally, given these issues it must be recognized that the exact etiology, or even the most likely etiology, of any specific cancer in any one individual can be difficult or impossible to ascertain. As a result, the cause for the vast majority of cancers is idiopathic (i.e. unknown).

B. Kidney (Renal) Cancer

Kidney cancer is generally described as a single entity in broad epidemiologic studies (e.g. (Siegel, Giaquinto, and Jemal 2024)); however, it is critical to note that this broad description represents a variety of distinct malignancies composed of multiple histologic subtypes arising from the kidney. The diagnosis of a cancer is typically based on the appearance of the tissue (from a biopsy or surgical specimen) under the microscope as assessed by an expert pathologist. Different cancers have different appearances, but these differences may be quite subtle. More recently, specialized staining and molecular analyses has clarified that cancers that were once thought to be a single entity, or disease, are really composed of multiple separate and distinct cancers, each with its own causative factors, prognosis, and treatment.

The most common cancers arising in the kidney are upper tract urothelial cancer (UTUC) and renal carcinoma (also known as renal cell cancer). The latter is further subdivided into over 20 distinct histologies (Gansler et al. 2018; Moch et al. 2022). The most common renal carcinoma subtype, comprising approximately 70% of all renal cancers, is clear cell (or conventional) renal carcinoma (Gansler et al. 2018). The next most common is papillary renal cancer comprising 10-15% of renal cancers, which traditionally was subdivided into “Type I” and “Type II”, but more recent studies demonstrate that this subclassification masks an even greater number of molecular defined cancers (Moch et al. 2022). More rare renal cancer subtypes typically comprising <5% of cases include chromophobe, collecting duct, and medullary renal cancers. Some subtypes, such as clear cell papillary, have only recently been recognized and described.

There are approximately 82,000 new cases of renal cancer in the United States annually, occurring typically in the sixth to eighth decade of life with a median age of 65 (NCI 2024a). Based on this SEER data, the incidence of renal cancer in men <50 is 5.5/100,000/year and 90.4/100,000/year in men 65 and older. It is approximately two times more common in men than in women. Overall, the lifetime risk for developing kidney cancer in men is about 1 in 43 (2.3%) and for women is about 1 in 73 (1.4%) (Siegel, Giaquinto, and Jemal 2024). The incidence of renal cancer has been increasing. The etiology for this increased incidence rate is unknown but may be partially explained by increased detection of small asymptomatic cancers.

Established etiologic factors for renal cancer that I have considered are (1) obesity; (2) smoking; (3) hypertension; (4) chronic kidney disease; (5) diabetes; (6) occupational exposures to cadmium, asbestos, petroleum byproducts, and trichloroethylene; and (7) heavy use of over the counter analgesics [See also (Scelo and Larose 2018) and Goodman report]. Other recognized risk factors that I have considered based on the above description of oncogenesis are (8) genetic predisposition syndromes; and (9) chronic infection and inflammation.

1) Obesity. The relative risk of developing renal cancer for obese individuals is reported as 1.97 (CI: 1.56 – 2.50), with risk increasing with body mass index (BMI) (Adams et al. 2008). Other studies report relative risks from 1.2 to 3.0. High BMI has been estimated to be responsible for 29% of all incident renal cancers (Safiri et al. 2020).

2) Smoking is an established risk factor, for which the relative risk in current smokers and former smokers are 1.36 (CI: 1.19-1.56), and 1.16 (CI: 1.08-1.25), respectively (Cumberbatch et al. 2016; Tsivian et al. 2011).

3) Hypertension is an established risk factor with a relative risk of 1.67 (CI: 1.46-1.90) (Hidayat et al. 2017)

4) Chronic kidney disease is a risk factor, especially in patients with end-stage kidney disease and those that develop cystic disease as a complication of long term dialysis (El-Zaatari and Truong 2022; Truong et al. 1995). Some studies suggest that less severe chronic kidney disease may also be associated with a slight increased risk of renal cancer with a relative risk of 1.81 (CI: 1.51 – 2.17) for patients with grade 3b renal dysfunction (see below for definitions) (Lowrance et al. 2014).

5) Diabetes is associated with development of renal cancer but has been difficult to disentangle from typically concomitant obesity and hypertension. Nevertheless, some studies do suggest an independent contribution with a relative risk of 1.12 (CI: 0.99 – 1.27) to 1.29 (CI: 1.05 – 1.58) (Larsson and Wolk 2011).

