Exhibit 475

Expert Report of Harry Paul Erba, M.D., Ph.D.

Robert J. Fiolek v. United States
7:23-cv-00062-D-BM
U.S. District Court for the Eastern District of North Carolina

Prepared By:

Harry Paul Erba, M.D., Ph.D.

April 8, 2025

TABLE OF CONTENTS

Plaintiff: Robert J. Fiolek

Case: *Robert J. Fiolek v. United States*, No: 7:23-cv-00062-D-BM (U.S. District Court, Eastern District of North Carolina).

I. Executive Summary

I prepared this report in response to the United States' request for my opinion as a hematologist and leukemia specialist on whether Mr. Robert Fiolek's chronic lymphocytic leukemia (CLL) was, in fact, caused by his exposure to the water at the Camp Lejeune military base in North Carolina. I was also asked to comment on Dr. Damian Laber's February 7, 2025, report and whether Mr. Fiolek's CLL or CLL treatment led to his bladder cancer.

In formulating my opinions in this case, I have determined the following:

1. It is highly unlikely that Mr. Fiolek's CLL was caused by his distant, intermittent exposure to the water at Camp Lejeune. Not only is there insufficient evidence of an association between CLL and the contaminants alleged in the Camp Lejeune water, but Mr. Fiolek's demographic profile has many widely accepted features associated with a higher risk of developing CLL: advanced age, gender, ethnicity, family history of leukemia, and obesity. Despite these associated demographic features, there are no environmental factors or genetic events that are known to cause CLL.

2. CLL is associated with an increased risk of second malignancies. However, there is no data to support the specific association of bladder cancer (or urothelial carcinoma in general) with CLL. On the other hand, Mr. Fiolek's biological mother's death at age 50 from bladder cancer, his prior smoking history, male gender, and advanced age at diagnosis (84-years-old) are all known risk factors for bladder cancer.

I base these opinions on my review of the relevant case materials and literature, decades of training and experience in hematology and oncology, and over 30 years of clinical diagnosis and treatment of CLL patients. I reserve the right to supplement these opinions if additional information is given to me after the date of this report. I hold all of these opinions to a reasonable degree of medical certainty.

II. Qualifications

I am a board-certified hematologist and oncologist at Duke University School of Medicine and a Member of the Duke Cancer Institute in Durham, North Carolina. I graduated in 1979 from Yale University with a Bachelor of Science degree in Biology. I earned my Medical Degree and Doctor of Philosophy Degree in Biophysics from Stanford University School of Medicine in California in 1988. I completed my internal medicine internship, internal medicine residency, and hematology and oncology fellowship at the Brigham and Women's Hospital, Dana Farber Cancer Institute, and Harvard Medical School. I am a Professor of Medicine in the Division of Hematologic

Malignancies and Cellular Therapy in the Department of Medicine at Duke University. I serve as the Director of the Leukemia Program at Duke University. I have served as the Chair of the Southwest Oncology Group Leukemia Committee (SWOG) since 2012.[1] I have been a member of the National Cancer Institute (NCI) Leukemia Steering Committee since 2012. I am also the Co-Chair of the Senior Scientific Council of the NCI-sponsored MyeloMATCH precision medicine initiative in acute myeloid leukemia (AML) and myelodysplastic syndromes, a role that I have occupied since 2019.

Since 1996, my clinical and research career has focused on the diagnosis and treatment of adults with acute leukemias, myelodysplastic syndromes, and myeloproliferative neoplasms, first at the University of Michigan (1996-2012), then at the University of Alabama at Birmingham (2012-2018), and currently at Duke University (2018-present). I currently care for over 100 patients annually with AML, acute lymphoblastic leukemia (ALL), myelodysplastic syndromes, chronic myeloid leukemia (CML), and other myeloproliferative diseases in the Duke Blood Cancer Center outpatient clinic and on the Hematologic Malignancies Inpatient Service at Duke University Hospital. Before relocating to Duke University on July 1, 2018, I also cared for patients with CLL for over 20 years at the University of Michigan and the University of Alabama at Birmingham. Although I now spend much of my clinical time treating patients with acute leukemia, I am currently treating a CLL patient at the Duke Blood Cancer Institute with the combination of obinutumomab and venetoclax. As Chair of the SWOG Leukemia Committee I have contributed to the clinical research studies leading to the approval of the current treatments for CLL. I am certified in Hematology by the American Board of Internal Medicine.

My current curriculum vitae is attached as Appendix A. It includes a list of my peer-reviewed publications during my entire academic life, including for the last ten (10) years. A list of the materials I considered in drafting this report is attached as Appendix B. I received $500 for each hour of service, including for my time spent testifying in a deposition or at trial. I have never been retained as an expert witness before my work in this and related cases in the Camp Lejeune litigation. I have never been deposed or testified at trial.

III. An Overview of Leukemia

Leukemia is a cancer arising from cells in the blood and bone marrow. To understand the origin of leukemia, one must be familiar with normal blood cell formation. There are two major subtypes of blood cells, myeloid and lymphoid. The myeloid cells include granulocytes (neutrophils, monocytes, eosinophils and basophils), platelets, and red blood cells. The lymphoid cells include B lymphocytes, T lymphocytes, and natural killer cells. The mature myeloid cells all have a finite life span in the blood: neutrophils remain in the blood for hours, platelets for 7-10 days, and red blood cells for 100 days. These cells are essential to human life. The granulocytes provide an innate defense against bacterial, fungal, and parasitic pathogens (in other words, infectious organisms). Platelets are essential for the first stages of blood clotting to prevent exsanguination due to

[1] SWOG is one of the cooperative groups funded by the NCI to perform clinical research for people with cancer in the United States and its territories.

disruption of the blood vessels. Finally, red blood cells carry oxygen from the lungs to the tissues of the body which is essential for energy production in these cells. B and T lymphocytes provide defense against viral pathogens, producing antibodies or cellular responses, respectively.

The bone marrow is responsible for constantly producing these mature blood cells throughout life. There is a finite pool of bone marrow stem cells and progenitor cells that are capable of self-renewal and differentiation into these myeloid or lymphoid cells. Leukemia is due to acquired changes in the genes (mutations) that govern the normal differentiation of the stem and progenitor cells into the mature blood cells. These cells may also acquire mutations in genes that lead to the accumulation of leukemic cells. Depending on the type of progenitor cell (myeloid or lymphoid), these cancers are classified as myeloid (myelogenous) or lymphocytic (lymphoblastic) leukemia. In both cases, the bone marrow will ultimately not be able to continue its normal function of blood formation.

Myeloid and lymphocytic leukemia are also classified as either acute or chronic based on the rate of disease progression, the type of cancer cells that accumulate, and treatment methodology. Acute leukemias are cancers that rapidly expand in the bone marrow and require immediate chemotherapy (within days of initial presentation of the patient). With some exceptions, most adult patients with acute leukemia will require hematopoietic stem cell transplant (also known as bone marrow transplant or blood and marrow transplant) after achieving an initial complete remission as the only potentially curative option. The two major types of acute leukemia are acute myeloid leukemia and acute lymphoblastic leukemia.

Chronic leukemias progress more slowly. In chronic leukemias, patients have a greater number of mature blood cells. The two major types of chronic leukemia are chronic myeloid leukemia (CML) and chronic lymphocytic leukemia (CLL).

A. CLL as a form of Non-Hodgkin Lymphoma

CLL is characterized by an accumulation of mature B lymphocytes in the blood, bone marrow, lymph nodes, and spleen. These lymphocytes are not functional. CLL results in suppression of the immune system. These patients have reduced ability to make antibodies and to respond to vaccinations. CLL and small lymphocytic lymphoma (SLL) are biologically equivalent diseases. If the diagnosis is made by detecting the neoplastic B lymphocytes in the blood or the bone marrow, the cancer is called CLL. On the other hand, if the diagnosis is made by biopsy of an organ of the immune system, such as lymph nodes, spleen, or other organs, the cancer is considered a subtype of non-Hodgkin lymphoma, currently called small lymphocytic lymphoma. Over the years, pathologists have realized that this is an oversimplification, since the same cancer cells can be found in lymph nodes, blood, and bone marrow, but the diagnosis was based on the first tissue to be biopsied. Oncologists treating these patients realized that the prognosis and treatment of CLL and SLL are similar. Therefore, CLL has been re-classified as a subtype of non-Hodgkin lymphoma.

The World Health Organization now classifies this subtype of non-Hodgkin lymphoma as CLL/SLL. The name CLL has been used for many decades. However, the name of this specific subtype of non-Hodgkin lymphoma has changed several times over the last 100 years.

Most recently, the Revised European American Lymphoma (REAL) classification and the World Health Organization (WHO) diagnostic criteria have considered CLL and SLL to be two presentations of the very same cancer. SLL is characterized by lymph node involvement with less than 5,000 neoplastic B lymphocytes per microliter of blood. CLL is defined as having over 5,000 neoplastic B cells per microliter of blood with or without other organ involvement. Monoclonal B lymphocytosis (MBL) of uncertain significance is diagnosed by the presence of less than 5,000 CD5 positive, CD23 positive monotypic B cells per microliter of blood. MBL is NOT considered cancer, but MBL patients may develop CLL/SLL many years later. MBL has been identified in 3.5% of people over 40 years of age [Rawstron AC, et al. Blood 2002; 100: 635-639].

Given the evolution of lymphoma diagnosis and classification over the last 50 years, older epidemiologic and animal toxicology reports can be difficult to apply in the current era. Furthermore, the etiology of all non-Hodgkin lymphoma is not necessarily the same. Antigenic stimulation has been hypothesized to underlie several subtypes of lymphoma.

B. Epidemiology and risk factors associated with the development of CLL

The annual incidence of CLL in the United States is 6.75 and 3.65 cases per 100,000 men and women, respectively. Although the incidence of CLL and AML are similar, the prevalence of CLL is higher due to the longer life expectancy of these patients. CLL accounts for 25-35% of all leukemia cases. CLL is a disease of advancing age; the median age at diagnosis of CLL is 70 years. CLL is less common in Asian countries, and the incidence remains low even after immigration to the Western countries. The incidence of CLL in African Americans and Asian Pacific Islander Americans is lower than in Caucasian Americans. There is also a familial tendency with a higher-than-expected frequency of CLL among first degree relatives of CLL patients. These, and other, observations suggest that genetic factors are likely to predispose to CLL [Swerdlow SH, et al. WHO Classifications of Tumours of Haematopoietic and Lymphoid Tissues, 2008; 4th edition, page 180]. Therefore, advanced age, gender, ethnicity (European vs African/Asian ancestry), and family history of CLL are the most widely accepted risk factors associated with the development of CLL. Ultimately, however, the cause or causes of CLL is unknown, and a specific causative agent or genetic event has not been identified.

Environmental exposures are clearly associated with cancer risk. However, the American Cancer Society only recognizes radon exposure as a potential risk factor for CLL. Agent Orange and pesticides have been suggested as risk factors for development of CLL, but these associations have not been confirmed (see www.cancer.org/cancer/types/chronic-lymphocytic-leukemia/causes-risks-prevention/risk-factors). Volatile organic chemicals ("VOCs") are not listed as possible risk factors for the development of CLL on the American Cancer Society website.

The InterLymph Non-Hodgkin Lymphoma Subtypes Project evaluated the incidence of specific non-Hodgkin lymphoma subtypes according to self-reported medical history, family history, occupation, and lifestyle [Morton LM, et al. J Natl Cancer Inst Monogr. 2014; 48: 130-144]. "Risks differed statistically significantly among lymphoma subtypes for medical history factors (autoimmune diseases, hepatitis C virus seropositivity, eczema, and blood transfusion), family

history of leukemia and multiple myeloma, alcohol consumption, cigarette smoking, and certain occupations, whereas generally homogeneous risks among subtypes were observed for family history of lymphoma, recreational sun exposure, hay fever, allergy, and socioeconomic status." This observation again illustrates that the subtypes of non-Hodgkin lymphoma are distinct pathologic entities and cannot be necessarily considered as one. Any self-reported family history of leukemia was associated with a 2.41 relative risk of development of CLL; the confidence interval was statistically significant, 1.85 – 3.14. Although CLL could have accounted for most of this effect, any family history of leukemia was associated with a higher risk of CLL.

Obesity has been associated with an increased risk of cancer in general. Obesity is defined as a body mass index greater than or equal to 30 kg/m^2. J.J. Castillo and colleagues performed a meta-analysis of studies evaluating the relation between obesity and the risk of leukemia and the associated mortality [Castillo JJ, et al. Leuk Res. 2012; 36: 868-875]. They first identified 1,778 manuscripts dealing with obesity and leukemia. They narrowed their meta-analysis analysis to 16 prospective cohort studies on the incidence of leukemia associated with obesity. Ten of these studies reported specifically on CLL. A statistically significant increased risk was only observed in obese men (not just overweight, and not in women). The incidence increased by 1.3% for every 1 kg/m^2 increase in the body mass index. The linear relation between the incidence of CLL and body mass index supports a direct relation. Marshall Lichtman, president of the American Society of Hematology in 1989, concluded in his peer-reviewed investigation of obesity and hematologic malignancies, that there is a significant association between obesity and the risk of chronic lymphocytic leukemia [see pages 1093 and 1097 of Lichtman, M. The Oncologist 2010; 15: 1083-1101].

CLL is preceded by an expansion of clonally related B cells with an immunophenotype identical to CLL cells (see section on CLL diagnosis below for definition), termed monoclonal B cell lymphocytosis (MBL). MBL is arbitrarily defined as less than 5000 monoclonal B cells per microliter of blood (values above 5000 per microliter define CLL). People with higher levels of MBL are at higher risk of developing CLL. Landgren and colleagues conducted a prospective cohort study based on 77,469 healthy adults enrolled in the population-based, U.S. Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial. Forty-five participants were subsequently diagnosed with CLL during the period of longitudinal observation. Using highly sensitive flow cytometry, 44 of these 45 CLL patients (98%) had MBL prior to the diagnosis of CLL. MBL was detected up to 6.4 years prior to CLL diagnosis in these individuals. Therefore, virtually all CLL patients have MBL for years prior to diagnosis. The annual risk of progression of MBL to CLL has been estimated to be 1-2% (see review by Shanafelt TD, et al. Leukemia 2010; 24: 512-520).

The pathogenesis of CLL is unknown. However, antigen interactions mediated by the B-cell receptor immunoglobulin are critical for the survival and proliferation of CLL malignant cells. In the largest analysis to date of over 29,000 samples from patients with CLL (see Agathangelidis A, et al. Blood 2021; 137: 1366), there was limited use of the available immunoglobulin V, D, and J segments in the CLL samples compared to normal B lymphocytes. For example, MBL are more likely to have immunoglobulin gene rearrangements with the IgHV-3 sequences. Since the V, D and J segments of the immunoglobulin molecule determine antigen binding, this stereotypy

suggests the hypothesis that CLL is initiated by expansion of B lymphocytes in response to a limited number of commonly occurring antigens in the body or in the environment. Taken together, these observations suggest that CLL is initially due to autoimmunization (reaction against common endogenous antigens in the patient's own body) or a commonly encountered antigen in the environment followed by other genetic events leading to cancer. The subsequent genetic events leading to cancer have not been elucidated.

C. Diagnosis and Prognosis of CLL

Most patients with CLL are asymptomatic at the time of initial diagnosis. The diagnosis is made after discovery of an elevated white blood cell count, and specifically, an elevated number of small, mature blood lymphocytes. The diagnosis of CLL is commonly established by flow cytometric analysis of the cells in any tissue involved by the small, mature lymphocytes characteristic of CLL. Flow cytometry detects the presence or absence of specific cell markers. These CD ("clusters of differentiation") markers provide a specific signature for each subtype of non-Hodgkin lymphoma. This signature is called an immunophenotype. The characteristic immunophenotype of CLL cells is positive for CD5 and CD23 on monotypic mature B cells with expression of CD19, CD20, and low-level expression of either kappa or lambda light chain surface immunoglobulin. The immunophenotype is distinct from other subtypes of non-Hodgkin lymphomas that may also be present in the blood, marrow, and lymph nodes, such as lymphoplasmacytic lymphoma, marginal zone lymphoma, mantle cell lymphoma, lymphoblastic lymphoma, and others.

The prognosis of CLL varies according to stage. There are five stages in the Rai staging system, commonly used in the United States. Stage 0 refers to patients with only an elevated peripheral blood white blood cell count with over 5000 CLL cells per microliter; this is called lymphocytosis. Stage I includes patients with lymphocytosis and enlarged lymph nodes (lymphadenopathy), stage II includes patients with lymphocytosis and enlargement of the spleen and/or liver (splenomegaly and/or hepatomegaly), stage III is lymphocytosis with anemia, and stage IV is lymphocytosis with thrombocytopenia. Stage 0 is considered low risk, stages I and II are intermediate risk, and stages III and IV are high risk. The stage informs the decision to initiate therapy (see below).

Once the diagnosis has been established, other studies are performed to provide further prognostic information and to guide initial treatment decisions. Recurrent alterations in the chromosomes in CLL cells have been recognized and are prognostically important. Deletion of the long arm of chromosome 13 [del(13q)] is the most common chromosomal change and associated with a more favorable prognosis. On the other hand, deletion of the long arm of chromosome 11 [del(11q)] or the short arm of chromosome 17 [del(17p)] are associated with a poor prognosis. Three copies of chromosome 12 (trisomy 12, or +12) is associated with an intermediate prognosis. These changes are detected by either fluorescence in situ hybridization (FISH) or metaphases chromosome analysis (karyotype). Mutations in specific genes also impact prognosis. Mutations of the *TP53* gene are associated with a worse outcome.

The expression levels of two proteins by the neoplastic cells, CD38 and ZAP-70, have been associated with the prognosis of CLL patients. The presence of CD38 and/or ZAP-70 expression has been associated with higher white blood cell counts, lower platelet counts, lower hemoglobin,

higher Rai stage disease, and worse overall survival [Hus I, et al. Annals of Oncol. 2006; 17(4): P683-690]. The expression levels of these two proteins were difficult to standardize, and both eventually fell out of favor as prognostic markers in CLL. The expression of ZAP-70 and/or CD38 were found to correlate with CLL cells carrying an unmutated immunoglobulin gene (see next paragraph).

CLL has been shown to be a neoplasm affecting either pre-germinal center B cells or post germinal center B cells. Shortly before birth, our B cells are programmed to recognize and respond to foreign antigens (proteins, sugars, or lipids not found in our body). However, when a B cell enters a lymphoid organ (e.g. lymph node) and engages a foreign antigen in a germinal center, DNA changes (somatic mutations) occur in the antibody-producing gene of the pre-germinal center B cell. The resulting B cells, that produce an antibody with the greatest affinity for a foreign antigen, are selectively expanded in number. This normal process results in an immune system capable of selectively and efficiently eliminating any foreign antigen. We can distinguish these pre-germinal B cells from post-germinal B cells by sequencing the DNA in the immunoglobulin gene (the gene that makes the antibody). CLL derived from pre-germinal center (unmutated) B cells have a worse prognosis compared with the post-germinal center (mutated) B cells.

The Rai stage, cytogenetic abnormalities in the CLL cells, presence or absence of *TP53* mutations in the CLL cells, and the mutational status of the immunoglobulin gene in the CLL cells are now included in prognostic models.

D. Treatment of CLL

Many patients with CLL often do NOT require treatment at the time of diagnosis (as in the case of Mr. Fiolek). Early treatment of asymptomatic CLL patients has not been shown to improve survival in the past. Patients with Rai stage 0 disease (lymphocytosis alone) are typically not treated, unless there is a rapid rise in the lymphocyte count or constitutional symptoms. Patients with Rai stage I and II disease (adenopathy, splenomegaly) may be treated, but typically only if the lymphoid organ enlargement is painful, cosmetically unacceptable to the patient (e.g. enlarged lymph nodes in the neck), obstructing the intestines or the airway, or obstructing ducts draining urine from the kidneys or bile from the liver. Treatment is recommended for patients with anemia and thrombocytopenia (Rai stage III and IV) due to bone marrow failure. A significant minority of CLL patients may never require therapy before dying of unrelated causes. These patients typically will have either Rai stage 0 or stage I disease at diagnosis. The prognostic factors discussed in the previous section are associated with the risk of progression to higher stages of the disease over time. The SWOG Leukemia Committee S1905 study is actively recruiting asymptomatic CLL patients with high-risk features and evaluating earlier intervention with modern, time-limited therapy (venetoclax and obinatuzumab, see below).

Historically, CLL was treated with single agent, oral chemotherapy drugs (DNA alkylating agents such as chlorambucil and cyclophosphamide) and corticosteroids (prednisone). Most responses were only partial responses and were not durable. Other chemotherapy agents became available over time including the intravenously administered purine analogs (fludarabine, cladribine, and pentostatin) and bendamustine. These agents were more effective but caused more suppression of

normal blood counts as well as the immune system, leading to more frequent infectious complications. Monoclonal antibodies directed against CD20 on the surface of CLL cells were developed as well (e.g., rituximab, obinutuzumab). These agents cause antibody-dependent cell-mediated toxicity, by engaging the immune system to attack the neoplastic CLL cells. Rituximab and obinutuzumab frequently can cause infusion reactions, especially with the first administration (as in the case of Mr. Fiolek). Patients may experience fever, shaking chills, low blood pressure, shortness of breath, low blood oxygen levels, wheezing, hives, and back pain. Infusion reactions are common and can be successfully managed in most cases by slowing the infusion and administering corticosteroids and antihistamines. Most patients can continue to receive these monoclonal antibodies even in the event of a serious reaction with the first dose.

Combination regimens became the standard of care for initial therapy of CLL for at least two decades (1995 through 2015). The most used immunochemotherapeutic regimens were fludarabine, cyclophosphamide, and rituximab (FCR), bendamustine and rituximab (BR), and oral chlorambucil with obinutuzumab. The selection of the specific regimen depended on the fitness of the patient to receive aggressive immunochemotherapy regimens. The latter was evaluated in older CLL patients with comorbid illnesses (who would not tolerate more aggressive chemotherapies such as fludarabine regimens). The combination of chlorambucil with obinutuzumab resulted in higher rates of complete remission and superior progression free survival compared with either chlorambucil alone or chlorambucil with the first generation anti-CD20 monoclonal antibody, rituximab [see Goede V, et al. N Engl J Med. 2014; 370(12): 1101-1110].

Most recently, cytotoxic chemotherapy drugs have been replaced by oral, targeted therapies. The two most popular regimens for initial therapy are the oral inhibitors of the Bruton tyrosine kinase (BTK) inhibitors and the BCL2 inhibitor venetoclax with the anti-CD20 monoclonal antibody, obinutuzumab. Ibrutinib, the first BTK inhibitor to be approved by the FDA, demonstrated superiority to single agent chlorambucil as initial therapy for CLL. The overall response rate has higher (86% versus 35%), progression free survival was better (84% lower risk of progression or death), and the overall survival was longer (98% versus 85% at 2 years) with ibrutinib versus chlorambucil, respectively [see Burger JA, et al. N Engl J Med 2015; 373: 2425]. But BTK inhibitors are associated with significant risks including atrial fibrillation (heart rhythm abnormality), excessive bleeding, and high blood pressure. CLL patients usually take the oral BTK inhibitors indefinitely in the absence of unacceptable toxicity, progression, or loss of response. There are now several FDA-approved, second generation BTK inhibitors for CLL including acalabrutinib, zanubrutinib, and pirtobrutinib. The second generation BTK inhibitors may have less risk of the common toxicities observed with ibrutinib, such as atrial dysrhythmia and bleeding tendency. The second generation BTK inhibitors may still be effective in patients developing resistance to ibrutinib.

The combination of venetoclax and obinutuzumab is a time-limited regimen for initial therapy, limited to only one year duration and then discontinued. This regimen leads to an overall response of 85% and complete remission rate in 50% of CLL patients with other comorbid illnesses. The progression free survival and response rates were superior with venetoclax and obinutuzumab compared with the chemotherapy agent chlorambucil with obinutuzumab [Fischer K, et al. N Engl

J Med 2019; 380: 2225]. The risks associated with venetoclax therapy include tumor lysis syndrome (kidney failure and cardiac arrhythmias due to rapid destruction of the malignant cells) and low white blood cell count (as occurred in Mr. Fiolek, requiring dose reductions). Patients begin obinutuzumab prior to venetoclax, and the dose of venetoclax is escalated slowly over a month, to minimize the risk of tumor lysis syndrome.

The BTK inhibitors and the BCL2 inhibitor venetoclax have improved the overall survival and progression free survival of CLL patients requiring initial therapy compared with immunochemotherapy regimens [see Shanafelt TD, et al. Blood 2022; 140(2): 11 and Woyach JA et al. N Engl J Med 2018; 379: 2517]. Allogeneic hematopoietic stem cell transplantation is very rarely considered now for CLL patients. Nevertheless, these regimens are not curative. Other forms of cellular immunotherapy are in development including chimeric antigen receptor T cells (CAR-T) and bispecific T cell engagers (BiTE).

IV. Summary of Exposure

Mr. Fiolek's exposure history to the water at Camp Lejeune is summarized on pages 14-16 of the Plaintiff Specific Causation Report prepared by Dr. Damian Laber. It is also summarized in the Expert Report of Dr. Judy S. LaKind. Although the reports differ as to certain details, Mr. Fiolek's time at Camp Lejeune was intermittent and limited to the 1960s.

V. Mr. Fiolek's Relevant Medical History

Although the diagnosis of CLL was formally made in August 2014, there is laboratory evidence of the disease at least seven years before the diagnosis. The earliest complete blood count (CBC) in the available medical record on 01/13/2000 (00062_FIOLEK_0000000298) was completely normal with a white blood cell (WBC) count 6,500 per microliter, absolute lymphocyte count (ALC) 2,200 per microliter, hemoglobin 14.6 gram/dL, and platelet count 219,000. Laboratory results have been tabulated in the CCHC record between 12/18/2007 and 09/22/2017 (00062_FIOLEK_CCHC_0000000062–150). The earliest CBC in the CCHC record on 12/18/2007 had a mild elevation of the white blood cell (WBC) count (11,000 per microliter) due to a very mild absolute lymphocytosis (increase in lymphocytes); the ALC was 4,200 per microliter (00062_FIOLEK_CCHC_0000000149). Although not clinically significant, these results should have prompted further discussion with the patient and possibly evaluation. The ALC remained high normal or just above normal for years.

Dr. Kristina Gintautiene, Mr. Fiolek's primary care provider, evaluated Mr. Fiolek on 07/15/2013. At that time, he was feeling well without complaints (00062_FIOLEK_0000000223). She notes that he had been diagnosed with obstructive sleep apnea, but he admitted to being non-compliant with CPAP at night due to the discomfort associated with wearing the CPAP mask (this comment has been documented at other times in the medical record). Following this first visit, she ordered a laboratory evaluation completed on 08/01/2013. The WBC count had increased to 13,200, and the ALC had increased to 8,500 per microliter (00062_FIOLEK_0000000237). There was no comment regarding the abnormal WBC and lymphocyte counts during subsequent visits until July

2014. Dr. Gintautiene evaluated Mr. Fiolek again on 07/31/2014 to discuss the results of abnormal laboratory findings identified on laboratory evaluation on 07/29/2014. At that time, he again had no symptoms, specifically denying fever, night sweats, unintentional weight loss, fatigue, and adenopathy (00062_FIOLEK_0000000212). The ALC increased further to 27,300 per microliter on 07/29/2024 (00062_FIOLEK_0000000229). After noticing increased WBC counts and ALC, she referred Mr. Fiolek to Dr. John Cho, a hematologist and oncologist, for evaluation (see referral letter dated 07/31/20214, 00062_FIOLEK_CCHC_0000000707). Dr Cho saw Mr. Fiolek for the initial consultation on 08/20/2014 (00062_FIOLEK_CCHC_0000000374). Mr. Fiolek told Dr. Cho that he had been told about the abnormal WBC count "years ago" (Cho Dep., 51:16-22).

Dr. Cho reviewed the blood film and felt the cells were consistent with "L2 CLL". The diagnosis of CLL was confirmed by peripheral blood flow cytometry, dated 08/20/2014. The peripheral blood lymphocytes were positive for CD5, CD19, CD20, CD23, and surface kappa light chain restriction, diagnostic of CLL (00062_FIOLEK_CCHC_0000000698). The cells were negative for CD38. The cells were negative for ZAP-70 expression (00062_FIOLEK_CCHC_0000000697).[2] At this time, Dr. Cho and Mr. Fiolek decided to engage in a "watchful waiting" approach, because Mr. Fiolek was not having physical symptoms from his CLL.

He had further evaluation of the CLL during his consultation with Dr. Matthew Foster at University of North Carolina (UNC) at Chapel Hill. On the day of the consultation, the ALC was 2,100 (normal, 1,500 – 5,000 per microliter). Somatic hypermutation of the immunoglobulin heavy chain variable region gene was performed at the Mayo Clinic. The CLL cells carried an IgHV 3-72*01 gene; the DNA sequence varied by 1.3% of the nucleotides from the germline sequence (00062_FIOLEK_0000010607). Because that was less than the 2.0% threshold for determining hypermutation status, the sample was considered to have an unmutated IgHV gene. However, the pathologist did comment that the value was close to the 2% threshold, and did indicate some variation from germline; therefore, the pathologist recommended caution in the interpretation of this value and prognosis. The CLL cells do NOT express an immunoglobulin IgHV gene associated with the worst prognosis (IgHV3-21). The cytogenetic analysis detected three chromosomal changes in the CLL cells: additional material on the short arm of chromosome X, additional material on the short arm of chromosome 18, and a derivative of a (X:11) chromosome translocation, resulting in loss of material from the long arm of chromosome 11. The FISH analysis also detected loss of the ATM gene (chromosome 11q) in 28% of the cells and homozygous loss of both copies of the long arm of chromosome 13 in twenty percent (20%) of the cells (00062_FIOLEK_0000010620). Even though the lymphocyte count was in the normal range, the cytogenetic analysis and the somatic hypermutation analysis both confirmed the persistence of the CLL cells on this date (after the obinutuzumab infusion and after discontinuation of the ibrutinib).

In summary, Mr. Fiolek's CLL had features associated with both favorable (Rai stage 0-1 disease, absence of the IgHV3-21 gene in the B cell receptor, absence of ZAP70 and CD38 expression) and unfavorable (three cytogenetic changes by metaphase chromosome karyotype, deletion of

[2] Contrary to Dr. Cho's testimony (Cho Dep., 64:6-17), ZAP-70 *negative* CLL is associated with a *better* prognosis than ZAP-70 *positive* disease. However, as explained above, ZAP-70 expression has fallen out of favor as a tool to evaluate prognosis of CLL for several reasons.

chromosome 11q, “unmutated” IgHV gene) prognosis. Mutational analysis has not been done in this case. The risk associated with progression of and death from CLL does not determine the timing of initial therapy.

Because there was no indication to begin therapy, he was observed following the diagnosis of CLL on 08/20/2014. Mr. Fiolek soon asked if the CLL could be attributed to the drinking water at Camp Lejeune (message on 09/18/2014). Dr Cho replied through his clinic staff that “there is no way to know for sure whether or not the water contributed to [his] CLL diagnosis.... [A]ge is also a factor.” (00062_FIOLEK_CCHC_ 0000000369).

Between 2015 and 2016, Mr. Fiolek’s WBC count increased rapidly, rising from 69,600 on 10/20/2015 to 139,000 by 06/16/2016. He also became more symptomatic, developing abdominal and back pain with nausea. A CT scan of the abdomen and pelvis performed on 09/02/2016 revealed mesenteric, periaortic, retroperitoneal, and inguinal lymphadenopathy as well as splenomegaly (00062_FIOLEK_CEMC_0000005290).

This prompted Dr. Cho to recommend initial therapy with chlorambucil and obinutuzumab [Goede V, et al. N Engl J Med. 2014; 370(12): 1101-1110]. Dr. Cho started allopurinol on 09/06/2015 to prevent tumor lysis syndrome and ordered ibrutinib. Mr. Fiolek met with Kimberly Hess, Dr. Cho’s nurse, on 10/28/2015 to review the treatment plan (00062_FIOLEK_CCHC_0000000347). A left internal jugular venous power port was placed on 11/02/2015 in anticipation of therapy (00062_FIOLEK_CCHC_0000000651).

A prescription for chlorambucil (Leukeran) by mouth on days 1 and 15 of the 28-day cycles was filled and delivered to Mr. Fiolek, but he never started the drug. On the day he started treatment, his WBC count was 77,400, ALC 64,300, and platelet count 95,000 (00062_FIOLEK_ CCHC_0000000110-111). On 12/01/2015, he received obinutuzumab (Gazyva) 100 mg by intravenous injection with the plan to give the remainder of the dose (900 mg) on day #2. However, within an hour of starting the first dose, he developed rigors, shortness of breath, and rapid heart rate (Jeraldine Fiolek Dep., 50:15-23), and the infusion was discontinued. The medical record also describes severe back pain during the infusion reaction. He was felt to have a hypersensitivity reaction to the obinutuzumab. The plan to give both obinutuzumab and chlorambucil was abandoned. As a result, Mr. Fiolek never received any chlorambucil. His white blood cell and platelet counts appeared to remain stable for at least 3.5 months after the incomplete infusion of obinutuzumab.

Dr. Cho saw Mr. Fiolek in clinic on 09/09/2016 (00062_FIOLEK_CCHC_0000000306). He documented cervical and axillary lymph node enlargement in his physical exam, but he did not detect splenomegaly by physical examination. Dr. Cho prescribed single agent ibrutinib (Imbruvica) 280 mg (two 140 mg tablets) by mouth once daily beginning on 09/09/2016. The initial dose of ibrutinib for CLL is 420 mg once daily according to the FDA prescribing information. He continued to take 280 mg once daily. On 10/07/2016, Dr. Cho noted decreased cervical and axillary adenopathy (00062_FIOLEK_CCHC_0000000297). On the other hand, the WBC count and ALC both increased as expected to 261,300 and 236,000, respectively

(00062_FIOLEK_CCHC_0000000091), due to translocation of the neoplastic lymphocytes from the lymph nodes to the peripheral blood.

The following treatment history is well summarized by Dr. Matthew Foster in his UNC consultation note on 07/03/2017 (00062_FIOLEK_0000010581). On 11/10/2016, Mr. Fiolek developed chest heaviness and shortness of breath. He was admitted. He was diagnosed with atrial fibrillation with a rapid ventricular response. His WBC count was 200,300, ALC 193,400, hemoglobin 14.8 gram/dL and platelet count 109,000 (00062_FIOLEK_CEMC_0000005443). Pharmacologic cardiac stress test on 11/11/2016 did not demonstrate any ischemia (00062_FIOLEK_CEMC_0000005450). An echocardiogram demonstrated normal left ventricular function with sclerotic aortic valve, but there was no evidence of aortic stenosis at this time (00062_FIOLEK_CEMC_0000005452-5454). CT chest angiography was negative for pulmonary emboli at this time; there was no adenopathy in the chest (00062_FIOLEK_CEMC_0000005447-5448). He received a single dose of diltiazem by intravenous infusion and the cardiac rhythm returned to normal sinus rhythm. He was discharged from the hospital on diltiazem (rate control), flecainide (anti-arrhythmic, coumadin (anticoagulation), and enoxaparin (Lovenox) (anticoagulation) (Discharge note 00062_FIOLEK_CEMC_0000005426-5429).

Dr. Gorman, cardiology consultant, attributed the atrial fibrillation to ibrutinib (see consultation note at 00062_FIOLEK_CEMC_0000005423-5426). However, since Mr. Fiolek admitted to not wearing the prescribed apparatus to treat sleep apnea, uncontrolled obstructive sleep apnea may have also contributed to the development of atrial fibrillation (see below in section marked, “Other medical problems unrelated to CLL”). In this regard, it is worth noting that Mr. Fiolek’s hemoglobin was frequently high-normal. A high-normal hemoglobin is typical of uncontrolled sleep apnea due to nighttime hypoxia (low blood oxygen), but unusual in CLL patients on therapy. Mr. Fiolek continued to have atrial fibrillation three years after discontinuation of ibrutinib despite therapy. More recently, an echocardiogram in 2024 demonstrates severe enlargement of his left atrium, a known risk factor for paroxysmal atrial fibrillation.

Because Mr. Fiolek developed atrial fibrillation and was now on diltiazem, Dr. Cho reduced the ibrutinib dose to 140 mg every other day from 11/18/2016 through 02/06/2017. He increased the dose to 140 mg by mouth once daily (50% dose reduction due to continuation of diltiazem and drug-drug interaction) from 02/07/2017 through 03/23/2017. On 03/23/2017, Mr. Fiolek was noted to have progressive lower extremity edema and easy bruising (both attributed to ibrutinib). On 03/25/2017, Mr. Fiolek had a mechanical fall while walking his dog. He was evaluated in the Emergency Room on 03/25/2017 (00062_FIOLEK_CEMC_0000005678-5680). He had injuries to his right elbow and occipital scalp (head). Head CT shows soft tissue abnormality in the right parieto-occipital region, but no fracture or intracranial abnormality. He required five staples for closure of the head laceration. There was a subcutaneous hematoma that was spontaneously draining. He saw Dr. Cho on 03/31/2017; the ibrutinib was restarted but at a reduced dose 140 mg every other day due to the interaction with diltiazem and now more significant bleeding (00062_FIOLEK_CCHC_0000000230-234). From 03/27/2017 through 04/27/2017, he continued ibrutinib 140 mg every other day. The dose was increased to daily on 04/27/2017. Over this time,

the bleeding from the occipital wound decreased, and the laceration healed by 06/14/2017 (00062_FIOLEK_CEMC_0000005108).

Mr. Fiolek continued to have significant lymphedema in both arms and both legs attributed to ibrutinib. Therefore, ibrutinib was discontinued on 06/02/2017. Dr. Cho did not detect any adenopathy or splenomegaly on this date (00062_FIOLEK_CCHC_0000000204-207). On 06/02/2017, there was still leukocytosis and lymphocytosis; the WBC count was 29,300, ALC 23.9, hemoglobin 13.5 gram/dL, and platelet count 105,000 (00062_FIOLEK_CCHC_0000000067-68). He was evaluated by Dr. Matthew Foster at UNC on 07/03/2017. On that day, without any documented interval therapy over the preceding month since discontinuation of ibrutinib, the WBC count had decreased to 7,400, and the ALC decreased to 2,100. Dr. Foster recommended observation at that time. He also recommended venetoclax if Mr. Fiolek's CLL later progressed (00062_FIOLEK_0000010580). As a second option, he suggested another anti-CD20 antibody, ofatumumab, could be used with chlorambucil, with proper prophylaxis for infusion reactions.

Mr. Fiolek was placed on a "watch and wait" observational protocol again after termination of the ibrutinib therapy. He developed progressive lymphocytosis and thrombocytopenia. On 05/31/2018, his WBC count was 50,800, HGB 14.9 gram/dL, and platelet count 81,000 (00062_FIOLEK_CEMC_0000006483). Ultimately, the decision was made to restart therapy.

The dose of venetoclax is slowly increased to avoid tumor lysis syndrome. Mr. Fiolek was admitted for observation after the first oral venetoclax doses on 10/16/2018; he had been off therapy for 16 months. On admission, his WBC count had increased further to 63,700 and platelet count decreased to 70,000. The initial order for 20 mg once daily can be found on 00062_FIOLEK_CEMC_0000006530. There was no evidence of tumor lysis syndrome, and he was discharged home. On 10/13/2018, the WBC count was 48,600, hemoglobin 13.8 gram/dL, and platelet count 72,000 (00062_FIOLEK_CEMC_0000006948). He was readmitted on 10/23/2018 for the next dose ramp up on 10/23/2018. Dr. Cho's order for venetoclax 50 mg daily can be found on 00062_FIOLEK_CEMC_0000006791. Dr. Cho was able to escalate the venetoclax to the recommended daily dose of venetoclax (400 mg, four 100 mg tablets once daily).