6) Occupational exposures to cadmium, asbestos, and petroleum byproducts, and trichloroethylene has been associated with renal cancer. Studies of occupational exposure oftentimes do not distinguish between specific chemical exposures making it more difficult to assign causation (Mandel et al. 1995). The specific chemical most strongly associated with renal cancer is trichloroethylene used as a metal cleanser and degreaser, which confers a relative risk of 1-2, but only in occupational settings with high cumulative exposures [See Goodman report for further details].

7) Heavy use of over the counter analgesics have also been associated with development of renal cancer, but the associations have been inconsistent across different studies implicating or not implicating acetaminophen for example (Cho et al. 2011; Karami et al. 2016). Additionally, statistically significant associations have generally been reported with more than 10 years of regular (more than 7 tablets weekly) use (Cho et al. 2011). Phenacetin, the agent with the strongest epidemiological data (Antoni et al. 2014), is associated with upper tract urothelial cancer UTUC and has generally not been available in the United States.

8) Genetic predisposition syndromes for renal cancer have been identified, but most of these are rare with Von-Hippel-Lindau disease (VHL), occurring in approximately 1/27,000 – 1/43,000 live births, being most common and the one associated with clear cell renal cancer (Binderup et al. 2022). As noted above, patients with genetic predisposition syndromes

often develop multiple independent cancers in the kidney, which is extremely rare in renal cancers not due to a genetic predisposition syndrome.

9) Chronic infection and inflammation is considered a common etiologic factor in many cancers. Inflammatory conditions associated with renal cancer include chronic hepatitis C, with a relative risk of 1.77 (CI: 1.05 – 2.98) (Gordon et al. 2010), and a history of kidney stones, which are often associated with infection, with a relative risk of 1.41 (CI: 1.11 – 1.80) for renal cancer only in men and a relative risk of 2.14 (CI: 1.35 – 3.40) for urothelial cancer across both sexes (Cheungpasitporn et al. 2015).

Despite multiple potential etiologies, the major factors are obesity for which the population attributable risk in North America is approximately 29% and smoking for which the attributable risk is approximately 18% (in other words the fraction of renal cancer patients for whom obesity and smoking is a contributing risk factor for their renal cancer), with the population attributable risk for all other factors, including environmental toxin exposure, being negligible (Safiri et al. 2020). Notably many patients have multiple risk factors such as smoking, obesity, diabetes, and hypertension, since these factors tend to occur together, making assignation of causation for any one factor impossible in such cases. Finally, and as discussed above for cancer in general, risk factors increase the odds of developing a cancer, but it is not possible to distinguish the causative roles, if any, of specific risk factors in an individual patient. As such, the cause or etiology for most patient's specific cancer is unknown ("idiopathic" in medical parlance).

Historically, the most common presenting symptoms for renal cancer are gross hematuria i.e. visible blood in the urine, an abdominal mass noted by the patient or their physician, pain, and weight loss. The latter three are typically the result of locally advanced or metastatic disease and an increasing number of renal cancers are diagnosed incidentally during imaging for an unrelated cause (i.e. detection of a renal mass on a radiologic procedure performed for other indications). This in turn likely explains at least some of the increased population incidence of renal cancer noted above.

Notably, there is a long list of possible causes for gross hematuria, including kidney stones, glomerulonephritis (a specific class of non-malignant kidney diseases), infection, and exercise induced hematuria such that the majority of individuals with hematuria do not have a urinary tract malignancy.

Treatment of localized renal cancer typically involves radical nephrectomy or partial nephrectomy in which only the cancer is removed sparing normal kidney tissue. A radical nephrectomy involves complete removal of the kidney and occasionally the adjacent adrenal gland and some lymph nodes. An issue with complete removal of the kidney is that there is some decrement in renal function, which can have its own health impacts, especially in patients with pre-existing renal disease (see below). As such, partial nephrectomy in which only the cancerous tumor is removed, sparing normal renal tissue, has been increasingly utilized. The choice of radical versus partial nephrectomy is generally based on the size and location of the cancer within the kidney, as well as baseline renal function and experience of the surgeon.

Traditionally, partial or radical nephrectomy have been performed utilizing large abdominal incisions with techniques termed as "open." While this approach is still required for technically more complex resections, the vast majority of nephrectomies are currently performed using a typically robotic,

laparoscopic approach. The lack of a large incision makes surgical recovery more rapid and decreases the risk of some complications such as abdominal wall hernias (Zhou and Carlson 2018). Occasionally, ablative techniques using radiofrequency, ultrasound, or freezing are also utilized, especially in patients in whom surgery is considered too risky. The exact technical approach to treatment of the primary renal cancer is based on surgical experience, body habitus (the shape and size of a person's body) and tumor location and in general has limited to no impact on long term cancer outcome.