Mr. Fiolek has required dose reductions due to leukopenia, neutropenia, and thrombocytopenia since initiation of the therapy. Low blood counts are known adverse effects associated with venetoclax. There appears to be disagreement between the exact doses documented in the progress notes and those documented in the McKesson records and medication list. For example, in Dr. Cho's progress note on 04/24/2024, he documents "At this time, we will have the patient now decrease to the final dose reduction of 150 mg a day. He will be taking one capsule a day." (see 00062_FIOLEK_CEMC_0000009334). The dose reduction was due to low WBC and platelet counts. However, the medication list on that date indicates Mr. Fiolek was taking two 100 mg tablets of venetoclax once daily. Venetoclax is NOT available as a single 150 mg capsule or tablet. According to McKesson accounts, he has been prescribed 100 mg tablets in recent years. He started at four 100 mg tablets once daily after the initial dose ramp up. Over the next six years there have been dose reductions to 300 mg once daily (first documented on 11/20/2018 for leukopenia (low

WBC count) (for example see 00062_FIOLEK_CEMC_0000007190), then to 200 mg once daily, and most recently to 100 mg once daily.

He has tolerated venetoclax remarkably well with excellent control of the CLL according to progress notes by Dr. John Cho between 06/22/2020 and 10/23/2023. (*See* progress notes 00062_FIOLEK_CEMC_0000007608-09 (06/22/2020), 0000000390 (09/02/2020), 0000000543 (06/03/2021), 0000000717 (08/26/2022), 0000000715 (12/23/2022), and 0000000803 (10/24/2023); Cho Dep. 120:21-121:4 ("He was having absolutely no side effects with it."), 124:11-23)). A sample of Mr. Fiolek's blood counts on venetoclax are listed below in Table 1:

Table 1 – Sample of Mr. Fiolek's Blood Counts on Venetoclax

Date of Sample	Blood Counts	Medical Record Citation
03/19/2020	WBC 3.9, HGB 15.5, PLT 105,000, ANC 2.8, ALC 0.5	00062_FIOLEK_CEMC_0000007165
06/22/2020	WBC 4.3, HGB 14.8, PLT 97,000	00062_FIOLEK_CEMC_0000007569
09/02/2020	WBC 4.1, HGB 14.7, PLT 108,000	00062_FIOLEK_CEMC_0000007569
12/02/2020	WBC 3.9, HGB 15.0, PLT 105,000, ALC 0.6	00062_FIOLEK_CEMC_0000007693 00062_FIOLEK_CEMC_0000000464
03/03/2021	WBC 3.7, HGB 14.9, PLT 111,000	00062_FIOLEK_CEMC_0000007693
07/30/2021	WBC 5.0, HGB 15.2, PLT 79,000	00062_FIOLEK_CEMC_0000007769
02/14/2022	WBC 3.5, HGB 15.0, PLT 123,000, ANC 2.3, ALC 0.6	00062_FIOLEK_CEMC_0000008238
12/23/2022	WBC 3.6, HGB 14.8, PLT 102,000	00062_FIOLEK_CEMC_0000008786
04/24/2023	WBC 3.8, HGB 15.2, PLT 102,000	00062_FIOLEK_CEMC_0000008847
06/18/2024	WBC 4.3, HGB 15.1, PLT 88,000, ANC 3.0, ALC 0.5	00062_FIOLEK_CEMC_0000009301
08/13/2024	WBC 4.1, HGB 13.9, PLT 124,000, ANC 2.8, ALC 0.6	00062_FIOLEK_CEMC_0000009301
11/04/2024	WBC 3.7, HGB 16.0, PLT 95,000	00062_FIOLEK_CEMC_0000010774
11/08/2024	WBC 3.4, HGB 15.9, PLT 107,000	00062_FIOLEK_CEMC_0000010843

The WBC count and absolute neutrophil counts (ANC) listed in Table 1 are low normal and of no clinical consequence. The hemoglobin is normal; he is not anemic. In fact, the hemoglobin is high-normal, potentially reflecting nocturnal hypoxia due to obstructive sleep apnea and documented poor compliance with CPAP. The platelet count is mildly decreased (considered grade 1 thrombocytopenia), and of no clinical consequence. The absolute lymphocyte count is low due to prior therapy with obinutuzumab, ibrutinib, and venetoclax. Remarkably, he has only had a single documented infection while taking venetoclax. He was diagnosed with dermatomal herpes zoster (shingles) on the right side of his body by Dr. Kristina Rowe on 12/03/2021 (00062_FIOLEK_CEMC_0000001431-1433). He was treated with a seven-day course of acyclovir 800 mg five times daily.

In review of the Biologics by McKesson account records, Mr. Fiolek's co-payment for ibrutinib and venetoclax from 09/08/2016 through 06/24/2024 was initially $24 and has increased over the years to $43 (00062_FIOLEK_0000010988-11678).

VI. Mr. Fiolek's Other Medical Issues

Mr. Fiolek has had several other major health issues while taking venetoclax, but that are not related to either CLL or its treatment. These include: (i) bladder cancer; (ii) cardiopulmonary issues; and (iii) miscellaneous other medical problems.

A. Mr. Fiolek's Bladder Cancer

On 02/13/2024, he was evaluated for the first time by Dr. Wardell for gross hematuria (visually apparent blood in his urine) (00062_FIOLEK_CEMC_0000001326). CT scan of the abdomen and pelvis on 03/05/2024 only demonstrated colonic diverticulosis and gall stones (00062_FIOLEK_CEMC_0000009376). There was no evidence of CLL on this CT scan; there was no splenomegaly or adenopathy. Mr. Fiolek saw Dr. Jeffrey Goodwin, urologist, for an initial consultation on 03/07/2024 (00062_FIOLEK_CEMC_0000001314-1319). Dr. Goodwin notes episodic hematuria for the prior two months. Dr. Goodwin also notes that the "patient is on Eliquis", even though Dr. Cho's progress notes indicated the apixaban would be discontinue after six months of therapy in October 2022. Dr. Cho's progress notes on 12/23/2022 (00062_FIOLEK_CEMC_0000000715) and 10/24/2023 (00062_FIOLEK_CEMC_0000000803) still list Eliquis. Dr. Goodwin's progress note lists Eliquis in the medication list on 03/07/2024. On a follow-up visit with Dr. Wardell on 11/04/2024, Eliquis is no longer listed on the medications list (00062_FIOLEK_CEMC_0000010407-10409). It is not clear if the apixaban (Eliquis) was discontinued in October 2022 as planned or at some time later. It should be noted that the electronic medical record will continue to list active medications until removed by an authorized provider (physician or advanced practice provider).

The urine cytology on 03/08/2024 detected atypical cells (00062_FIOLEK_CEMC_0000009401). Therefore, he underwent a repeat CT scan with hematuria protocol on 04/02/2024. There was dilation of the distal left ureter and lobular filling defects in the left ureter (00062_FIOLEK_CEMC_000009432). He underwent cystoscopy with transurethral resection of a bladder tumor on 04/19/2024. The operative report (00062_FIOLEK_CEMC_0000009483)

describes a papillary tumor involving the bladder trigone and left ureteral orifice with minimal involvement of the left bladder wall. Two grams of the chemotherapy agent gemcitabine were instilled in the bladder at the end of the procedure. The admission note for this surgical procedure only mentions Mr. Fiolek's family history of bladder cancer as a risk factor, and not CLL (00062_FIOLEK_CEMC_0000009476).

He started therapy with intravesical BCG. He received 50 mg with each treatment (one third the standard dose due to a national BCG shortage). He received the first installation on 04/28/2024 (00062_FIOLEK_CEMC_0000001280), the second installation on 06/04/2024 (00062_FIOLEK_CEMC_0000001278), and the third on 06/11/2024 (00062_FIOLEK_CEMC_0000001277). He saw Dr. Marc Bjurlin at the UNC Genitourinary Multidisciplinary Clinic on 05/24/2024 (see 00062_FIOLEK_0000010550-10552 for detailed assessment and recommendations). Dr. Bjurlin recommended either placement of a stent in the left ureter followed by BCG therapy or robotic left ureteretectomy followed by BCG. Mr. Fiolek chose to return to his local urologist Dr. Goodwin for treatment.

When Dr. Goodwin received the UNC Genitourinary Oncology consultation note, he repeated the cystoscopy and placed a left ureteral stent on 07/02/2024. Dr. Goodwin instilled two grams of gemcitabine into the bladder at the end of the procedure. Mr. Fiolek then received six further doses of intravesical BCG 50 mg (one third dose due to national shortage) on 08/13/2024 (00062_FIOLEK_CEMC_0000010492), 08/20/2024 (00062_FIOLEK_CEMC_0000010486), 09/03/2024 (00062_FIOLEK_CEMC_0000010480), 09/10/2024 (00062_FIOLEK_CEMC_0000010473), 09/24/2024 (00062_FIOLEK_CEMC_0000010453), and 10/01/2024 (00062_FIOLEK_CEMC_0000010447). Repeat cystoscopy was performed on 11/15/2024. There was no evidence of disease in the bladder and the left ureteral orifice was widely patulous. There were small nodular areas in the left distal ureter consistent with disease; there was no evidence of persistent urothelial carcinoma in the bladder wall. Biopsies were taken and the areas were subsequently treated with laser. The remainder of the more proximal left ureter was examined and found to be free of disease. The left ureteral stent was removed. (00062_FIOLEK_CEMC_0000010549). The pathologic examination of the left distal ureteral nodules was diagnostic of high grade invasive urothelial carcinoma; there was no muscularis in the specimen (00062_FIOLEK_CEMC_0000010585). The cytologic examination was positive for atypical cells (00062_FIOLEK_CEMC_0000010586). Mr. Fiolek tolerated the procedure well except for diarrhea for a few days following the procedure (00062_FIOLEK_CEMC_ 0000010387). Dr. Goodwin saw Mr. Fiolek on 11/27/2024 (00062_FIOLEK_CEMC_ 0000010392) to discuss the operative findings and referred Mr. Fiolek back to the UNC Genitourinary Oncology Clinic for recommendations. Dr. Bjurlin saw Mr. Fiolek at UNC on 02/03/2025 and recommended a repeat ureteroscopy; a surgical resection of the ureter; and further treatment with intravesical gemcitabine and docetaxel. (00062_FIOLEK_UNC_0000000146).

B. Mr. Fiolek's Cardiopulmonary Issues

Mr. Fiolek has had three major cardiopulmonary issues. The first of these is the atrial fibrillation, initially attributed to ibrutinib. An implanted loop recorder was placed on 07/27/2017 to document episodes of paroxysmal atrial fibrillation (00062_FIOLEK_CEMC_0000005847). He continued diltiazem (for ventricular rate control), flecainide (anti-arrhythmic), and coumadin (as anticoagulation to prevent thromboembolic complications). After discontinuation of ibrutinib, but before initiation of venetoclax, he had more cardiac symptoms. He was evaluated in the CEMC Emergency Room for chest pain on 04/02/2018 (00062_FIOLEK_CEMC_0000005999). His WBC count was 31,500, hemoglobin 13.9 gram/dL, and platelet count 84,000. Mr. Fiolek was evaluated by Dr. Angela Park, cardiologist, on 05/07/2018 (00062_FIOLEK_CEMC_0000006199). She noted increase burden of atrial fibrillation with episodes of shortness of breath and increasing lower extremity edema (swelling), requiring diuresis with furosemide. Nonetheless, Dr. Park was not convinced that the shortness of breath and edema were due to the atrial fibrillation. She changed the diltiazem to metoprolol to help decrease the lower leg swelling. She recommended cardiac catheterization to exclude heart failure and coronary artery disease.

He was admitted from 06/04/2018 through 06/07/2018 for the left and right cardiac catheterization. The right and left cardiac catheterization performed by Dr. Jessup during this admission showed no evidence of significant coronary artery disease, and the filling pressures and cardiac output were normal (00062_FIOLEK_CEMC_0000006219-6221). The flecainide was discontinued, and he started dofetilide (Tikosyn), an anti-arrhythmic medication, during this hospitalization (see discharge note 00062_FIOLEK_CEMC_0000006216).

Despite dofetilide therapy, Mr. Fiolek continued to have symptomatic atrial fibrillation confirmed by the implanted loop recorder. Dr. Park recommended cardiac ablation on 03/19/2020 as documented in the admission note by Mallory Salter, NP, on 05/15/2020 (00062_FIOLEK_CEMC_0000007276). On 06/02/2020 he underwent cardiac electrophysiology study with cryoablation for pulmonary vein isolation and radiofrequency ablation for atrial flutter (00062_FIOLEK_CEMC_0000007346 for procedure note). The pre-procedure transesophageal echocardiogram did not demonstrate a left atrial appendage thrombus. Incidentally, the aortic valve "opened well with trace to mild regurgitation"; there was no mention of stenosis (00062_FIOLEK_CEMC_0000007317). The implantable loop recorder did not demonstrate any atrial fibrillation following the ablation. At the clinic visit with Dr. Angela Park on 06/04/2021, the dofetilide (Tikosyn) was discontinued (00062_FIOLEK_CEMC_0000007893). Dr. Park's progress note indicates that the anti-coagulant apixaban (Eliquis) had been discontinued at "the last visit". A new loop recorder (due to end-of-life of the first loop recorder) was implanted on 06/18/2021 (00062_FIOLEK_CEMC_0000007895). This second implantable loop recorder also did not detect any episodes of atrial fibrillation up to and including the last transmission on 06/06/2024. Therefore, on 10/30/2024, his cardiologist recommended against replacement of the implantable loop recorder at the end-of-the-life of the current implant.

The second major event occurred on 04/15/2022. He woke at 3 a.m. short of breath (a condition known as paroxysmal nocturnal dyspnea). He was diagnosed with multiple pulmonary emboli (blood clots in the lungs), flash (sudden) pulmonary edema, and severe aortic stenosis (aortic valve

area 0.9 cm2). There was no evidence of deep venous thrombosis in either leg by venous Doppler ultrasound (00062_FIOLEK_CEMC_0000008476-8477). He was treated with full dose apixaban (Eliquis, an oral anti-coagulant) and the diuretic agent furosemide to remove fluid from the lungs with clinical improvement (see 00062_FIOLEK_CEMC_0000008454 for discharge summary). He had been off anti-coagulation since 2021. He was felt to be at risk of thromboembolic disease due to CLL according to the hospital notes. However, at that time, his WBC count was 3.6, hemoglobin 14.8 gram/dL, and platelet count 98,000. He subsequently was evaluated by Dr. Cho. Dr. Cho ordered a venous Doppler ultrasound of the port, evaluating for a catheter-associated thrombosis; this study was negative for thrombosis (00062_FIOLEK_CEMC_0000008807). In retrospect, a CT scan of the chest, abdomen and pelvis had been done on 03/21/2022 in preparation for a trans-aortic valve replacement (TAVR). The CT scan did not find any high-grade stenosis of the aorta and iliac vessels. There was mention of moderate circumferential bladder wall thickening, without mention of localized bladder wall thickening or hydronephrosis. The radiologist recommended correlation with urinalysis. There was no adenopathy identified on the scan (00062_FIOLEK_CEMC_00000008267-8268). There is no evidence of macroscopic hematuria during the admission according to the nursing assessment of urine output (00062_FIOLEK_CEMC_0000008514), even though he had started apixaban. A urinalysis was not done during this admission according to the discharge summary (00062_FIOLEK_CEMC_0000008612-8615). The apixaban was discontinued following a six-month course in October 2022 according to Dr. Cho's progress note (00062_FIOLEK_CEMC_0000008792).

The third cardiac issue is aortic stenosis. He has been followed by Dr. Scott Sample for this issue. On 02/11/2022, Dr. Sample evaluated Mr. Fiolek (00062_FIOLEK_CEMC_0000008110-8117), recommending evaluation for aortic valve replacement. The echocardiogram on 02/21/2022 demonstrated a sclerotic aortic valve with a mean trans-valve pressure gradient 19 mm Hg and peak trans-valve gradient 30.8 mm Hg consistent with mild to moderate aortic stenosis with mild aortic regurgitation. The left ventricular function was preserved (ejection fraction 50-55%). The cardiac catheterization on 02/25/2022 (00062_FIOLEK_CEMC_0000008131) detected mild aortic stenosis and non-obstructive coronary artery disease. However, the TAVR procedure has not been scheduled due to his other medical problems including pulmonary emboli and urothelial carcinoma. A repeat echocardiogram on 12/03/2024 demonstrates stable cardiac function and stable mild to moderate aortic stenosis with mild aortic regurgitation (00062_FIOLEK_CEMC_0000010372-10375). The peak trans-valvular pressure gradient was slightly higher compared to 02/21/2022 (now 38 mm Hg), but the mean gradient was identical (19 mm Hg). There was diastolic dysfunction, mild concentric left ventricular hypertrophy, and low normal left ventricular function; the left atrium was now severely dilated.

C. Miscellaneous Other Medical Problems:

Finally, Mr. Fiolek also has experienced miscellaneous other medical problems that do not appear to be relevant to this case. These are briefly summarized below:

- 08/03/1971: Motorcycle accident on base with fracture of right femur and patella. Right patella removed on 08/03/1971 (00062_FIOLEK_0000000117).

- 05/26/1998: Nuclear medicine pharmacologic (Cardiolite) stress test for evaluation of chest pain: reversible defect consistent with minimal apical ischemia (00062_FIOLEK_CEMC_0000004548).
- 01/21/2000: Orthopedic surgery admission for right total knee arthroplasty/replacement by Dr. Brian Battersby (Discharge note 00062_FIOLEK_CEMC_0000004743). WBC 6.5 with 33.9% lymphocytes (normal).
- 02/26/2004: Sleep study for evaluation of snoring, apnea, and myoclonic jerks at night (00062_FIOLEK_CEMC_0000004883-4975). Prescribed nasal CPAP for mild obstructive sleep apnea on (03/08/2004 sleep study interpretation with CPAP (00062_FIOLEK_CEMC_0000004958). Mr. Fiolek has been poorly compliant with CPAP by his own admonition (for example, see a progress note on 08/12/2019 00062_FIOLEK_CEMC_0000006997).
- 07/19/2010: Esophagogastroduodenoscopy (EGD) for evaluation of epigastric pain: hiatal hernia and erosive gastritis, deformed antrum consistent with prior peptic ulcer disease, and erosive duodenitis. Treated with dexlansoprazole and sucralfate. (00062_FIOLEK_CCHC_0000000416). Pathology report on 00062_FIOLEK_CEMC_0000005160).
- 09/02/2010: Doppler ultrasound for right lower leg swelling: No deep venous thrombosis, but prominent Baker cyst (00062_FIOLEK_CEMC_0000005187).
- 04/12/2012: Upper GI series with small bowel follow through detected small hiatal hernia and narrow duodenum 00062_FIOLEK_CEMC_0000005239).
- 08/07/2012: Pathology report of gastric biopsy shows slight chronic inflammation (00062_FIOLEK_CEMC_0000005263).
- 01/16/2017: Dysphagia evaluation by barium swallow: Negative (00062_FIOLEK_CEMC_0000005648)
- 02/07/2017: Speech therapy evaluation for dysphagia: Negative.
- 02/02/2018: Pulmonary function tests: Normal DLCO (gas exchange), normal lung volumes, mild expiratory air flow obstruction without significant change post bronchodilator (00062_FIOLEK_CEMC_0000005934).
- 08/30/2019: Esophagogastroduodenoscopy (EGD) demonstrated gastritis (00062_FIOLEK_CEMC_0000007035).
- 10/27/2021: Laceration of the left fourth finger on a knife. Closed with Steri-strips alone (00062_FIOLEK_CCHC_0000000185).
- 01/26/2023: Admission for evaluation of sudden onset diplopia (double vision) and imbalance. The symptoms resolved by the next day. The MRI and CT scans of the brain were unremarkable. This was likely a reversible ischemic neurologic defect (RIND) versus a transient ischemic attack (TIA). (See discharge note 00062_FIOLEK_CEMC_0000009026.)
- 09/12/2024: Evaluation for dizziness and vertigo. Head CT was unremarkable. Diagnosis benign paroxysmal positional vertigo (BPPV). (00062_FIOLEK_CEMC_0000010463).

VII. Analysis

A. It is highly unlikely that Mr. Fiolek's distant and intermittent exposure to water at Camp Lejeune caused his CLL.

As stated above, it is my opinion that it is highly unlikely that Mr. Fiolek's distant and intermittent exposure to water at Camp Lejeune in the 1960s caused his CLL.

There is no known cause or causes for CLL. There is insufficient evidence linking the specific contaminants at Camp Lejeune to CLL. Furthermore, Mr. Fiolek has known demographic features associated with a higher risk of CLL compared with people without these features. The median age at diagnosis of CLL is 70 years. Mr. Fiolek was 74 years old at the time of his initial diagnosis. Men are 1.8 times as likely to be diagnosed with CLL compared with women (6.75 and 3.65 cases per 100,000 men and women, respectively). He is Caucasian, although without a thorough genealogy we cannot state if he has any African or Asian ancestry. His half-sister had leukemia, specifically acute lymphoblastic leukemia (ALL), as noted in Mr. Fiolek's deposition. (Fiolek Dep. 93:18-22.) The medical record also states his brother had leukemia, but Mr. Fiolek denies this in his deposition. (Fiolek Dep., Vol. I, 99:7-23.) He is considered to have severe obesity based on the reported body mass index (BMI 35-40 kg/m^2) around the time of his CLL diagnosis: BMI 37.6 kg/m^2 on 07/15/2013 (00062_FIOLEK_000000223-225), BMI 38.06 kg/m^2 (00062_ FIOLEK_000000217-218) on 01/16/2014, and BMI 36.77 kg/m^2 (00062_ FIOLEK_000000241-244) on 08/20/2014.

Bove and colleagues (see Bove FJ, et al. Environmental Health 2014; 13: 10) evaluated the mortality of Marines and Navy personnel who began service between 1975 and 1985 and were exposed to contaminated drinking water at Camp Lejeune in a retrospective cohort study. The mortality data were collected from 1979 to 2008 from death registries and the cause of death from the National Death Index. The control cohort were Marines and Navy personnel stationed at Camp Pendleton in California during the same time. This cohort study does not distinguish between death due to the multiple subtypes of acute and chronic leukemia. A shared generic name (such as leukemia) does not indicate a shared pathophysiologic mechanism. You cannot tell any specific risk for any single leukemia subtype based on a risk estimated for leukemia as a group.

In such a retrospective cohort study, it is important to conduct a multivariate analysis that includes all other potential covariates that may impact the results. Even setting aside the issue of estimating risk for all leukemia subtypes combined, a study should still adjust for potential confounders. The models would need to include age, gender, ethnicity, obesity, and family history of leukemia. These are known demographic features that affect the incidence of CLL. The Bove analysis includes the first three, but not obesity or family history. Furthermore, since CLL has a long natural history with or without therapy, the incidence of CLL, rather than mortality related to CLL, would provide a better assessment of any potential risk for this disease.

The standardized mortality rate for all leukemia was significantly lower in both the Camp Lejeune and Camp Pendleton populations compared with the general population [0.74 (95% CI 0.57, 0.95) and 0.78 (95% CI 0.60, 0.99), respectively]. There was not a statistically significant

difference in leukemia-related mortality in the Camp Lejeune and Camp Pendleton population. Furthermore, the relation between cumulative exposure and leukemia-related mortality was not linear; the calculated hazard ratios were lower at the higher exposures to TCE, benzene and TVOC than the lower exposures.

	Low exposure	Medium exposure	High exposure	Cumulative exposure	Log_{10} cumulative exposure
			c. Leukemias (N=66)		
TCE	2.00 (1.00, 4.00) N=16	1.54 (0.71, 3.36) N=11	1.81 (0.85, 3.85) N=13	.00002 (−0.00004, 0.00008) p=.46	.0801 (−0.0093, 0.1695) p=.08
Benzene	2.54 (1.27, 5.08) N=17	1.46 (0.66, 3.20) N=11	1.69 (0.77, 3.67) N=12	.00168 (−0.00158, 0.00494) p=.31	.1276 (0.0020, 0.2532) p=.05
TVOC	2.50 (1.24, 5.03) N=19	1.33 (0.56, 3.14) N=9	2.33 (1.08, 5.03) N=15	.00001 (−0.00003, 0.00005) p=.44	.0950 (0.0032, 0.1868) p=.04

Bove and colleagues (see Bove FJ, et al. Environmental Health Perspective 2024; 132: 107008-1-15) also evaluated the incidence of cancers with longer follow up in the Camp Lejeune and Camp Pendleton cohorts (https://doi.org/10.1289/EHP14966). In this evaluation, they included diagnoses obtained from cancer registries, a more reliable source of data than death registries, between 1996 and 2017. The Marine and Navy personnel were on base between 1975 and 1985. There was NO association between exposure to the contaminated water supply at Camp Lejeune between 1975 and 1985 and the subsequent development of all leukemia subtypes COMBINED between 1996 and 2017 (first line of table below). This analysis distinguishes between the various subtypes of leukemia. There was NO association between contaminated water supply at Camp Lejeune with the subsequent development of CLL [adjusted HR 1.02 (0.79, 1.32)].

	Camp Lejeune			Camp Pendleton
Cancer outcome	Cases (*n*)	Unadjusted HR (95% CI)	Adjusted HR (95% CI) CIR	Cases (*n*)
Leukemias	314	1.06 (0.91, 1.24)	1.07 (0.91, 1.25) 1.4	319
Lymphoid cancers	979	1.03 (0.95, 1.13)	1.02 (0.94, 1.12) 1.2	1,018
Hodgkin lymphoma	108	1.01 (0.78, 1.31)	1.01 (0.77, 1.31) 1.7	114
Non-Hodgkin lymphoma	550	1.00 (0.89, 1.13)	1.01 (0.90, 1.14) 1.3	588
Mantle Cell	27	1.21 (0.70, 2.09)	1.26 (0.73, 2.19) 3.0	24
Follicular	130	1.03 (0.81, 1.31)	1.07 (0.84, 1.36) 1.6	135
Diffuse large B-cell	160	0.88 (0.72, 1.09)	0.89 (0.72, 1.10) 1.5	194
Burkitt	15	1.33 (0.62, 2.84)	1.53 (0.71, 3.30) 4.6	12
Marginal zone B-cell	43	1.41 (0.89, 2.21)	1.45 (0.92, 2.28) 2.5	33
Multiple myeloma	185	1.22 (0.99, 1.51)	1.13 (0.91, 1.40) 1.5	163
Acute lymphocytic leukemia	23	0.97 (0.55, 1.70)	0.94 (0.53, 1.67) 3.2	25
Chronic lymphocytic leukemia	114	1.01 (0.78, 1.30)	1.02 (0.79, 1.32) 1.7	122
Myeloid cancers (including polycythemia vera, myelodysplastic and myeloproliferative syndromes)	239	1.21 (1.00, 1.45)	1.24 (1.03, 1.49) 1.4	213
Myeloid cancers (including myelodysplastic and myeloproliferative syndromes)	186	1.19 (0.96, 1.46)	1.19 (0.97, 1.47) 1.5	169
Acute myeloid leukemia[a]	104	1.36 (1.02, 1.81)	1.38 (1.03, 1.85) 1.8	82
Chronic myeloid leukemia	39	0.75 (0.50, 1.12)	0.74 (0.49, 1.12) 2.3	56
Myelodysplastic and myeloproliferative syndromes	49	1.66 (1.07, 2.60)	1.68 (1.07, 2.62) 2.4	32
Polycythemia vera	53	1.29 (0.87, 1.93)	1.41 (0.94, 2.11) 2.2	44

Mr. Fiolek, like most patients presenting with CLL, did not initially require therapy. The disease process was very likely present at the time of the first complete blood count showing an elevation of both the white blood cell count and lymphocyte count. The first time a CBC detected a mild elevation of the white blood cell count (11,000 per microliter) with a very mild increase in the absolute lymphocyte count (4,200 per microliter) was on 12/18/2007. If flow cytometry had been done at this time, the peripheral blood lymphocytes would almost definitely have the typical immunophenotype of CLL (expression of CD5, CD19, CD20, CD23 and surface immunoglobulin). However, he would not have been considered to have CLL at that time. CLL is

defined as having over 5000 monoclonal B cells per microliter blood. He would be considered to have monoclonal B lymphocytosis. All patients with CLL have prior monoclonal B cell lymphocytosis (MBL); however, MBL does not always progress to CLL. However, he had a higher risk of progression to CLL based on the degree of MBL in 2007.

Mr. Fiolek has had an excellent and durable response with venetoclax therapy. In the event of a relapse, Mr. Fiolek could still be treated with other monoclonal antibodies like rituximab or ofatumumab (as suggested by Dr. Matthew Foster in his UNC consultation report in 2017). He could receive newer BTK inhibitors that have been shown to be less likely to cause atrial fibrillation. There are also novel agents in development including bispecific T cell engagers (BiTE) and chimeric antigen receptor T cells (CAR-T). In fact, the life expectancy of older CLL patients treated with targeted therapies such as venetoclax and the BTK inhibitors on clinical trials is similar to that of an age- and gender-matched general population (see Molica S, et al. Cancers 2024; 16: 1085). In short, Mr. Fiolek's CLL is unlikely to shorten his life expectancy.

B. It is unlikely that Mr. Fiolek's CLL or CLL treatment caused his bladder cancer.

As stated above, it also is my opinion as an oncologist and hematologist that it is unlikely that Mr. Fiolek's CLL or CLL treatment caused his subsequent bladder cancer.

Mr. Fiolek has known risk factors for bladder cancer (a subset of urothelial carcinoma), including family history of bladder cancer in his mother at a relatively young age, his personal use of tobacco, advanced age, and male gender. In general, secondary cancers are 2-3 times more likely to develop in patients with CLL. We recommend standard surveillance for other cancers in our patients with CLL, especially dermatologic evaluation for both melanoma and non-melanomatous cancers.

That said, bladder cancer is not included as a secondary cancer in CLL patients on the American Cancer Society website made available to patients. The ACS website lists the following second cancers as more likely to occur in CLL: skin cancer, melanoma, cancer of the larynx, lung cancer, colon cancer, Kaposi sarcoma, soft tissue sarcoma (https://www.cancer.org/cancer/types/chronic-lymphocytic-leukemia/after-treatment/second-cancers). The risk of bladder cancer in patients with CLL is not clear; some studies did not report an increased risk (see Sayin S, et al. Asian Pac J Cancer Prev. 2023; 24: 1971-77). The recent analysis by Bond and colleagues from the Ohio State University did detect a higher incidence of bladder cancer in their CLL patient population: expected risk 1.34, secondary cancer risk 1.7, confidence intervals 1.2 – 8.7 (see Bond DA, et al. Leukemia 2020; 34: 3197-3205). However, four of the five bladder cancer patients had a prior history of tobacco use, like Mr. Fiolek, which is a confounding variable. Furthermore, the authors do not comment on whether any of these five patients had been treated with cyclophosphamide, an alkylating agent used in the treatment of CLL. Sixty percent of the patients in their cohort had received an alkylating agent; Mr. Fiolek has not.

VIII. Response and Rebuttal to Dr. Laber's Report

I disagree with some observations regarding Mr. Fiolek's medical history made by Dr. Laber in his report (dated Feb. 7, 2025).

First, Dr. Laber notes that Mr. Fiolek was initially treated with a combination of chlorambucil and obinutuzumab. He does recognize that Mr. Fiolek had a severe infusion reaction to obinutuzumab therapy, "but recovered and was able to complete therapy" (see page 12 of Dr. Laber's report). In fact, Mr. Fiolek only received a fraction of the first dose of obinutuzumab. Mr. Fiolek never started chlorambucil (although he did have the prescription) and did not complete even the first of six planned cycles of obinutuzumab.

In his analysis of Mr. Fiolek's case, Dr. Laber concludes that Mr. Fiolek did not have a response to intravesical BCG and gemcitabine "due to the presence of immune dysregulation of his CLL" (see page 17 of Dr. Laber's report). However, Mr. Fiolek did have a complete disappearance of the bladder wall tumor; however, the tumor involving the left ureter persisted. Urothelial carcinoma is known as a field defect, potentially arising in any region of the urinary collecting system. The lack of response in the left ureter, but not the bladder wall, is more likely related to drug delivery. In fact, Mr. Fiolek first received three doses of intravesical BCG before his urologist received the recommendations from the UNC Genitourinary Tumor Board. UNC physicians recommended placement of a stent in the left ureter before giving intravesical BCG. The reason for this suggestion is that the normal urine flow from the kidney into the renal pelvis followed by the left ureter into the bladder would diminish (if not completely prevent) the BCG from reaching the ureteral tumor from the bladder. The stent was placed to potentially eliminate the urinary current in the left ureter and allow more efficient drug delivery to this site. Despite the placement of the stent, the left ureteral tumor did not respond to six additional doses of intravesical BCG, but the bladder wall tumor did.

Second, Dr. Laber and some of Plaintiffs' general causation experts cite the New Jersey study of exposure to VOCs in drinking water and the incidence of leukemia and non-Hodgkin lymphoma [Cohn P, et al. Environ Health Perspect. 1994; 102: 556-561]. There are several methodological issues with this population-based study that limit the applicability of the conclusions to this case.

Specifically, the authors could not adjust their models for all known risks associated with a higher incidence of CLL. The authors were able to comment on the effect of age and gender, but the available data precluded an analysis based on other known risks for CLL including obesity and family history of leukemia. Although self-reported ethnicity was collected in the New Jersey State Cancer Registry, the potential effect of ethnicity was not described in the report. It is conceivable that the regions of higher VOC exposures also had higher prevalence of other demographic characteristics associated with CLL. A multivariate analysis including all known risks for CLL would be required to conclude that the VOC exposure was the cause of CLL in these people. Since the reported relative risks are so close to unity (i.e., 1.0), an imbalance in other known risk factors could potentially affect the conclusions. The incident cases of primary leukemia and lymphoma were collected between 1979 and 1987, but the first time that the VOC levels were measured was in 1984-1985. It may be reasonable to assume that the water supply was contaminated prior to the

first rounds of mandatory water testing; however, additional cases were not collected after 1987. If the exposure to VOC contamination of the New Jersey water supply was responsible for the reported higher incidence of CLL in this cohort, these people likely already had MBL, given the natural history of MBL and progression to CLL reviewed by Shanafelt and colleagues (Shanafelt TD, et al. Leukemia 2010; 24: 512-520). Given the limited timing of the collection of leukemia cases from the New Jersey State Cancer Registry, this analysis does not allow us to conclude that an exposure to VOC may be a cause of CLL decades later, as in this case. Although the authors point out that the geographic regions evaluated in this study did not "exhibit major population influx" during the 1970-1980 period, there was no attempt to evaluate each reported case of cancer with time of residency in one of the New Jersey counties.

With these methodological weaknesses we can now evaluate the results in the analysis by Cohn et al. Some cases of CLL could have been included in the low-grade NHL group, if the diagnosis was made by lymph node biopsy and called small lymphocytic lymphoma. The relative risk of developing low-grade lymphoma was numerically higher with trichloroethylene (TCE) exposure, but not statistically increased. The relative risk was numerically lower with the higher TCE exposure compared to lower. The lack of a relation between exposure dose and risk of low-grade lymphoma further argues against a causal relation. The relative risk of CLL was numerically, but not statistically, higher even at the higher level of TCE exposure. There was no relation between CLL and perchloroethylene (PCE). In fact, the relative risk of CLL was numerically (but not statistically) lower with exposure to PCE than without.

Despite other reports in the literature similar to that of Cohn et al. (1996) and given methodological issues common to many population-based epidemiologic studies, there remains no known cause of CLL. The American Cancer Society does not recognize any definite environmental agent as causative of CLL.

Dr. McCabe also addresses evidence citing the effects of VOCs on the immune system. (See pgs. 19-22 of Dr. McCabe's General Causation Report – Camp Lejeune Water Volatile Organic Chemicals and Non-Hodgkin's Lymphoma and Leukemia (Feb. 7, 2025)). Immune dysfunction is hypothesized to be a contributing factor for the development of neoplasia (cancer) in general due to decrease in immune surveillance. However, not all cancers are associated with deficiencies in our immune system. For example, congenital immunodeficiency states are not associated with CLL. Immunosuppressive therapy with drugs such as the calcineurin inhibitors, methotrexate, and azathioprine is associated with subsequent development of skin cancers and myeloid neoplasms, but again not CLL. There is no clinical data to suggest immune injury of any kind as a cause of CLL. In Mr. Fiolek's case, there was also no evidence of an immune disorder before the diagnosis of CLL. Mr. Fiolek was not known to have frequent infections before the diagnosis of CLL. In fact, after the diagnosis of CLL, and despite treatment, he has only had three documented infections: Staphylococcus aureus cellulitis at the time of the head trauma, dermatomal herpes zoster (shingles), and Candida (yeast) oro-pharyngitis. Mr. Fiolek also never had an autoimmune disease. The pathogenesis of CLL is unknown, but the current favored hypothesis suggests an exaggerated response to autoantigens or common environmental antigens—not immune dysfunction following possible exposures to VOCs.

Lympho-hematopoietic cancers are often grouped together in epidemiologic evaluation of potential risk factors. This practice may allow for a greater number of subjects and events to be analyzed, increasing the statistical power of the analysis. However, grouping may obscure an actual effect in a smaller subset of the population. The practice also presupposes that these factors are known to play a pathogenic role in every subtype of the disease. This is clearly not always true. For example, familial predisposition syndromes such as ataxia telangiectasia and Wiskott-Aldrich Syndrome are associated with non-Hodgkin lymphoma. However, these congenital immunodeficiencies have been mostly associated with high grade B cell lymphoma, especially in children, and often associated with the Epstein-Barr virus, but not low-grade indolent lymphoma or CLL. Autoimmune disorders such as rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE) are associated with non-Hodgkin lymphoma, but again these autoimmune diseases are associated with more aggressive B cell lymphoma such as large B cell lymphoma, not CLL (see review by S. Yadlapati and P. Efthimiou. BioMed Research International 2016). One study from the Swedish Cancer Registry (Baecklund E, et al. Arthritis and Rheumatism 2003; 48: 1543-50) found "an increased incidence of one specific lymphoma subtype, [diffuse large B cell lymphoma], in RA patients, as well as a possible association with RA disease activity." Sjogren's syndrome has been associated with mucosal-associated lymphoid tissue (MALT) lymphoma, but not CLL. Finally, immunosuppressive therapy following organ transplantation or for the treatment of autoimmune diseases increases the risk of both aggressive lymphoma and myeloid neoplasms. However, clinical studies have not associated the development of CLL with prior exposure to immunosuppressive therapies. Animal model studies are cited by the general causation experts, demonstrating the negative effects of VOC on immune cells and immune function. I agree with the evidence that these chemical agents cause DNA damage and immune defects in animal models. Nonetheless, there is no clinical data that other DNA damaging agents (like chemotherapy) or any immunosuppressive therapy is associated with CLL.

IX. Conclusions

Based on my review of this case, I have reached the following conclusions concerning Mr. Fiolek's case to a reasonable degree of medical certainty:

1. Mr. Fiolek has at least four factors associated with a greater risk for the development of CLL: advanced age, male gender, European ancestry, and obesity. Although not apparently CLL, he also has a family history of leukemia, which has been cited as a risk factor for CLL by the InterLymph Project. There is insufficient data in the literature to implicate VOCs, such as those found in the water supply at Camp Lejeune, in the development of CLL. Despite the epidemiological available data, CLL has no known cause. It is my opinion therefore that Mr. Fiolek's CLL is highly unlikely to be related to or caused by his exposure to any contaminants in the water at Camp Lejeune.

2. Although CLL has been associated with the subsequent development of other cancers, Mr. Fiolek has a personal history of tobacco use and close family history of bladder cancer, which are known risk factors. The American Cancer Society does not recognize bladder

cancer as specifically associated with CLL. Furthermore, because his CLL is not related to exposure to the contaminants in the Camp Lejeune water, I cannot conclude that the bladder cancer was related to any exposure either.

Therefore, I believe it is highly unlikely that any potential exposures to the VOCs in the water at Camp Lejeune in the 1960s caused Mr. Fiolek's CLL or bladder cancer. Mr. Fiolek has responded well to his CLL treatment and, given his current age of 85, I am more concerned that Mr. Fiolek's other significant (but unrelated) health problems, such as his aortic stenosis, may become more significant, if not life-threatening, problems in the near future. The recommendation for surgical resection of the left distal ureter is complicated by his high risk of surgical morbidity and mortality based on his advanced age, aortic stenosis, history of atrial fibrillation, and history of pulmonary embolism.