Following nephrectomy or partial nephrectomy, additional adjuvant systemic therapy to prevent recurrence (including chemotherapy and immunotherapy) has not been utilized; although, some more recent studies suggest that there may be some value to adjuvant immunotherapy (Choueiri et al. 2024). Recommended standard follow up and monitoring of renal cancer following nephrectomy or partial nephrectomy is CT scans of the chest, abdomen and pelvis every 6 months for 3 years followed by annual scans up to 5 - 6 years post-surgery. Although renal cancer can occasionally recur beyond 5 and even beyond 10 years, routine scanning beyond 5 or 6 years is generally not recommended.

Prognosis and survival of localized renal cancer is highly dependent on stage and renal cancer subtype. Staging is based on both extent and size of the tumor within the kidney, presence of spread to lymph nodes, and presence of metastatic disease (TNM system).

Primary tumor (T)	
T category	**T criteria**
TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
T1	Tumor ≤7 cm in greatest dimension, limited to the kidney
T1a	Tumor ≤4 cm in greatest dimension, limited to the kidney
T1b	Tumor >4 cm but ≤7 cm in greatest dimension, limited to the kidney
T2	Tumor >7 cm in greatest dimension, limited to the kidney
T2a	Tumor >7 cm but ≤10 cm in greatest dimension, limited to the kidney
T2b	Tumor >10 cm, limited to the kidney
T3	Tumor extends into major veins or perinephric tissues, but not into the ipsilateral adrenal gland and not beyond Gerota's fascia
T3a	Tumor extends into the renal vein or its segmental branches, or invades the pelvicalyceal system, or invades perirenal and/or renal sinus fat but not beyond Gerota's fascia
T3b	Tumor extends into the vena cava below the diaphragm
T3c	Tumor extends into the vena cava above the diaphragm or invades the wall of the vena cava
T4	Tumor invades beyond Gerota's fascia (including contiguous extension into the ipsilateral adrenal gland)
Regional lymph nodes (N)	
N category	**N criteria**
NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Metastasis in regional lymph node(s)
Distant metastasis (M)	

M category	**M criteria**		
M0	No distant metastasis		
M1	Distant metastasis		
Prognostic stage groups			
When T is...	**And N is...**	**And M is...**	**Then the stage group is...**
T1	N0	M0	I
T1	N1	M0	III
T2	N0	M0	II
T2	N1	M0	III
T3	NX, N0	M0	III
T3	N1	M0	III
T4	Any N	M0	IV
Any T	Any N	M1	IV

Adapted from the AJCC Cancer Staging Manual, Eighth Edition (2017) published by Springer International Publishing. Corrected at 4th printing, 2018.

The five-year cancer-specific survival rates for patients with clear cell renal cancer stage I, II, and III disease are >90%, 75%, and 60-70% respectively. Specific factors associated with recurrence and worse survival include renal pelvis and vena cava involvement and lymph node positivity, which are incorporated into the staging system. Clear cell renal cancers are also graded according to the Fuhrman/ISUP system, which is based on the appearance of the cancer under the microscope. High grade disease is also associated with a higher risk of recurrence. Risk of recurrence beyond 10 years for clear cell renal cancers is 6%, with the major risk factor being lymph node positivity, for which there is a 6-fold higher risk of such a late recurrence (Miyao et al. 2011). Recurrence 20 years after nephrectomy are reported but are rare.

Prognosis and outcome of renal cancers that are not clear-cell are generally similar to clear cell renal cancer, but can be markedly different for specific subtypes. For example, medullary renal cancers are extremely aggressive with the majority of patients developing metastases and dying from their disease within 2 years (Ezekian et al. 2017), whereas chromophobe renal cancers metastasize only very rarely (Volpe et al. 2012). Data for rare subtypes, and especially for subtypes that have only been described more recently, is often incomplete and typically not included in descriptions of general renal cancer outcomes based on TNM staging.

A major potential long-term complication of nephrectomy is decreased renal function. Renal dysfunction, or chronic kidney disease (CKD), is generally graded by the estimated glomerular filtration rate (GFR), which is based on serum creatinine levels:

- G1 = ≥ 90 ml/min/1.73 m^2 (normal)
- G2 = 60-89 ml/min/1.73 m^2 (mildly decreased)
- G3a = 45-59 ml/min/1.73 m^2 (mildy to moderately decreased)
- G3b = 30-44 ml/min/1.73 m^2 (moderately to severely decreased)

- G4 = 15-29 ml/min/1.73 m^2 (severely decreased)
- G5 = <15 ml/min/1.73 m^2 (kidney failure)

The implications and outcomes for patients with CKD include hypertension, fluid retention, electrolyte imbalances and in the worst case scenario need for dialysis. Overall, and depending on the patient's age, the relative risk for all-cause mortality among patients with isolated G3a CKD is 1.2 (CI: 1.0 – 1.5) – 1.9 (CI: 1.4 – 2.5), with a specific relative risk of cardiovascular mortality of 1.3 (CI: 0.6 – 3.2) – 1.4 (CI: 1.2 – 1.8), and risk of developing the need for dialysis of 3.1 (CI: 1.1 – 8.3) – 3.4 (CI: 1.6 – 7.2), which for the former reflects an increased risk from 48/10,000 to 65/10,000 and the latter reflects an increased risk from 5.7/10,000 to approximately 18.6/10,000 (Levey et al. 2011).

Notwithstanding the aforementioned, the most common causes for CKD are hypertension, diabetes, hypercholesterolemia and smoking. Chronic non-steroidal anti-inflammatory drug use, with medications such as ibuprofen, may also increase the risk of chronic renal disease. However, in patients with modest renal dysfunction, it is only high dose use, on the order of 3.5 or more 200mg ibuprofen pills daily (i.e. 700 mg or more), that is significantly associated worsening renal function (Gooch et al. 2007).

V. Overview of Plaintiff Case

Mr. Howard was born on [redacted]/59 and was stationed at Camp Lejeune from 9/77 – 2/79 (see LaKind report). Details of clinical presentation are not clear from the provided records, but on 11/18/08 he was found to have a large renal mass on imaging and underwent an open radical nephrectomy on 12/3/08. Pathology revealed a 4.2 x 4.0 x 4.0 cm. renal cell carcinoma, clear cell type, tumor grade (Fuhrman grades 1-4) 2, but no invasion of perinephric fat or renal veins, and without evidence of lymph node involvement. Per modern staging criteria this would be considered a Stage I cancer (pT1bN0Mx).

Based on the presence of pulmonary nodules there was an initial concern for metastatic disease, but with lack of any change in their size or appearance on subsequent monitoring, with the last CT on 7/23/20 and as acknowledged by the plaintiff, these are now considered to be benign. More specifically, small pulmonary nodules are relatively common and can be caused by a variety of benign conditions, including prior infections. Malignant metastatic nodules would not remain stable for 12 years.

Mr. Howard underwent routine post-operative care and monitoring, initially more frequently due to the pulmonary nodules but then every 6 months until approximately 4/15 at which time routine chest X-rays only continued. Post-operatively Mr. Howard's creatinine was normal at 1.1 mg/ml and as late as 7/24/20, his estimated GFR was normal at 95 ml/min/1.73m^2. Routine physician visits have also demonstrated that he has not developed any hypertension.

Over the years Mr. Howard has been diagnosed with basal cell cancer of the skin (2/19), hypercholesterolemia (7/24/15), hypothyroidism (7/17), hearing loss/tinnitus (4/10); and a non-cancerous tubular adenoma that was removed on colonoscopy (7/17 and 3/21). As is standard, follow up colonoscopies every 3 years have been recommended. Bladder cystoscopies performed in 3/21 revealed only a benign adenoma. He also suffered a severe bicycle crash in 8/16/20 complicated by a pneumothorax and subsequent near fatal pulmonary embolism.

In 8/23 he was diagnosed with diffuse large B-cell lymphoma, germinal center type with a R-IPI score 2, which is considered low/intermediate risk. He completed 6 cycles of pola-R-CHP on 1/29/24 and as of 5/10/24 was considered to be in complete remission with no evidence of disease.

From a social history perspective, he smoked for 2 years while in the marines and has no family history of cancer; although, he is estranged from his father and thus paternal history is unknown.

VI. Opinion

In order to assess likely and unlikely causes for any one individual's renal cancer I assess whether any of the known causes apply to the individual, whether that individual's cancer presentation is typical for known causes, and to what degree other potential causes need to be considered in this context. Additionally, I consider the complex multi-step and somewhat random nature of oncogenesis discussed above, as well as the increased risk attributable to and the clinical significance of any known potential causative factor. For example, a known factor, such as smoking, is likelier to be a cause if that factor is persistent and long standing. Conversely, a known factor might still be unlikely to be a cause if exposure is brief and clinically minimal.