APPENDIX A

DUKE UNIVERSITY MEDICAL CENTER

CURRICULUM VITAE

Harry Paul Erba, MD PhD

Primary academic appointment: Hematologic Malignancies and Cellular Therapy

Primary academic department (not DUAP): Medicine

Secondary appointment (if any) - (department): N/A

Present academic rank and title (if any): Professor of Medicine

Date and rank of first Duke Faculty appointment: 07/01/2018

Medical Licensure: North Carolina License, # 2018-01322

Date of License: 05/25/2018

Specialty certification(s) and dates (Month/Day/Year):

ABIM, Board Certified, Internal Medicine (09/25/1991-12/31/2011)

ABIM, Board Certified, Hematology, (11/10/1994-Present)

ABIM, Board Certified, Medical Oncology, (11/09/1995-12/31/2015)

Citizen of United States

Education and Training

Education	Institution	Date (Year)	Degree
High School	North Haven	1975	HS Diploma
College	Yale University	9/1975-5/1979	BS, Biology
Graduate or Professional School	Stanford University School of Medicine	9/1981-6/1988	MD, Ph.D.

Scholarly societies (Alpha Omega Alpha, Sigma Xi, Phi Beta Kappa; etc.):

1977 Sigma Xi
1978 Phi Beta Kappa

Professional training and academic career (chronologically, beginning with first postgraduate position):

Institution	Position/Title	Dates
Internships and Residencies:		
Harvard Medical School	Clinical Fellow in Medicine	6/1988-6/1991
Brigham and Women's Hospital	First-Year Resident Physician	6/1988-6/1989
Brigham and Women's Hospital	Second-Year Resident Physician	7/1989-6/1990
Fellowships:		
Brigham and Women's Hospital	Clinical Fellow in Medicine	7/1990-6/1991
Brigham and Women's Hospital	Research/Clinical Fellow in Medicine	6/1991-7/1992
Harvard Medical School	Research Fellow in Medicine	6/1991-6/1993

Academic, Administrative, and Clinical Appointments

Instructor in Medicine, Harvard Medical School	7/1993-6/1996
Assistant Professor of Internal Medicine, University of Michigan Medical School	6/1996-8/2005
Associate Director, Hematology/Oncology Fellowship, University of Michigan	6/1996-12/05
Associate Professor of Internal Medicine, University of Michigan Medical	9/2005-6/2012
Professor of Internal Medicine, University of Alabama at Birmingham (UAB)	7/2012-4/2018
Director, Hematologic Malignancy Program, UAB Division of Hem & Oncology	7/2012-4/2018
Chair, Hematologic Malignancy Working Group, UAB Cancer Center	7/2012-4/2018
Associate Director, Clinical Research, UAB Comprehensive Cancer Center	3/2013-4/2018
Alfred F. LoBuglio Endowed Chair for Translational Cancer Research, UAB	9/2012-4/2018
Professor of Medicine, Duke University	7/2018-Present
Medical Director, Hematologic Malignancies Inpatient Services, Duke Hospital	1/2019-5/2023
Director, Leukemia Program, Duke Cancer Institute	7/2019-present

Hospital Appointments

7/1993-6/1996	Assistant Physician, Harvard University Health Services
7/1993-6/1996	Associate Staff Physician, Department of Medical Oncology, Dana-Farber Cancer Institute
7/1992-6/1996	Associate Physician, Brigham and Women's Hospital
7/1996-6/2012	Attending Physician, University of Michigan Health Systems
7/2012-4/2018	Attending Physician, University of Alabama at Birmingham Hospital
7/2018-Present	Attending Physician, Duke University Medical Center

Publications (Peer-reviewed Manuscripts):

1. Varley JM, MacGregor HC, **Erba HP**. Satellite DNA is transcribed on lampbrush chromosomes. Nature 1980; 283: 686-8.

2. Varley JM, McGregor HC, Nardi I, Andrews C, **Erba HP**. Cytological evidence of transcription of highly repeated DNA sequences during the lampbrush stage Triturus cristatus carnifex. Chromosoma 1980; 80: 289-307.

3. Stephensen EC, **Erba HP**, Gall JG. Characterization of a cloned histone gene cluster of the newt Notopthalmus viridescens. Nucleic Acids Res 1981; 9: 2281-95.

4. Stephensen EC, **Erba HP**, Gall JG. Histone gene clusters of the newt Notopthalmus are separated by long tracts of satellite DNA. Cell 1981; 24: 639-47.

5. Gall JG, Stephensen EC, **Erba HP**, Diaz MO, Barsacchi-Pilone G. Histone genes are located at the sphere loci of newt lampbrush chromosomes. Chromosoma 1981; 84:159-71.

6. **Erba HP**, Gunning P, Kedes L. Nucleotide sequence of the human gamma cytoskeletal actin mRNA: anomalous evolution of vertebrate non-muscle actin genes. Nucleic Acids Res 1986; 14: 5275-94.

7. **Erba HP**, Eddy R, Shows T, Kedes L, Gunning P. Structure, chromosome location, and expression of the human gamma-actin gene: differential evolution, location, and expression of the cytoskeletal beta- and gamma-actin genes. Mol Cell Biol 1988; 8: 1775-89.

8. Ng S-Y, **Erba HP**, Latter G, Kedes L, Leavitt J. Modulation of microfilament protein composition by transfected cytoskeletal actin genes. Mol Cell Biol 1988; 8: 1790-94.

9. Taylor A, **Erba HP**, Muscat G, Kedes L. Nucleotide sequence and expression of the human skeletal alpha-actin gene: evolution of functional regulatory domains. Genomics 1988; 3: 323-36.

10. Cross GS, Wilson C, **Erba HP**, Woodland HR. Cytoskeletal actin gene families of Xenopus borealis and Xenopus laevis. J Mol Evol 1988; 27: 17-28.

11. Aster J, Pear W, Hasserjian R, **Erba HP**, Sklar J. Functional Analysis of the TAN-1 Gene, a Human Homologue of Drosophila Notch. Cold Spring Harbor Symposia on Quantitative Biology 1995; 59:125-36.

12. Paciocco G, Bossone E, **Erba HP**, Rubenfire M. Reversible Pulmonary Hypertension in POEMS Syndrome. Canadian Journal of Cardiology 2000; 16: 1007-12.

13. Ganz P, Moinpour C, Pauler D, **Erba HP**, Fisher R. Health Status and Quality of Life in Patients with Early-Stage Hodgkin's Disease Treated on Southwest Oncology Group Study 9133. J Clin Oncol 2003; 21: 3512-9.

14. **Erba HP**. Recent Progress in the Treatment of Myelodysplastic Syndrome in Adult Patients. Curr Opin Oncol 2003; 15: 1-9.

15. **Erba HP**. Treatment Options for Newly Diagnosed Patients with Chronic Lymphocytic Leukemia (Review). Curr Hematol Rep 2004; 3: 47-53.

16. O'Brien S, Berman E, Ghalla K, **Erba HP**, Wetzler M et al. Chronic Myelogenous Leukemia. J Natl Compr Canc Netw 2005; 3: 732-555.

17. Collins CD, DePestel DD, Stuntebeck ER, **Erba HP**, Stevenson JG. Cost Analysis of a Ferbrile Neutropenia Algorithm with Respect to Empirical Antifungal Therapy in Adult Hematology/Oncology Patients: PIN5. Value in Health 2005; 8: 306.

18. O'Donnell MR, Appelbaum FR, Baer MR, **Erba HP**, Tallman MS et al. Acute Myeloid Leukemia. Clinical Practice Guidelines in Oncology. J Natl Compr Canc Netw 2006; 4: 16-36.

19. Greenberg PL, Baer MR, Bennett JM, **Erba HP**, Tallman MS et al. Myelodysplastic Syndromes. Clinical Practice Guidelines in Oncology. J. Natl Compr Canc Netw 2006; 4: 58-77.

20. Greineder CF, Nelson PW, Dressel AL, **Erba HP**, Younger John G. In Vitro and In Silico Analysis of Annexin V Binding to Lymphocytes as a Biomarker in Emergency Department Sepsis Studies. Acad Emerg Med Sep 2007; 14: 763-71.

21. O'Brien S, Berman E, Bhalla K, **Erba HP**, Wetzler M et al. Chronic Myelogenous Leukemia. J Natl Compr Canc Netw 2007; 5: 474-96.

22. Shehab N, DePestel DD, Mackler E, **Erba Harry P**. Institutional Experience with Voriconazole Compared with Liposomal Amphotericin B as Empiric Therapy for Febrile Neutropenia. Pharmacotherapy 2007; 27: 970-9.

23. Crawford J, Althaus B, Armitage J, **Erba HP**, Wong MK, et al. Myeloid Growth Factors. Clinical Practice Guidelines in Oncology. J Natl Compr Canc Netw 2007; 5(2):188-202.

24. Saddler C, Ouillette P, Kujawski L, M, **Erba HP**, Malek SN. Comprehensive Biomarker and Genomic Analysis Identifies p53 Status as the Major Determinant of Response to MDM2 Inhibitors in Chronic Lymphocytic Leukemia. Blood 2007; 111: 1584-93.

25. **Erba HP**. Prognostic Factors in Elderly Patients with AML and the Implications for Treatment. Hematology 2007; 420-8.

26. **Erba HP**. The Combination of Xanafide and Cytarabine has Unique Activity in Acute Myeloid Leukemia. Touch Briefings-US Oncological Disease. 2007; Issue II: 43-4.

27. Ouillette P, **Erba HP**, Malek SN. Integrated Genomic Profiling of Chronic Lymphocytic Leukemia Identifies Subtypes of Deletion 13q14. Cancer Res 2008; 68: 1012-21.

28. **Erba HP**, Kopecky KJ, Kirschbaum MH, Appelbaum FR. Phase II Studies of Different Schedules and Doses of the Farnesyltransferase Inhibitor Tipifarnib (R115777, Zarnestra) for Patients of Age 70 or Older with Previously Untreated Acute Myeloid Leukemia (AML): North American Intergroup Study S0432. Ann Hematol 2008; 87 (supplement 1): S57-S59.

29. Kujawski L, Ouillette P, **Erba HP**, Malek S. Genomic Complexity Identifies Patients with Aggressive Chronic Lymphocytic Leukemia. Blood 2008; 112: 1993-2003.

30. Greenberg PL, Attar E, Battiwalla M, **Erba, HP**, Westervelt P. Myelodysplastic Syndromes. J Natl Compr Canc Netw 2008; 6(9): 902-26.

31. O'Donnell MR, Appelbaum FR, Coutre SE, **Erba, HP**, White FL. Acute Myeloid Leukemia. J Natl Compr Canc Netw 2008; 6(10): 962-93.

32. Radich JP, Zelenetz AD, Chan WC, **Erba HP**, Winter JN. NCCN Task Force Report: Molecular Markers in Leukemias and Lymphomas. J Natl Compr Canc Netw 2009; 7 supplement 4:S1-23, S35-6.

33. Crawford J, Armitage J, Balducci L, **Erba HP**, Wong MK. Myeloid Growth Factors. J Natl Compr Canc Netw 2009; 7(1): 64-83.

34. O'Brien S, Berman E, Borghaei H, **Erba HP**, Wetzler M. NCCN Clinical Practice Guidelines in Oncology: Chronic Myelogenous Leukemia. J Natl Compr Canc Netw 2009; 7(9): 984-1023. PMID: 1987641

35. Chauncey TR, Gundacker H, Shadman M, **Erba HP**, Appelbaum FR. Sequential Phase II Southwest Oncology Group Studies (S0112 and S0301) of Daunorubicin and Cytarabine by Continuous Infusion, without and with Cyclosporin, in Older Patients with Previously Untreated Acute Myeloid Leukaemia. Br J Haemat 2010; 148: 48-58.

36. Kantarjian, HM, **Erba HP**, Claxton D. Phase II Study of Clofarabine Monotherapy in Previously Untreated Older Adults with Acute Myeloid Leukemia and Unfavorable Prognostic Factors. J Clin Oncol 2010; 28(4): 549-555. PMID: 20026805

37. Long J, Parkin B, Ouillette P, **Erba HP**, Malek S. Multiple Distinct Molecular Mechanisms Influence Sensitivity and Resistance to MDM2 Inhibitors in Adult Acute Myelogenous Leukemia. Blood 2010; 116(1): 71-80. PMID: 20404136.

38. Parkin B, Ouillette P, Wang Y, **Erba HP**, Malek S. NF1 Inactivation in Adult Acute Myelogenous Leukemia. Clin Cancer Res 2010; 16(16): 4135-47. PMID: 20505189.

39. Parkin B, **Erba HP**, Malek S. Acquired Genomic Copy Number Aberrations and Survival in Adult Acute Myelogenous Leukemia. Blood 2010; 116(23): 4958-67. PMID: 20729456.

40. **Erba HP**. Has There Been Progress in the Treatment of Older Patients with Acute Myeloid Leukemia? Best Pract Res Clin Haematol 2010; 23(4): 495-501. PMID: 21130413.

41. Kantarjian HM, **Erba HP**, Faderl S. Phase II Study of Clofarabine Monotherapy in Previously Untreated Older Adults with Acute Myeloid Leukemia and Unfavorable Prognostic Factors. J Clin Oncol 2010; 28(4): 521-3. PMID: 20026805

42. Wang M, Medeiros BC, **Erba HP**, Swords RT. Targeting Protein Neddylation: A Novel Therapeutic Strategy for the Treatment of Cancer. Expert Opinion in Therapeutic Targets 2011; 15: 253-63.

43. Levis M, Ravandi F, Wang ES, **Erba HP**, Smith BD. Results from a Randomized Trial of Salvage Chemotherapy Followed by Lestaurtinib for Patients with FLT3 Mutant AML in First Relapse. Blood 2011; 117: 3294-3301.

44. Li M, Collins R, Jiao Y, Ouillette P, Bixby D, **Erba HP**, Vogelstein B, Kinzler KW, Papadopoulos N, Malek SN. Somatic Mutations in the Transcriptional Co-repressor Gene BCORL1 in Adult Acute Myelogenous Leukemia. Blood 2011; 118(22): 5914-59171.

45. Saiya-Cork K, Collins R, Parkin B, **Erba HP**, Malek SN. A Pathobiological Role of the Insulin Receptor in Chronic Lymphocytic Leukemia. Clinical Cancer Research 2011; 17: 2679-92.

46. Sekeres MA, Maciejewski JP, **Erba HP**, Kalaycio ME. A Phase 2 Study of Combination Therapy with Arsenic Trioxide and Gemtuzumab Ozogamicin in Patients with Myelodysplastic Syndromes or Secondary Acute Myeloid Leukemia. Cancer 2011; 117: 12553-61. PMID: 20960521.

47. Magenau J, Tobai H, **Erba HP**, Mineishi S. Clofarabine and Busulfan Conditioning Facilitates Engraftment and Provides Significant Antitumor Activity in Non-remission Hematologic Malignancies. Blood 2011; 118: 4258-64.

48. **Erba HP**, Pham DC, Zaiden R, Vu H, Tai S. Improving Frontline Treatment for Chronic Myeloid Leukemia: Emerging Evidence for use of Nilotinib and Dasatinib. Clin Adv Hematol Oncol 2011; 9: v734-45.

49. Claxton D, **Erba HP**, Faderl S, Kantarjian H. Outpatient Consolidation Treatment with Clofarabine in a Phase 2 Study of Older Adult Patients with Previously Untreated Acute Myelogenous Leukemia. Leuk and Lymph 2012; 53: 435-40.

50. Borate U, Absher D, **Erba HP,** Pasche B. Potential for Whole Genome Sequencing for Determining Risk and Personalizing Therapy: Focus on AML. Expert Rev. Anticancer Ther. 2012; 12 (10): 1289-1297.

51. Roth BJ, Krilov L, Adams S, Aghajanian CA, Bach P, Braiteh F, Brose MS, Ellis LM, **Erba HP**, George DJ, Gilbert MR, Jacobson JO, Larsen EC, Lichtman SM, Partridge AH, Patel JD, Quinn DI, Robison LL, von Roenn JH, Samlowski W, Schwartz GK, and Vogelzang NJ. Clinical Cancer Advances 2012: Annual Report on Progress against Cancer from the American Society of Clinical Oncology. J Clin Oncol. 2013; 31 (1): 131-161.

52. Petersdorf SH, Kopecky KJ, Slovak M, Willman C, Nevill T, Brandwein J, Larson RA, **Erba HP**, Stiff PJ, Stuart RK, Walter RB, Tallman MS, Stenke L, Appelbaum FR. A Phase 3 Study of Gemtuzumab Ozogamicin during Induction and Post-Consolidation Therapy in Younger Patients with Acute Myeloid Leukemia. Blood. 2013; 121 (24): 3454-4860.

53. **Erba HP**, Sayar H, Juckett M, Lahn M, Andre V, Callies S, Schmidt S, Kadam S, Brandt JT, Van Bockstaele D, Andreeff M. Safety and Pharmacokinetics of the Antisense Oligonucleotide (ASO) LY2181308 as a Single-Agent or in Combination with Idarubicin and Cytarabine in Patients with Refractory or Relapsed Acute Myeloid Leukemia (AML). Invest New Drugs. 2013; 31(4): 1023-1034.

54. Ganz PA, Moinpour CM, Pauler DK, Kornblith AB, Gaynor ER, Balcerzak SP, Gatti GS, **Erba HP**, McVoy S, Press OW, Fisher RI. Health Status and Quality of Life in Patients with Early-Stage Hodgkin's Disease Treated on Southwest Oncology Group Study 9133. J Clin Oncol 2013; 21(18): 3512-9.

55. Ravandi R, **Erba HP**, Pollyea DA. Expert Insights into the Contemporary Management of Older Adults with Acute Myeloid Leukemia. Cancer Control. 2013; 20(4Suppl):5-16.

56. Nand S, Othus M, Godwin JE, Willman CL, Norwood TH, Howard DS, Coutre SE, **Erba HP**, Applebaum FR. A Phase 2 Trial of Azacitidine and Gemtuzumab Ozogamicin Therapy in Older Patients with Acute Myeloid Leukemia. Blood. 2013; 121 (20): 3432-9.

57. Jain N, Curran E, lyengar NM, Diaz-Flores E, Kinnavakkam R, Popplewell L, Kirschbaum MH, Karrison T, **Erba HP**, Green M, Poire X, Koval G, Shannon K, Reddy PL, Joseph L, Atallah EL, Dy P, Thomas SP, Smith SE, Doyle LA, Stakler WM, Larson RA, Stock W, Odenike O. Phase II Study of the Oral MEK Inhibitor Selumetinib in Advanced Acute Myelogenous Leukemia: A University of Chicago Phase II Consortium Trial. Clinical Cancer Res. 2014; 20(2):490-8.

58. **Erba HP**, Othus M, Walter RB, Kirschbaum MH, Tallman MS, Larson RA, Slovak ML, Kopecky KJ, Gundacker HM, Applebaum FR. Four Different Regimens of Farnesyltransferase Inhibitor Tipifarnib in Older, Untreated Acute Myeloid Leukemia Patients: North American Intergroup Phase II Study SWOG S0432. Leuk Res. 2014; 38 (3):329-333.

59. Prebet T, Sun Z, Figueroa ME, Kettering R, Melnick A, Greenberg P, Juckett M, Smith M, Malick L, Paietta E, Czader M, Gabrilove J, **Erba HP**, Gore S, Tallman M. Prolonged administration of azacitidine with or without entinostat for myelodysplastic syndrome and acute myeloid leukemia with myelodysplasia-related changes: Results of the US Leukemia Intergroup trial E1905. Journal of Clinical Oncology. 2014; 32(12):1242-2348.

60. Zeidan AM, Lee JW, Prebet T, Greenberg P, Sun Z, Juckett M, Smith MR, Paietta E, Gabrilove J, **Erba HP**, Tallman MS, Gore SD. Comparison of the prognostic utility of the revised International Prognostic Scoring System and the French Prognostic Scoring System in azacitidine-treated patients with myelodysplastic syndromes: E 1905: Br J Haemat. 2014; 166(3):352-359.