Given the medical history and aforementioned discussion regarding renal cancer etiology, it is my opinion that Mr. Howard's renal cancer was unlikely due to Camp LeJeune water. This is based evaluation of the aforementioned etiologic factors for renal cancer.

1) Obesity. Per the provided medical records Mr. Howard is not obese.

2) Smoking. Mr. Howard had only a brief smoking history while in the military. Like many cancers associated with environmental exposure, brief short term smoking has not been reliably linked to renal cancer (Hunt et al. 2005).

3) Hypertension. There is no evidence for hypertension prior to renal cancer diagnosis.

4) Chronic kidney disease. Mr. Howard had normal kidney function prior to his nephrectomy and did not have cystic disease of the kidney at the time of diagnosis.

5) Diabetes: Mr. Howard did not have a history of diabetes prior to his RCC diagnosis

6) Occupational exposure to cadmium, asbestos, and petroleum byproducts. These etiologic factors have not been demonstrated to be relevant outside of occupational settings in which prolonged and high exposure levels have been documented. Mr. Howard has no history of such occupational exposure. See also Goodman report and Lipscomb report regarding trichloroethylene exposure as risk factor and LaKind and Bailey reports regarding plaintiff exposure and risk estimates.

7) Heavy use of non-steroidal anti-inflammatory drugs, acetaminophen and phenacetin. Mr. Howard does not have any history of using any analgesic of more than 7 pills weekly for 10 or more years, which is the defined heavy use most consistently associated with renal cancer (Cho et al., 2011). Additionally, the most well documented cancer associated with these agents is upper tract urothelial cancer and not clear cell renal cancer.

8) Genetic predisposition syndromes. There is no evidence for a genetic predisposition in Mr. Howard's case; although, no formal testing was ever conducted which is at least at this time considered to be a reasonable standard of care for relatively young patients diagnosed with cancer.

9) Chronic infection and inflammation. There is no evidence for any pre-diagnostic chronic kidney infection or inflammation in Mr. Howard's case.

Importantly, as noted above, most renal cancers, even if there are predisposing factors, must be considered to be idiopathic in nature. That is simply because the vast majority of patients who have the most significant risk factors (i.e. smoking and obesity) do not develop renal cancer and even patients, like Mr. Howard, who have no clear risk factors, develop renal cancer. It is also critical to re-emphasize that a "risk-factor" for a cancer only increases the odds of developing such a cancer and the presence of such a risk factor does not automatically mean that it is the cause of any individual's cancer, especially if the increased risk is minimal (see also Goodman report; Bailey report). Furthermore, Mr. Howard was in the typical age range for a renal cancer.

Additionally, Mr. Howard has not suffered any significant long term health consequences of his renal cancer. More specifically:

1) Overall risk of recurrence for his stage I cancer more than 15 years after nephrectomy is close to nil and no routine monitoring is recommended. Furthermore, as attested to by his physicians and acknowledged by Mr. Howard, his pulmonary nodules, which have not changed in over 12 years, are benign, and do not reflect metastatic cancer.
2) His post-operative renal function was normal and continues to be normal.
3) Mr. Howard does not have diabetes or hypertension and thus the risk for developing renal dysfunction is quite low.
4) I am unaware of any medical evidence that a history of renal cancer or nephrectomy can cause non-Hodgkin's lymphoma in general or diffuse large B-cell lymphoma specifically.
5) I am unaware of any medical evidence that a history of renal cancer or nephrectomy can cause hypothyroidism.

As such, Mr. Howard's renal cancer is unlikely to be related to Camp Lejeune exposures and likely idiopathic in nature, which is the case in more than 50% of patients. Furthermore, its successful treatment has minimal to no impacts on his current or future health status.