61. Zeidan AM, Lee JW, Prebet T, Greenberg P, Sun Z, Juckett M, Smith MR, Paietta E, Gabrilove J, **Erba HP**, Katterling RP, Tallman MS, Gore SD. Platelet count doubling after the first cycle of azacitidine

therapy predicts eventual response and survival in patients with myelodysplastic syndromes and oligoblastic acute myeloid leukaemia but does not add to prognostic utility of the revised IPSS: On behalf of the Eastern Cooperative Oncology Group (ECOG) and North American Leukemia Intergroup. Br J Haemat. 2014; 167(1): 62-68.

62. Schimmer AD, Raza A, Carter TH, Claxton D, **Erba HP,** DeAngelo DJ, Tallman MS, Goard C, Borthakur G. A Multicenter Phase I/II Study of Obatoclax Mesylate Administered as a 3 hour or 24-Hour Infusion in Older Patients with Previously Untreated Acute Myeloid Leukemia. PLos One 2014; 9(10): e108694. Epub 2014 Oct 6.

63. **Erba HP**. Finding the optimal combination therapy for the treatment of newly diagnosed AML in older patients unfit for intensive therapy. Leuk Res. 2015; 39(2):183-9.

64. Lindsley RC, Mar BG, Mazzola E, Grauman PV, Shareef S, Allen SL, Pigneux A, Wetzler M, Stuart RK, **Erba HP**, Damon LE, Powell BL, Lindeman N, Steensma DP, Wadleigh M, DeAngelo DJ, Neuberg D, Stone RM, Ebert BL. Acute myeloid leukemia ontogeny is defined by distinct somatic mutations. Blood. 2015; 125(9): 1367-76.

65. Swords RT, **Erba HP**, DeAngelo DJ, Bixby DL, Altman JK, Maris M, Hua Z, Blakemore SJ, Faessel H, Sedarati F, Dezube BJ, Giles FJ, Medeiros BC. Pevonedistat (MLN4924), a First-in-Class NEDD8-activating enzyme inhibitor, in patients with acute myeloid leukemia and myelodysplastic syndromes: A Phase 1 Study. Br J Haematol. 2015; 169(4): 534-43. Epub 2015 Mar 2.

66. Dipersio JF, **Erba HP**, Larson RA, Luger SM, Tallman MS, Brill JM, Vuagnizus G, Rouits E, Sorensen JM, Zanna C. Oral Debio1143 (AT406), an Antagonist of Inhibitor of Apoptosis Proteins, Combined with Daunorubicin and Cytarabine in Patients with Poor-Risk Acute Myeloid Leukemia--Results of a Phase 1 Dose-Escalation Study. Clin Lymphoma Myeloma Leuk. 2015; 15(7): 443-449. Epub 2015 Mar 5.

67. Medeiros BC, Othus M, Fang M, Appelbaum FR, **Erba HP**. Cytogenetic heterogeneity negatively impacts outcomes in patients with acute myeloid leukemia. Haematologica. 2015; 100(3): 331-5.

68. Othus M, Applebaum FR, Petersdorf SH, Kopecky KJ, Slovak M, Nevill T, Brandwein J, Larson RA, Stiff PJ, Walter RB, Tallman MS, Stenke L, **Erba HP**. Fate of Patients with newly diagnosed acute myeloid leukemia who fail primary induction therapy. Biol Blood Marrow Transplant. 2015; 21(3): 559-64.

69. **Erba HP**. Molecular monitoring to improve outcomes in patient with chronic myeloid leukemia. Am J Hematol. 2015; 100(3): 242-9.

70. Michaelis LC, **Erba HP**. Recent developments in the treatment of older individuals with acute myeloid leukemia: 2014. Curr Opin Hematol. 2015; 22(2): 108-15.

71. Stone RM, Mazzola E, Nueberg D, Allen SL, Pigneux A, Stuart RK, Wetzler M, Rizzieri D, **Erba HP**, Damon L, Jang JH, Tallman MS, Warzocha K, Masszi T, Sekeres MA, Egyed M, Horst HA, Selleslag D, Solomon SR, Venugopal P, Lundberg AS, Powell B. Phase III Open-Label Randomized Study of Cytarabine in Combination with Amonafide L-Malate or Daunorubicin as Induction Therapy for Patients with Secondary Acute Myeloid Leukemia. J Clin Oncol. 2015; 33(11): 1252-7.

72. Othus M, Appelbaum FR, Petersdorf SH, Kopecky KJ, Slovak M, Nevill T, Brandwein J, Larson RA, Stiff PJ, Walter RB, Tallman MS, Stenke L, **Erba HP**. Fate of patients with newly diagnosed acute myeloid leukemia who fail primary induction therapy. Biol Blood Marrow Transplant. 2015; 21(3): 559-64. doi: 10.1016/j.bbmt.2014.10.025. Epub 2014 Dec 20. PubMed PMID: 25536215; PubMed Central PMCID: PMC4386840

73. Ravandi F, Ritchie EK, Sayar H, Lancet JE, Craig MD, Vey N, Strickland SA, Schiller GJ, Jabbour E, **Erba HP**, Pigneux A, Horst H-A, Recher C, Klimek VM, Cortes J, Roboz GJ, Odenike O, Thomas X, Havelange V, Maertens J, Derigs H-G, Heuser M, Damon L, Powell B, Gaidano G, Carella A-M, Wei A, Hogge D, Craig AR, Fox JA, Ward R, Smith JA, Acton G, Mehta C, Stuart RK, Kantarjian HM. Vosaroxin plus cytarabine versus placebo plus cytarabine in patients with first relapsed or refractory acute

myeloid leukaemia (VALOR): a randomized, controlled, double-blind, multinational, phase 3 study. Lancet Oncol 2015; 16(9): 1025-1036. Epub 2015 Jul 30.

74. Walter RB, Othus M, Lowenberg B, Ossenkoppele GJ, Petersdorf SH, Pabst T, Vekemans, Appelbaum FR, **Erba HP**, Estey EH. Empiric definition of eligibility criteria for clinical trials in relapsed/refractory acute myeloid leukemia: analysis of 1,892 patients from HOVON/SAKK and SWOG. Haematologica 2015; 100(10): e409-411. Epub 2015 Jul 9

75. Prebet T, Sun Z, Ketterling RP, Zeidan A, Greenberg P, Herman J, Juckett M, Smith MR, Malick L, Paietta E, Czader M, Figueroa M, Gabrilove J, **Erba HP**, Tallman MS, Litzow M, Gore SD. Azacitidine with or without Entinostat for the treatment of therapy-related myeloid neoplasm: further results of the E1905 North American Intergroup study. Br J Haematol 2016; 172(3): 384-391. Epub 2015 Nov 18

76. Achilles NJ, Othus M, Phelan K, Zhang S, Cooper K, Godwin JE, Appelbaum FR, Radich JP, **Erba HP**, Nand S, Zeleznik-Le NJ. Association between early promoter-specific DNA methylation changes and outcome in older acute myeloid leukemia patients. Leuk Res 2016; 42: 68-74. Epub 2016 Jan 15.

77. Steensma DP, Abedi M, Bejar R, Cogle CR, Foucar K, Garcia-Manero G, George TI, Grinblatt D, Komrokji R, Ma X, Maciejewski J, Pollyea DA, Savona MR, Scott B, Sekeres MA, Thompson MA, Swern AS, Nifenecker M, Sugrue MM, **Erba HP**. Connect MDS/AML: Design of the Myelodysplastic Syndromes and Acute Myeloid Leukemia Disease Registry, a Prospective Observational Cohort Study. 2016 Aug 19 16:652(10): 1186/s12885-016-2710-6.

78. Othus M, Mukherjee S, Sekeres MA, Godwin J, Petersdorf S, Appelbaum F, **Erba HP**, Estey E. Prediction of CR following a second course of '7+3' in patients with newly diagnosed acute myeloid leukemia not in CR after a first course. Leukemia 2016; 30(8): 1779-1780. doi: 10.1038/leu.2016.48

79. Ravandi R, Othus M, O'Brien S, Forman SJ, Ha CS, Wong JYC, Tallman MS, Paietta E, Racevskis J, Uy GL, Horowitz M, Takebe N, Little R, Borate U, Kebriaei P, Kingsbury L, Kantarjian HM, Radich JP, **Erba HP**, Appelbaum FR. US intergroup study of chemotherapy plus dasatinib and allogeneic stem cell transplant in Philadelphia chromosome positive ALL. Blood Advances 2016; 1(3): 250-259.

80. Othus M, Wood BL, Stirewalt DL, Estey EH, Petersdorf SH, Appelbaum FR, **Erba HP**, Walter RB. Effect of Measurable ("Minimal") Residual Disease (MRD) Information on Prediction of Relapse and Survival in Adult Acute Myeloid Leukemia. Leukemia 2016; 30(10): 2080-2083.

81. Pine AB, Lee E-J, Sekeres M, Steensma DP, Zelterman D, Prebet T, DeZern A, Komrokji R, Litzow M, Luger S, Stone R, **Erba HP**, Garcia-Manero G, Lee AI, Podoltsev NA, Barbarotta L, Kasberg S, Hendrickson JE, Gore SD, Zeidan AM. Wide variations in blood product transfusion practices among providers who care for patients with acute leukemia in the United States. Transfusion 2017; 57(2): 289-295. Epub 2016 Nov 22.

82. Moinpour CM, Unger, JM, Ganz PA, Kornblith AB, Gaynor ER, Bowers MA, Gatti GS, Kaminski MS, **Erba HP**, Wang T, Yoon J, Press OW, Fisher RI. Seven-year follow-up for energy / vitality outcomes in early-stage Hodgkin's disease patients treated with subtotal lymphoid irradiation versus chemotherapy plus radiation: SWOG S9133 and its QOL companion study, S9208. J Cancer Surviv 2017; 11(1): 32-40. Epub 2016 Jul 12.

83. Swords RT, Watts J, **Erba HP**, Altman JK, Maris M, Anwer F, Hua Z, Stein H, Faessel H, Sedarati F, Dezube BJ, Giles FJ, Medeiros BC, DeAngelo DJ. Expanded safety analysis of pevonedistat, a first-in-class NEDD8-activating enzyme inhibitor, in patients with acute myeloid leukemia and myelodysplastic syndromes. Cancer. 2017 Feb 21. doi: 10.1002/cncr.30626.

84. Minagawa K, Jamil MO, Al-Obaidi M, Pereboeva L, Salzman D, **Erba HP**, Lamb LS, Bhatia R, Mineishi S, Di Stasi A. Correction: In Vitro Pre-Clinical Validation of Suicide Gene Modified Anti-CD33 Redirected Chimeric Antigen Receptor T-Cells for Acute Myeloid Leukemia. PLoS One. 2017 Feb 15; 12(2): e0172640. doi: 10.1371/journal.pone.0172640.

85. Mantha S, Goldman DA, Devlin SM, Lee J-W, Zannino D, Collins M, Douer D, Iland HJ, Litzow MR, Stein EM, Appelbaum FR, Larson RA, Stone R, Powell BL, Geyer S, Laumann K, Rowe JM, **Erba H**, Coutre S, Othus M, Park JH, Wiernik PH, Tallman MS. Determinants of fatal bleeding during induction therapy for acute promyelocytic leukemia in the ATRA era. Blood 2017; 129(13): 1763-1767. Epub 2017 Jan 12.

86. Qu X, Othus M, Davison J, Wu Y, Yan L, Meshinchi S, Ostronoff F, Estey EH, Radich JP, **Erba HP**, Appelbaum FR, Fang M. Prognostic methylation markers for overall survival in cytogenetically normal patients with acute myeloid leukemia treated on SWOG trials. Cancer 2017; 123(13): 2472-2481. doi: 10.1002/cncr.30626.

87. Perl AE, Altman JK, Cortes J, Smith C, Litzow M, Baer MR, Claxton D, **Erba HP**, Gill S, Goldberg S, Jurcic JG, Larson RA, Liu C, Ritchie E, Schiller G, Spira AI, Strickland SA, Tibes R, Ustun C, Wang ES, Stuart R, Rollig C, Neubauer A, Martinelli G, Bahceci E, Levis M. Selective inhibition of FLT3 by gilteritinib in relapsed or refractory acute myeloid leukaemia: a multicentre, first-in-human, open-label, phase 1-2 study. Lancet Oncology 2017; 18(8): 1061-1075.

88. Sekeres MA, Othus M, List AF, Odenike O, Stone RM, Gore SD, Litzow MR, Buckstein R, Fang M, Roulston D, Bloomfield CD, Moseley A, Nazha A, Zhang Y, Velasco MR, Gaur R, Atallah E, Attar EC, Cook EK, Cull AH, Rauh MJ, Appelbaum FR, **Erba HP**. Randomized Phase II Study of Azacitidine Alone or in Combination with Lenalidomide or with Vorinostat in Higher-Risk Myelodysplastic Syndromes and Chronic Myelomonocytic Leukemia: North American Intergroup Study SWOG S1117. J Clin Oncol. 2017 Aug 20; 35(24):2745-2753. doi: 10.1200/JCO.2015.66.2510. Epub 2017 May 9. PubMed PMID: 28486043; PubMed Central PMCID: PMC5562170.

89. Pogosova-Agadjanyan EL, Moseley, A, Othus M, Appelbaum FR, Chauncey TR, Chen I-ML, **Erba HP**, Godwin JE, Fang M, Kopecky KJ, List AF, Pogosov GL, Radich JP, Willman CL, Wood BL, Meshinchi S, Stirewalt KD. Impact of Specimen Heterogeneity on Biomarkers in Repository Samples from Patients with Acute Myeloid Leukemia: A SWOG Report. Biopreserv Biobank 2017; 16(1): 42-52. Epub 2017 Nov 27.

90. Stein EM, Walter RB, **Erba HP**, Fathi AT, Advani AS, Lancet JE, Ravandi F, Kovacsovics T, DeAngelo DJ, Bixby D, Faderl S, Jillella AP, Ho P, O'Meara MM, Zhao B, Biddle-Snead C, Stein A. A phase 1 trial of vadastuximab talirine as monotherapy in patients with CD33 positive acute myeloid leukemia (AML). Blood 2018; 131(4): 387-396. Epub 2017 Dec 1

91. Swords RT, Coutre S, Maris MB, Zeidner JF, Foran JM, Cruz J, **Erba, HP**, Berdeja JG, Tam W, Vardhanabhuti S, Pawlikowska-Dobler I, Faesse HM, Dash AB, Sedarati F, Dezube BJ, Faller DV, Savona, MR. Pevonedistat, a first-in-class NEDD8-activating enzyme (NAE) inhibitor, combined with azacitidine, in patients with AML. Blood 2018; 131(13): 1415-1424. Epub 2018 Jan 18.

92. Walter RB, Michaelis LC, Othus M, Uy GL, Radich JP, Little RF, Hita S, Saini L, Foran JM, Gerds AT, Klepin HD, Hay AE, Assouline S, Lancet JE, Couban S, Litzow MR, Stone RM, **Erba HP**. Intergroup LEAP trial (S1612): A randomized phase 2/3 platform trial to test novel therapeutics in medically less fit older adults with acute myeloid leukemia. Am J Hematol. 2018; 93(2): E49-E52. PubMed PMID: 29164656.

93. Advani AS, Li H, Michaelis LC, Medeiros BC, Liedtke M, List AF, O'Dwyer K, Othus M, **Erba, HP**, Appelbaum FR. Report of the relapsed/refractory cohort of SWOG S0919: A phase 2 study of idarubicin and cytarabine in combination with pravastatin for acute myelogenous leukemia (AML). Leuk Res 2018; 67: 17-20. Epub 2018 Jan 31.

94. Statler A, Othus M, **Erba HP**, Chauncey TR, Radich JP, Coutre S, Advani A, Nand S, Ravandi F, Mukherjee S, Sekeres MA. Comparable Outcomes of Patients Eligible versus Ineligible for SWOG Leukemia Studies. Blood 2018. Epub 2018 Apr 4.

95. Halpern AB, Othus M, Huebner EM, Scott BL, Becker PS, Percival M-EM, Hendrie PC, Gardner KM, Chen TL, Buckley SA, Orlowski KF, Anwar S, Appelbaum FR, **Erba HP**, Estey EH, Walter RB. A phase 1/2 trial of GCLAM with dose-escalated mitoxantrone for newly diagnosed AML or other high-grade myeloid neoplasms. Leukemia 2018. Epub 2018 Apr 17.

96. Stahl M, Pine A, Hendrickson JE, Litzow MR, Luger SM, Stone RM, **Erba HP**, Kim TK, Sekeres MA, Steensma DP, Komrokji RS, Gore SD, Zeidan AM. Beliefs and practice patterns in hyperleukocytosis management in acute myeloid leukemia: a large U.S. web-based survey. Leuk Lymphoma 2018. Epub 2018 Apr 18.

97. DiNardo CD, Stein EM, de Botton S, Roboz GJ, Altman JK, Mims AS, Swords R, Collins RH, Mannis GN, Pollyea DA, Donnellan W, Fathi AT, Pigneux A, **Erba HP**, Prince GT, Stein AS, Uy GL, Foran JM, Traer E, Stuart RK, Arellano ML, Slack JL, Sekeres MA, Willekens C, Choe S, Wang H, Zhang V, Yen KE, Kapsalis SM, Yang H, Dai D, Fan B, Goldwasser M, Liu H, Agresta S, Wu B, Attar EC, Tallman MS, Stone RM, and Kantarjian HM. Durable Remissions with Ivosidenib in IDH1-Mutated Relapsed or Refractory AML. N Engl J Med 2018; 378: 2386-98. DOI: 10.1056/NEJMoa1716984.

98. Fathi AT, **Erba HP**, Lancet JE, Stein EM, Ravandi F, Faerl S, Wlater RB, Advani AS, DeAngelo DJ, Kovacsovics TJ et al. A phase I trial of vadastuximab talirine combined with hypomethylating agents in patients with CD33-positive AML. Blood 2018; 132 (1): 1125-1133.

99. Jamy O, Bae S, Costa LJ, **Erba HP**, Papadantonakis N. Outcomes of fludarabine, high dose cytarabine and granulocyte-colony stimulating factor (FLAG) as re-induction for residual acute myeloid leukemia on day 14 bone marrow. Leukemia Research 2018; 74: 64-67.

100. Othus M, Sekeres MA, Nand S, Garcia-Manero G, Appelbaum, **Erba HP**, Estey E. Relative survival following response to 7+3 versus azacytidine is similar in acute myeloid leukemia and high-risk myelodysplastic syndromes: an analysis of four SWOG studies. Leukemia 2018; 12 October 2018.

101. Othus M, Estey EH, Garcia-Manero G, Wood BL, Stirewalt DL, Godwin JE, Weick JK, Anderson JE, Appelbaum FR, **Erba HP**, Walter RB. Second cycle remission achievement with 7+3 and survival in adults with newly diagnosed acute myeloid leukemia: analysis of recent SWOG trials. Leukemia. 2019 Feb; 33(2):554-558. doi: 10.1038/s41375-018-0274-y. Epub 2018 Oct 12.

102. Woyach JA, Ruppert AS, Heerema NA, Zhao W, Booth AM, Ding W, Bartlett NL, Brander DM, Barr PM, Rogers KA, Parikh SA, Coutre S, Hurria A, Brown JR, Lozanski G, Blachly JS, Ozer HG, Major-Elechi B, Fruth B, Nattam S, Larson RA, **Erba H**, Litzow M, Owen C, Kuzma C, Abramson JS, Little RF, Smith SE, Stone RM, Mandrekar SJ, Byrd JC: Ibrutinib Regimens versus Chemo immunotherapy in Older Patients with Untreated CLL. N Engl J Med. 2018 Dec 27; 379(26):2517-2528. doi: 10.1056/NEJMoa1812836. Epub 2018 Dec 1.

103. Medeiros BC, Othus M, Tallman MS, The relationship between clinical trial accrual volume and outcomes in acute myeloid leukemia: A SWOG/ECOG-ACRIN study (S0106 and E1900). un Z, Fernandez HF, Rowe JM, Lazarus HM, Appelbaum FR, Luger SM, Litzow MR, **Erba HP**. Leuk Res. 2019 Mar; 78:29-33. doi: 10. 1016/j.leukres 2019.01.007. Epub 2019 Jan 17.

104. Stock W, Luger SM, Advani AS, Yin J, Harvey RC, Mullighan CG, Willman CL, Fulton N, Laumann KM, Malnassy G, Paietta E, Parker E, Geyer S, Mrózek K, Bloomfield CD, Sanford B, Marcucci G, Liedtke M, Claxton DF, Foster MC, Bogart JA, Grecula JC, Appelbaum FR, **Erba H**, Litzow MR, Tallman MS, Stone RM, Larson RA. A pediatric regimen for older adolescents and young adults with acute lymphoblastic leukemia: results of CALGB 10403. Blood. 2019 Apr 4; 133(14):1548-1559. doi: 10.1182/blood-2018-10-881961. Epub 2019 Jan 18.

105. LeBlanc TW, **Erba HP**. Shifting paradigms in the treatment of older adults with AML Semin Hematol. 2019 Apr; 56(2):110-117. doi: 10.1053/j.seminhematol.2019.02.002. Epub 2019 Feb 27. Review.

106. Ustun C, Le-Rademacher J, Wang HL, Othus M, Sun Z, Major B, Zhang MJ, Storrick E, Lafky JM, Chow S, Mrózek K, Attar EC, Nand S, Bloomfield CD, Cripe LD, Tallman MS, Appelbaum F, Larson RA, Marcucci G, Roboz GJ, Uy GL, Stone RM, Jatoi A, Shea TC, de Lima M, Foran JM, Sandmaier BM, Litzow MR, **Erba HP**, Hurria A, Weisdorf DJ, Artz AS. Allogeneic hematopoietic cell transplantation compared to chemotherapy consolidation in older acute myeloid leukemia (AML) patients 60-75 years in first complete remission (CR1): an alliance (A151509), SWOT, ECOG-ACRIN, and CIBMTR study. Leukemia 2019 Nov; 33(11):2599-2609. Doi: 10: 1038/s41375-019-0477-x. Epub 2019 May 9.

107. **Erba HP**, Becker PS, Shami PJ, Grunwald MR, Flesher DL, Zhu M, Rasmussen E, Henary HA, Anderson AA, Wang ES. Phase 1b study of the MDM2 inhibitor AMG 232 with or without trametinib in relapsed/refractory acute myeloid leukemia. Blood Adv. 2019 Jul 9; 3(13):1939-1949. doi: 10.1182/bloodadvances.2019030916.

108. Shanafelt TD, Wang XV, Kay NE, Hanson CA, O'Brien S, Barrientos J, Jelinek DF, Braggio E, Leis JF, Zhang CC, Coutre SE, Barr PM, Cashen AF, Mato AR, Singh AK, Mullane MP, Little RF, **Erba H**, Stone RM, Litzow M, Tallman M. Ibrutinib-Rituximab or Chemo immunotherapy for Chronic Lymphocytic Leukemia. N Engl J Med. 2019 Aug 1; 381(5):432-443. doi: 10.1056/NEJMoa1817073.

109. Shah G, Mikhail FM, Bachiasvili K, Vachhani P, **Erba HP**, Papadantonakis N. Outcomes of high-risk acute promyelocytic leukemia patients treated with arsenic trioxide (ATO)/all Trans' retinoic acid (ATRA) based induction and consolidation without maintenance phase: A case Series. Hematol Oncol Stem Cell Ther. 2019 Oct 14. pii: S1658-3876(19)30076-7. doi: 10.1016/j.hemonc.2019.08.006. [Epub ahead of print]

110. Nazha A, Sekeres MA, Bejar R, Rauh MJ, Othus M, Komrokji RS, Barnard J, Hilton CB, Kerr CM, Steensma DP, DeZern A, Roboz G, Garcia-Manero G, **Erba H**, Ebert BL, Maciejewski JP. Genomic Biomarkers to Predict Resistance to Hypomethylating Agents in Patients with Myelodysplastic Syndromes Using Artificial Intelligence. JCO Precis Oncol. 2019; 3. doi: 10.1200/po.19.00119. Epub 2019 Sep 20.

111. Perl AE, Martinelli G, Cortes JE, Neubauer A, Berman E, Paolini S, Montesinos P, Baer MR, Larson RA, Ustun C, Fabbiano F, **Erba HP**, Di Stasi A, Stuart R, Olin R, Kasner M, Ciceri F, Chou WC, Podoltsev N, Recher C, Yokoyama H, Hosono N, Yoon SS, Lee JH, Pardee T, Fathi AT, Liu C, Hasabou N, Liu X, Bahceci E, Levis MJ. Gilteritinib or Chemotherapy for Relapsed or Refractory FLT3-Mutated AML. N Engl J Med. 2019 Oct 31; 381(18):1728-1740. doi: 10.1056/NEJMoa1902688.

112. Merz LE, Perissinotti AJ, Marini BL, Burke PW, Crouch A, **Erba HP**, Bixby D. Lenalidomide plus Hypomethylating Agent as a Treatment Option in Acute Myeloid Leukemia with Recurrent Genetic Abnormalities-AMML with inv (3) (q21.3q26.2) or t (3:3) (q21.3:q26.2): GATA2.MECOM. Lymphoma Myeloma Leuk. 2020 Jan; 20(1):24-30. doi: 10.1016/j.clml.2019.09.615. Epub 2019 Sep 28.

113. Roboz GJ, DiNardo CD, Stein EM, de Botton S, Mims AS, Prince GT, Altman JK, Arellano ML, Donnellan W, **Erba HP**, Mannis GN, Pollyea DA, Stein AS, Uy GL, Watts JM, Fathi AT, Kantarjian HM, Tallman MS, Choe S, Dai D, Fan B, Wang H, Zhang V, Yen KE, Kapsalis SM, Hickman D, Liu H, Agresta SV, Wu B, Attar EC, Stone RM.Ivosidenib induces deep durable remissions in patients with newly diagnosed IDH1-mutant acute myeloid leukemia. Blood. 2019 Dec 16. pii: blood.2019002140. doi: 10.1182/blood.2019002140. [Epub ahead of print]

114. Pagel JM, Othus M, Garcia-Manero G, Fang M, Radich JP, Rizzieri DA, Marcucci G, Strickland SA, Litzow MR, Savoie ML, Spellman SR, Confer DL, Chell JW, Brown M, Medeiros BC, Sekeres MA, Lin TL, Uy GL, Powell BL, Bayer RL, Larson RA, Stone RM, Claxton D, Essell J, Luger SM, Mohan SR, Moseley A, **Erba HP**, Appelbaum FR. Rapid Donor Identification Improves Survival in High-Risk First-Remission Patients with Acute Myeloid Leukemia. JCO Oncol Pract. 2020 Jan 27:JOP1900133. doi: 10.1200/JOP.19.00133. [Epub ahead of print]

115. Sung AD, Jauhari S, Siamakpour-Reihani S, Rao AV, Staats J, Chan C, Meyer E, Gadi VK, Nixon AB, Lyu J, Xie J, Bohannon L, Li Z, Hourigan CS, Dillon LW, Wong HY, Shelby R, Diehl L, de Castro C, LeBlanc T, Brander D, **Erba H**, Galal A, Stefanovic A, Chao N, Rizzieri DA.Am J Hematol. Micro transplantation in older patients with AML: A pilot study of safety, efficacy, and immunologic effects. 2020 Jun; 95(6):662-671. doi: 10.1002/ajh.25781. Epub 2020 Mar 30.

116. Lancet JE, Moseley AB, Coutre SE, DeAngelo DJ, Othus M, Tallman MS, Litzow MR, Komrokji RS, **Erba HP**, Appelbaum FR A phase 2 study of ATRA, arsenic trioxide, and gemtuzumab ozogamicin in patients with high-risk APL (SWOG 0535). Blood Adv. 2020 Apr 28; 4(8):1683-1689. doi: 10.1182/bloodadvances.2019001278.

117. Zeidan AM, Boddu PC, Patnaik MM, Bewersdorf JP, Stahl M, Rampal RK, Shallis R, Steensma DP, Savona MR, Sekeres MA, Roboz GJ, DeAngelo DJ, Schuh AC, Padron E, Zeidner JF, Walter RB, Onida F,

Fathi A, DeZern A, Hobbs G, Stein EM, Vyas P, Wei AH, Bowen DT, Montesinos P, Griffiths EA, Verma AK, Keyzner A, Bar-Natan M, Navada SC, Kremyanskaya M, Goldberg AD, Al-Kali A, Heaney ML, Nazha A, Salman H, Luger S, Pratz KW, Konig H, Komrokji R, Deininger M, Cirici BX, Bhatt VR, Silverman LR, **Erba HP**, Fenaux P, Platzbecker U, Santini V, Wang ES, Tallman MS, Stone RM, Mascarenhas J.Lancet Haematol. Special considerations in the management of adult patients with acute leukemia's and myeloid neoplasms in the COVID-19 era: recommendations from a panel of international experts. 2020 Aug; 7(8):e601-e612. doi: 10.1016/S2352-3026(20)30205-2. Epub 2020 Jun 18.

118. Pogosova-Agadjanyan EL, Moseley A, Othus M, Appelbaum FR, Chauncey TR, Chen IL, **Erba HP**, Godwin JE, Jenkins IC, Fang M, Huynh M, Kopecky KJ, List AF, Naru J, Radich JP, Stevens E, Willborg BE, Willman CL, Wood BL, Zhang Q, Meshinchi S, Stirewalt DL. AML Risk Stratification Models Utilizing ELN-2017 Guidelines and Additional Prognostic Factors: A SWOG Report. Biomark Res. 2020 Aug 12; 8:29. doi: 10.1186/s40364-020-00208-1. eCollection 2020.PMID: 32817791

119. Shah G, Mikhail FM, Bachiasvili K, Vachhani P, **Erba HP**, Papadantonakis N. Outcomes of High-Risk Acute Promyelocytic Leukemia Patients Treated with Arsenic Trioxide (ATO)/all Trans Retinoic Acid (ATRA) Based Induction and Consolidation Without Maintenance Phase: A Case Series. Hematol Oncol Stem Cell Ther. 2020 Sep; 13(3):143-146. doi: 10.1016/j.hemonc.2019.08.006. Epub 2019 Oct 14.PMID: 31629725

120. Arber DA, **Erba HP.** Diagnosis and Treatment of Patients with Acute Myeloid Leukemia with Myelodysplasia-Related Changes (AML-MRC). Am J Clin Pathol. 2020 Nov 4; 154(6):731-741. doi: 10.1093/ajcp/aqaa107.PMID: 32864703

121. Uy GL, Aldoss I, Foster MC, Sayre PH, Wieduwilt MJ, Advani AS, Godwin JE, Arellano ML, Sweet KL, Emadi A, Ravandi F, **Erba HP**, Byrne M, Michaelis L, Topp MS, Vey N, Ciceri F, Carrabba MG, Paolini S, Huls GA, Jongen-Lavrencic M, Wermke M, Chevallier P, Gyan E, Récher C, Stiff PJ, Pettit KM, Löwenberg B, Church SE, Anderson E, Vadakekolathu J, Santaguida M, Rettig MP, Muth J, Curtis T, Fehr E, Guo K, Zhao J, Bakkacha O, Jacobs K, Tran K, Kaminker P, Kostova M, Bonvini E, Walter RB, Davidson-Moncada JK, Rutella S, DiPersio JF. Flotetuzumab as Salvage Immunotherapy for Refractory Acute Myeloid Leukemia. Blood. 2021 Feb 11; 137(6):751-762. doi: 10.1182/blood.2020007732.PMID: 32929488

122. Patel JL, Abedi M, Cogle CR, **Erba HP**, Foucar K, Garcia-Manero G, Grinblatt DL, Komrokji RS, Kurtin SE, Maciejewski JP, Pollyea DA, Revicki DA, Roboz GJ, Savona MR, Scott BL, Sekeres MA, Steensma DP, Thompson MA, Dawn Flick E, Kiselev P, Louis CU, Nifenecker M, Swern AS, George TI. Real-World Diagnostic Testing Patterns for Assessment of Ring Sideroblasts and SF3B1 Mutations in Patients with Newly Diagnosed Lower-Risk Myelodysplastic Syndromes. Int J Lab Hematol. 2021 Jun; 43(3):426-432. doi: 10.1111/ijlh.13400. Epub 2020 Nov 21.PMID: 33220019

123. Moseley A, Othus M, Garcia-Manero G, Appelbaum FR, **Erba HP**, Walter RB. Predicting Severe Toxicities with Intensive Induction Chemotherapy for Adult Acute Myeloid Leukemia: Analysis of SWOG Cancer Research Network Trials S0106 and S1203. Leuk Lymphoma. 2021 Jul; 62(7):1774-1777. doi: 10.1080/10428194.2021.1881512. Epub 2021 Feb 9.PMID: 33560164

124. DiNardo CD, Stein EM, Pigneux A, Altman JK, Collins R, **Erba HP**, Watts JM, Uy GL, Winkler T, Wang H, Choe S, Liu H, Wu B, Kapsalis SM, Roboz GJ, de Botton S. Outcomes of Patients with IDH1-Mutant Relapsed or Refractory Acute Myeloid Leukemia Receiving Ivosidenib Who Proceeded to Hematopoietic Stem Cell Transplant. Leukemia. 2021 Nov; 35(11):3278-3281. doi: 10.1038/s41375-021-01229-x. Epub 2021 Mar 26.PMID: 33772143

125. Xin Victoria Wang, Curtis A. Hanson, Renee C. Tschumper, Connie E. Lesnick, Esteban Braggio, Elisabeth M. Paietta, Susan O'Brien, Jacqueline C. Barrientos, Jose Francisco Leis, Cong Christine Zhang, Steven E. Coutre, Paul M. Barr, Amanda F. Cashen, Anthony R. Mato, Avina K. Singh, Michael P. Mullane, **Harry Erba**, Richard Stone, Mark R. Litzow, Martin S. Tallman, Tait D. Shanafelt, Neil E. Kay. Measurable Residual Disease Does Not Preclude Prolonged Progression-Free Survival in CLL Treated with Ibrutinib. Blood (2021) 138 (26): 2810–2827.

126. Anjali S. Advani, Eric Larsen, Kristina Laumann, Selina M. Luger, Michaela Liedtke, Meenakshi Devidas, Zhiguo Chen, Jun Yin, Matthew C. Foster, David Claxton, Kristin Coffan, Martin S. Tallman, Frederick R. Appelbaum, **Harry Erba**, Richard M. Stone, Stephen P. Hunger, Jennifer L. McNeer, Mignon L. Loh, Elizabeth Raetz, Naomi Winick, William Carroll, Richard A. Larson, Wendy Stock. Comparison of CAGLB 10403 (Alliance) and COG AALL0232 Toxicity Results in Young Adults with Acute Lymphoblastic Leukemia. Blood *Adv* (2021) 5 (2): 504–512.

127. Advani AS, Moseley A, O'Dwyer KM, Wood BL, Fang M, Wieduwilt MJ, Aldoss I, Park JH, Klisovic RB, Baer MR, Stock W, Bhave RR, Othus M, Harvey RC, Willman CL, Litzow MR, Stone RM, Sharon E, **Erba HP.** SWOG 1318: A Phase II Trial of Blinatumomab Followed by POMP Maintenance in Older Patients with Newly Diagnosed Philadelphia Chromosome-Negative B-Cell Acute Lymphoblastic Leukemia. J Clin Oncol. 2022 Feb 14:JCO2101766. doi: 10.1200/JCO.21.01766. Online ahead of print.PMID: 35157496

128. Wall, Anna; Advani, Anjali S; Stock, Wendy; **Erba, Harry P**; Muffly, Lori; Quiroz, Elisa; Appelbaum, Frederick R; Tallman, Martin S; Jacobson, Sawyer; Larson, Richard A; et al. Disparities in trial enrollment and outcomes of Hispanic adolescent and young adult acute lymphoblastic leukemia. UC Davis 2022.

129. Pullarkat, Vinod; Levis, Mark J.; Mannis, Gabriel N. ; Lin, Tara L.; Faderl, Stefan; Chakravarthy, Divya; Chandrasekaran, Vijayalakshmi; Cheung, Ronald S.; **Erba, Harry P**. Preliminary Results By Age Group of Treatment with CPX-351 Plus Venetoclax in Adults with Newly Diagnosed AML: Subgroup Analysis of the V-FAST Phase 1b Master Trial. Transplantation and Cellular Therapy, 2022-03-01, Volume 28, Issue 3, Pages S125-S125.

130. O'Brien, Susan; Wang, Xin Victoria; Barr, Paul M; Cashen, Amanda F; Little, Richard F; **Erba, Harry P**; Barrientos, Jacqueline C; Singh, Avina K; Mullane, Michael P; Tallman, Martin S; et al. Long-term outcomes for ibrutinib–rituximab and chemo immunotherapy in CLL: updated results of the E1912 trial. Blood Volume 140, Issue 2, 14 July 2022, Pages 112-120.

131. Pratz, KW; Kaplan, J; Levy, M; Bixby, D; Burke, PW; **Erba, H**; Wise-Draper, TM; Roboz, GJ; Papadantonakis, N; Rajkhowa, T; Hernandez, D; Dobler, I; Gregory, RC; Li, C; Wang, S; Stumpo, K; Kannan, K; Miao, H; Levis, M; A phase Ib trial of mivavotinib (TAK-659), a dual SYK/FLT3 inhibitor, in patients with relapsed/refractory acute myeloid leukemia. 108(3), 705–716. https://doi.org/10.3324/haematol.2022.281216.

132. Assouline, S., Michaelis, L. C., Othus, M., Hay, A. E., Walter, R. B., Jacoby, M. A., Schroeder, M. A., Uy, G. L., Law, L. Y., Cheema, F., Sweet, K. L., Asch, A. S., Liu, J., Moseley, A. B., Maher, T., Kingsbury, L. L., Fang, M., Radich, J., Little, R. F. & **Erba, H. P**., A randomized phase II/III study of 'novel therapeutics' versus azacitidine in newly diagnosed patients with acute myeloid leukemia (AML), high-risk myelodysplastic syndrome (MDS), or chronic myelomonocytic leukemia (CMML), age 60 or older: a report of the comparison of azacitidine and nivolumab to azacitidine: SWOG S1612. 2023, In: Leukemia and Lymphoma. 64, 2, p. 473-477 5 p.

133. Ibrahim Aldoss, Jun Yin, Anna Wall, Krzysztof Mrózek, Michaela Liedtke, David F. Claxton, Matthew C. Foster, Frederick R. Appelbaum, **Harry P. Erba**, Mark R. Litzow, Martin S. Tallman, Richard M. Stone, Richard A. Larson, Anjali S. Advani, Wendy Stock, Selina M. Luger. The impact of early PEG-asparaginase discontinuation in young adults with ALL: a post hoc analysis of the CALGB 10403 study. Blood Adv (2023) 7 (2): 196–204.

134. Anjali S. Advani, Anna Moseley, Kristen M. O'Dwyer, Brent L. Wood, Jae Park, Matthew Wieduwilt, Deepa Jeyakumar, George Yaghmour, Ehab L. Atallah, Aaron T. Gerds, Susan M. O'Brien, Jane L. Liesveld, Megan Othus, Mark Litzow, Richard M. Stone, Elad Sharon, **Harry P. Erba**. Dasatinib/prednisone induction followed by blinatumomab/dasatinib in Ph+ acute lymphoblastic leukemia. Blood Adv (2023) 7 (7): 1279–1285.

135. Era L. Pogosova-Agadjanyan, Xing Hua, Megan Othus, Frederick R. Appelbaum, Thomas R. Chauncey, **Harry P. Erba**, Matthew P. Fitzgibbon, Isaac C. Jenkins, Min Fang, Stanley C. Lee, Anna Moseley, Jasmine Naru, Jerald P. Radich, Jenny L. Smith, Brooke E. Willborg, Cheryl L. Willman, Feinan Wu, Soheil Meshinchi & Derek L. Stirewalt. Verification of prognostic expression biomarkers is improved by

examining enriched leukemic blasts rather than mononuclear cells from acute myeloid leukemia patients. Biomarker Research volume 11, Article number: 31 (2023).