VII. Responses to Plaintiff's Experts

A. General Responses

It is my opinion that plaintiff's experts make some fundamental errors in their causation assessment. First, plaintiff experts refer to the Bradford-Hill criteria assessing whether an association between exposure and subsequent health event (in this case renal cancer) is likely to be causative. For example, Dr. Del Pizzo states "[t]he Bradford Hill considerations are employed here for structural analysis to determine wither this particular association with Mr. Howard is causal, and specifically, whether that it is as likely as not that this exposure was the cause of Mr. Howard's kidney cancer." (Del Pizzo report at

16). These criteria, however, focus on potential causation within a ***population*** and do not necessarily apply to causation in an ***individual***. This becomes especially important when the relative risk associated with such an exposure is small and less than 2, which is acknowledged by plaintiff experts even under a worst-case scenario. In other words, within even an exposed population most of the patients with a specific cancer would have gotten that cancer even in the absence of exposure. To thus attribute any single individual's cancer to such an exposure, even if there are no other obvious known causative conditions, is not accurate.

Secondly, and relatedly, plaintiff experts ignore the implications of the multi-step and random events for oncogenesis in general and renal cancer specifically. For example, Dr. Smith concludes that "There simply is no other risk factor for Mr. Howard that is as likely as [Camp Lejeune] exposure in terms of a likelihood of being causally related to his kidney cancer." (Smith report at 12). As I have noted and plaintiff experts acknowledge, multiple genetic and other events must occur for a clinical cancer to develop and there is a certain randomness to each event and oncogenesis in general (a phenomenon known as "stochastic"). As such, clinicians like myself consider most cancers in any specific individual to be idiopathic, which is not even considered by plaintiff experts. In other words, it is far more likely than not that Mr. Howard would have developed his cancer even in the absence of any exposures. Plaintiff's experts not only fail to convincingly "rule out" idiopathic cause; they ignore it altogether.

Finally, plaintiff experts over-emphasize the role any toxin exposure in Camp LeJeune water may have played, despite incomplete information on true exposure, differences in opinion from exposure experts regarding level of exposure, and very small levels of increased risk, all the while minimizing the role other risk factors such as low-level smoking or mild obesity may play. For example, Dr. Smith notes that "2 pack-years represents a very low cumulative exposure, especially when compared to thresholds associated with significant cancer risk." (Smith report at 12). Dr. Josephson similarly describes Mr. Howard's two pack-year smoking history as "so remote and minimal as to be non-contributory." (Josephson report at 11). As I explain above, Mr. Howard's smoking history *is* a risk factor, but is not likely a "cause" because the extent of his smoking exposures were minimal. Similarly, even if Mr. Howard's exposure to Camp Lejeune water increased his risk of kidney cancer, I would not assign causality to those exposures because the vast majority of studies suggest that high levels of sustained exposure to such toxins in occupational settings is necessary, which is not the case for Mr. Howard. I have chosen to consistently eliminate ***all*** low risk level risk factors with limited clinical exposure as causative and have concluded that the etiology of Mr. Howard's renal cancer is idiopathic.

B. Specific Responses

I disagree with Dr. Smith's opinion that "Mr. Howard's diagnosis at age 49 and the size of his tumor (T1b) are unusual circumstances for sporadic RCC." (Smith report at 10). Dr. Smith claims that "[t]hese factors suggest a significant environmental contribution, particularly exposure to carcinogens like TCE." Dr. Smith's opinion overemphasizes the clinical significance of Mr. Howard's age at diagnosis because renal cancer is often seen in a wide range of age groups. Further, according to SEER data, 14% of renal cancer diagnoses occur in the 45-54 year old age group and the average annual percentage increase of renal cancer between 2000 -2006 for males in this age group was 3.2% (NCI 2024b). Clearly, younger-than-average individuals are increasingly being diagnosed with renal cancer, and this cannot be simply explained by exposure to toxins in Camp LeJeune water.

Dr. Smith's opinion also overemphasizes the clinical significance of Mr. Howard's tumor size. Idiopathic tumors are also often "aggressive" insomuch as they can be high grade and can metastasize, and degree of "aggressiveness" does not provide guidance as any specific exposure being causative. Additionally, smoking exposure, which both plaintiff experts and I have considered possibly contributory, would have the same degree of DNA-damaging properties and promotion of chronic inflammation.

I agree with Drs. Smith, Josephson, and Del Pizzo that the care Mr. Howard received was appropriate and that the cancer will not have an impact on his life expectancy. I also agree with Dr. Josephson that "Mr. Howard remains disease free 15 years removed from his original diagnosis and would be considered in remission for kidney cancer" (Josephson report at 12), and with Dr. Del Pizzo that Mr. Howard "has had no evidence of recurrent or metastatic disease relating to renal cell carcinoma." (Del Pizzo report at 4). A perhaps more accurate statement is that Mr. Howard is almost certainly cured of his renal cancer.

VIII. References

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