136. Brian A. Jonas, Jing-Zhou Hou, Gail J. Roboz, Caroline L. Alvares, Deepa Jeyakumar, John R. Edwards, **Harry P. Erba**, Richard J. Kelly, Christoph Röllig, Walter Fiedler, Deanna Brackman, Satya R. Siddani, Brenda Chyla, Jacqueline Hilger-Rolfe, Justin M. Watts. A phase 1b study of Venetoclax and alvocidib in patients with relapsed/refractory acute myeloid leukemia. (2023) https://doi.org/10.1002/hon.3159.

137. **HP Erba**, Pau Montesinos, Hee-Je Kim, et al. Quizartinib plus chemotherapy in newly diagnosed patients with FLT3-internal-tandem-duplication-positive acute myeloid leukaemia (QuANTUM-First): a randomised, double-blind, placebo-controlled, phase 3 trial. Lancet 2023; 401: 1571.

138. Sara Zarnegar-Lumley, Todd A. Alonzo, Robert B. Gerbing, Megan Othus, Zhuoxin Sun, Rhonda E. Ries, Jim Wang, Amanda Leonti, Matthew A. Kutny, Fabiana Ostronoff, Jerald P. Radich, Frederick R. Appelbaum, Era L. Pogosova-Agadjanyan, Kristen O'Dwyer, Martin S. Tallman, Mark Litzow, Ehab Atallah, Todd M. Cooper, Richard A. Aplenc, Omar Abdel-Wahab, Alan S. Gamis, Selina Luger, **Harry Erba,** Ross Levine, E. Anders Kolb, Derek L. Stirewalt, Soheil Meshinchi, Katherine Tarlock Characteristics and prognostic impact of IDH mutations in AML: a COG, SWOG, and ECOG analysis Blood Adv (2023) 7 (19): 5941–5953

139. Jacob S Appelbaum, Andrew H Wei, Sumithra J Mandrekar, Ing S Tiong, Chong Chyn Chua, Tse-Chieh Teh, Chun Yew Fong, Stephen B Ting, Daniela Weber, Axel Benner, Hannah Hill, Maral Saadati, Jun Yin, Richard M Stone, Guillermo Garcia-Manero, Harry P Erba, Geoffrey L Uy , Guido Marcucci, Richard A Larson, Abin Thomas, Sylvie D Freeman, Nuria Marquez Almuina, Konstanze Döhner, Ian Thomas, Nigel H Russel, Hartmut Döhner, Megan Othus, Elihu H Estey, Roland B Walter. Clinical evaluation of complete remission (CR) with partial hematologic recovery (CRh) in acute myeloid leukemia: a report of 7235 patients from seven cohorts. Leukemia 2024 Feb;38(2):389-392

140. Shanafelt TD, Wang XV, Hanson CA, Paietta E, O'Brien S, Barrientos J, Jelinek DF, Braggio E, Leis JF, Zhang CC, Barr PM, Cashen AF, Mato AR, Singh AK, Mullane MP, Little RF, Erba H, Stone RM, Litzow M, Tallman M, Kay NE Tolerability and long-term disease control by IGHV mutation status among patients with CLL on ibrutinib arm of E1912. Blood Adv 2025 Jan 14;9(1):224-228

141. Moseley A, LeBlanc M, Freidlin B, Shallis RM, Zeidan AM, Sallman DA, Erba HP, Little RF, Othus M Evaluating the impact of stratification on the power and cross-arm balance of randomized phase 2 clinical trials. Clin Trials 2025 Jan 15:17407745241304065

Chapters in books

1. Kelley's Essentials of Internal Medicine, Second Edition. Humes, H. David, ed. in- chief. **Erba, Harry P.**, Associate ed., Lippincott, Williams and Wilkins, 2001.

2. Conn's Current Therapy. Rakel, RE and Bope, ET, eds. **Erba, Harry P.**, W.B. Saunders Company, 2002.

3. Conn's Current Therapy. Rakel, RE and Bope, ET, eds. **Erba, Harry P.**, W.B. Saunders Company, 2003.

4. Hematology for the Medical Student. Schmaier, A and Petruzzelli, L, eds. Myeloid Stem Cell Disorders. **Erba Harry P.**, Lippincott Williams and Wilkins, March 2003:153-171.

5. Hematology for the Medical Student. Schmaier, A and Petruzzelli, L, eds. Acute Leukemia. **Erba, Harry P.**, Lippincott Williams and Wilkins, March 2003:173-184.

6. Hematology: Basic Principles and Practice. Hoffman R, Benz EJ, Silberstein LE, Heslop HE, Weitz JI, Salama ME, Abutalib SA, eds. Clinical Manifestations and Treatment of Acute Myeloid Leukemia. **Erba, Harry P.** Elsevier 2023: 950-976.

7. The International Consensus Classification of Myeloid and Lymphoid Neoplasms. Arber DA, Borowitz MJ, Cook JR, de Level L, Goodlad JR, Hasserjian RP, King RL, Kvasnicka HM, Orazi A, eds. Acute Myeloid

Leukemia with t(9;11)(p21.3;q23.3)/*KMT2A*::*MLLT3* and Other *KMT2A* Rearrangements. Tam W, **Erba HP**, Liu Y-C. Wolters Kluwer 2025: 202-207.

Consultant appointments: (Include US government, state, private organizations, etc.)

Daiichi Sankyo Pharmaceutical
Kura Oncology
Servier
Sumitomo Pharma

Honors and Awards

1978 -1979	Science and Engineering Awards, Yale University
1979	B.S. (summa cum laude), Yale University
1979 -1980	Fulbright-Hays Fellowship, University of Leicester, Leicester, England
1995	Scholar Award, American Society of Hematology
2002	Teacher of the Year, 2002, Division of Hematology/Oncology, Department of Internal Medicine, University of Michigan
2003	Teacher of the Year, 2003, Division of Hematology/Oncology, Department of Internal Medicine, University of Michigan
2004	Teacher of the Year, 2004, Division of Hematology/Oncology, Department of Internal Medicine, University of Michigan
2004	Outstanding Clinician Award, University of Michigan
2005	Teacher of the Year, 2005, Division of Hematology/Oncology, Department of Internal Medicine, University of Michigan
2007	Special Recognition and Appointment to the National Comprehensive Cancer Network (NCCN) Board of Producers
2008	Special Recognition and Appointment to the National Comprehensive Cancer Network (NCCN) Board of Producers
2012	League of Clinical Excellence, University of Michigan
2016	Teacher of the Year, 2016, Division of Hematology/Oncology, Department of Internal Medicine, University of Alabama at Birmingham
2017	Teacher of the Year, 2016, Division of Hematology/Oncology, Department of Internal Medicine, University of Alabama at Birmingham

Organizations and participation (Offices held, committee assignments, etc.):

Intramural Committee and Administrative Service

Harvard Collaborative Oncology Group, Lymphoma Committee (member)
Intern Selection Committee, Department of Medicine, Brigham and Women's Hospital
Protocol Review Committee, University of Michigan (member)
Leukemia Conference, University of Michigan (Organizer, 7/96 - 6/12)
Hematologic Malignancy Working Group, University of Alabama (Chair, 7/12 - 4/18)
Clinical Trials Operations Committee, University of Alabama at Birmingham (Chair, 3/13 - 4/18)

Extramural Committee, Organizational, and Volunteer Service

National Comprehensive Cancer Network, Clinical Guidelines Committee, Chronic Myelogenous Leukemia
National Comprehensive Cancer Network, Clinical Guidelines Committee, Myelodysplastic Syndromes
National Comprehensive Cancer Network, Clinical Guidelines Committee, Acute Leukemia
National Comprehensive Cancer Network, Clinical Guidelines Committee, Myeloid Growth Factors
Southwest Oncology Group (SWOG), Executive Officer (4/2005 – 10/2012)
SWOG Leukemia Committee, Chair (10/2012 - present)
NCI Leukemia Steering Committee, Member (10/2012 – present)
NCTN Myelo MATCH Initiative, Co-Chair, Senior Scientific Council (1/2019-present)

Scientific Steering Committees and DSMB Positions

Genzyme Oncology, Acute Myeloid Leukemia Steering Committee.
Sunesis Pharmaceuticals, VALOR Steering Committee
Janssen Research and Development, Chair, Independent Data Monitoring Committee, CNTO328 (siltuximab) MDS2001 protocol
Celgene, Chair, Scientific Steering Committee, AML/MDS Registry
Glycomimetics, Inc. Chair, Data and Safety Monitoring Committee, GMI-1271 Phase Ib Study
Daiichi Sankyo Inc., Co-Chair, Scientific Steering Committee, QuANTUM – First
AbbVie, Chair, Independent Review Committee for VIALE A and VIALE C

Memberships in Professional Societies

Active Member, American Society of Hematology

Active Member, American Society of Clinical Oncology

Member of the National Comprehensive Cancer Network (NCCN) Practice Guidelines Committees for acute myeloid leukemia, chronic myeloid leukemia, myelodysplastic syndromes, and myeloid growth factors (until 3/31/10).

Teaching Activities

1976 -1978	Teaching Assistant, Molecular Cytogenetics, Cold Spring Harbor Laboratory, Cold Spring Harbor, New York
1980	Teaching Assistant, Animal Cytology, School of Biological Sciences, University of Leicester, England

Stanford University:

1982	Teaching Assistant, Advanced Molecular Biology, department of Biochemistry, Stanford University
1982 -1983	Teaching Assistant, Cells and Tissues, Department of Structural Biology, Stanford University
1983	Teaching Assistant, Human Anatomy, Department of Structural Biology, Stanford University
1983 -1984	Tutor, Anatomy and Physiology, Primary Care Associate Program, Stanford University
1985	Lecturer, Anatomy of the Kidney, Renal Physiology, Stanford University

Harvard Medical School:

1989 -1990	Instruction of interns and students on the General Medicine Service, Brigham and Women's Hospital
1990 -1993	Instruction of students on Hematology Elective, Brigham and Women's Hospital
1993	Attending Physician, Hematology/Oncology Service, Brigham and Women's Hospital

University of Michigan:

1996 - 2012	Attending Rounds, Department of Internal Medicine
1996 - 2012	Clinical Outpatient Teaching, Department of Internal Medicine
1999 - 2012	M2 Hematology Course, Department of Internal Medicine, annually
2005 - 2002	Chief Rounds, Department of Internal Medicine, annually

Clinical activity - type of practice and estimate of time commitment:

1. AML Clinic (2 days/week)
2. AML disease focus clinical trials (5 days/week)
3. Attending, hematologic malignancies inpatient teaching service (8 weeks/year)

Participation in academic and administrative activities of the University and Medical Center:

1. Attend Grand Rounds for CME credits.
2. Medical Director, Hematologic Malignancies Inpatient Service.
3. Director, Leukemia program in the Division of Hematologic Malignancies and Cellular Therapy at Duke.

APPENDIX B

A. References

Agathangelidis A, et al. Higher-order connections between stereotyped subsets: implications for improved patient classification in CLL. *Blood*. 2021; 137 (10): 1365-1376. doi: 10.1182/blood.2020007039

Agraz-Doblas A, et al. Unraveling the cellular origin and clinical prognostic markers of infant B-cell acute lymphoblastic leukemia using genome-wide analysis. *Haematologica*. 2019; 104: 1176-1188. doi: 10.3324/haematol.2018.206375

American Cancer Society, *Second Cancers After Chronic Lymphocytic Leukemia*, https://www.cancer.org/cancer/types/chronic-lymphocytic-leukemia/after-treatment/second-cancers.html (last accessed Mar. 20, 2025)

American Cancer Society, *What Are the Risk Factors for Chronic Lymphocytic Leukemia?* https://www.cancer.org/cancer/types/chronic-lymphocytic-leukemia/causes-risks-prevention/risk-factors.html (last accessed Mar. 20, 2025)

Andersson AK, et al. The landscape of somatic mutations in infant MLL-rearranged acute lymphoblastic leukemias. *Nat Genet*. 2015; 47; 330-337. doi: 10.1038/ng.323

Baecklund E, et al. Lymphoma subtypes in patients with rheumatoid arthritis: increased proportion of diffuse large B cell lymphoma. *Arthritis Rheum*. 2003; 48: 1543-50. doi: 10.1002/art.11144

Bhatia S. Cause Specific Late Mortality after Allogeneic Stem Cell Transplant. *Hematology Am Soc Hematol Educ Program*. 2019; 2019(1): 626-629. doi: 10.1182/hematology.2019000004

Bond DA, et al. Second cancer incidence in CLL patients receiving BTK inhibitors. *Leukemia*. 2020; 34: 3197-3205. doi: 10.1038/s41375-020-0987-6

Bove FJ, et al. Cancer Incidence among Marines and Navy Personnel and Civilian Workers Exposed to Industrial Solvents in Drinking Water at US Marine Corps Base Camp Lejeune: A Cohort Study. *Environmental Health Perspective*. 2024; 132: 107008-1-15. doi: 10.1289/EHP14966

Bove FJ, et al. Evaluation of mortality among marines and navy personnel exposed to contaminated drinking water at USMC base Camp Lejeune: a retrospective cohort study. *Environmental Health*. 2014; 13: 10. doi: 10.1186/1476-069X-13-10

Brown J, et al. Sustained benefit of zanubrutinib vs ibrutinib in patients with R/R CLL/SLL: final comparative analysis of ALPINE. *Blood*. 2024; 144: 2706-2717. doi: 10.1182/blood.2024024667

Burger JA, et al. Ibrutinib as Initial Therapy for Patients with Chronic Lymphocytic Leukemia. *N Engl J Med.* 2015; 373: 2425. doi: 10.1056/NEJMoa1509388

Castillo JJ, et al. Obesity but not overweight increases the incidence and mortality of leukemia in adults: a meta-analysis of prospective cohort studies. Leuk Res. 2012; 36: 868-875. doi: 10.1016/j.leukres.2011.12.020

Cohn P, et al. Drinking Water Contamination and the Incidence of Leukemia and Non-Hodkin's Lymphoma. *Environ Health Perspect*. 1994; 102: 556-561. doi: 10.1289/ehp.94102556

Curtis RE, et al. Risk of leukemia after chemotherapy and radiation treatment for breast cancer. *N Engl J Med*. 1992; 326(26): 1745-51. doi: 10.1056/NEJM199206253262605

Davids MS, et al. Ibrutinib plus fludarabine, cyclophosphamide, and rituximab as initial treatment for younger patients with chronic lymphocytic leukaemia: a single-arm, multicentre, phase 2 trial. *Lancet Haematol*. 2019; 6: e419-e428. doi: 10.1016/S2352-3026(19)30104-8

Fischer K, et al. Venetoclax and Obinutuzumab in Patients with CLL and Coexisting Conditions. *N Engl J Med*. 2019; 380: 2225. doi: 10.1056/NEJMoa1815281

Francisco L, et al. Progressive decline in late mortality after hematopoietic cell transplantation (HCT) over 40 years – a report from BMTSS. *Blood*. 2016; 128: 691. doi: 10.1182/blood.V128.22.691.691

Fung HC, et al. A long-term follow-up report on allogeneic stem cell transplantation for patients with primary refractory acute myelogenous leukemia: impact of cytogenetic characteristics on transplantation outcome. *Biol Blood Marrow Transplant*. 2003; 9(12): 766-771. doi: 10.1016/j.bbmt.2003.08.004

Glass D, et al. The Health Watch Case–Control Study of Leukemia and Benzene: The Story so Far. *Ann. N. Y. Acad. Sci*. 2006; 1076: 80-89. doi: 10.1196/annals.1371.024

Goede V, et al. Obinutuzumab plus chlorambucil in patients with CLL and coexisting conditions. *N Engl J Med*. 2014; 370(12): 1101-1110. doi: 10.1056/NEJMoa1313984

Granfeldt Østgård LS, et al. Epidemiology and Clinical Significance of Secondary and Therapy-Related Acute Myeloid Leukemia: A National Population-Based Cohort Study. *J Clin Oncol*. 2015; 33(31): 3641-9. doi: 10.1200/JCO.2014.60.0890

Greil C, et al. Prognostic factors for survival after allogeneic transplantation in acute lymphoblastic leukemia. *Bone Marrow Transplant*. 2021; 56: 841-52. doi: 10.1038/s41409-020-01101-z

Hillmen P, et al. Zanubrutinib Versus Ibrutinib in Relapsed/Refractory Chronic Lymphocytic Leukemia and Small Lymphocytic Lymphoma: Interim Analysis of a Randomized Phase III Trial. *J Clin Oncol*. 2022; 41: 1035-1045. doi: 10.1200/JCO.22.00510

Huang KL, et al. Pathogenic Germline Variants in 10,389 Adult Cancers. *Cell*. 2018; 173(2): 355-370.e14. doi: 10.1016/j.cell.2018.03.039

Hus I, et al. The clinical significance of ZAP-70 and CD38 expression in B-cell chronic lymphocytic leukaemia. *Annals of Oncol*. 2006; 17(4): P683-690. doi: 10.1093/annonc/mdj120

Swerdlow SH, et al. WHO classification of Tumours of Haematopoietic and Lymphoid Tissues. 4th ed. Lyon: IARC; 2008, page 180.

Issa G, et al. Predictors of outcomes in adults with acute myeloid leukemia and KMT2A rearrangements. *Blood Cancer J*. 2021; 11: 162. doi: 10.1038/s41408-021-00557-6

Jonsdottir G, et al. Cumulative exposure to melphalan chemotherapy and subsequent risk of developing acute myeloid leukemia and myelodysplastic syndromes in patients with multiple myeloma. *Eur J Haematol*. 2021; 107(2): 275-282. doi: 10.1111/ejh.13650

Lichtman, M. Obesity and the risk for a hematological malignancy: leukemia, lymphoma, or myeloma. *The Oncologist*. 2010; 15: 1083-1101. doi: 10.1634/theoncologist.2010-0206

Michels SD, et al. Therapy-related acute myeloid leukemia and myelodysplastic syndrome: a clinical and morphologic study of 65 cases. *Blood*. 1985; 65: 1364-1372

Molica S, et al. Impact of Targeted Agents on Survival of Chronic Lymphocytic Leukemia Patients Fit for Fludarabine, Cyclophosphamide, and Rituximab (FCR) Relative to Age- and Sex-Matched Population. *Cancers*. 2024; 16: 1085. doi: 10.3390/cancers16061085

Morton LM, et al. Etiologic heterogeneity among non-Hodgkin lymphoma subtypes: the InterLymph Non-Hodgkin Lymphoma Subtypes Project. *J Natl Cancer Inst Monogr*. 2014; 48: 130-144. doi: 10.1093/jncimonographs/lgu013

National Cancer Institute, *Cancer Stat Facts: Leukemia – Acute Lymphocytic Leukemia (ALL)*, https://seer.cancer.gov/statfacts/html/alyl.html (last accessed Mar. 20, 2025)

National Cancer Institute, *Cancer Stat Facts: Leukemia – Chronic Lymphocytic Leukemia (CLL)*, https://seer.cancer.gov/statfacts/html/clyl.html (last accessed Mar. 20, 2025)

Rawstron AC, et al. Monoclonal B lymphocytes with the characteristics of "indolent" chronic lymphocytic leukemia are present in 3.5% of adults with normal blood counts. *Blood*. 2002; 100: 635-639. doi: 10.1182/blood.v100.2.635

Saygin C, et al. Therapy-related acute lymphoblastic leukemia is a distinct entity with adverse genetic features and clinical outcomes. *Blood Adv*. 2019; 3(24): 4228-4237. doi: 10.1182/bloodadvances.2019000925

Sayin S, et al. Evaluation of Second Primary Cancer Risk Among Chronic Lymphocytic Leukemia Patients: Multicenter Study. *Asian Pac J Cancer Prev*. 2023; 24(6): 1971-77. doi: 10.31557/APJCP.2023.24.6.1971

Shanafelt TD, et al. Ibrutinib-Rituximab or Chemoimmunotherapy for Chronic Lymphocytic Leukemia. *N Engl J Med*. 2019; 381(5): 432-443. doi: 10.1056/NEJMoa1817073

Shanafelt TD, et al. Long-term outcomes for ibrutinib-rituximab and chemoimmunotherapy in CLL: updated results of the E1912 trial. *Blood.* 2022; 140(2): 11. doi: 10.1182/blood.2021014960

Shanafelt TD, et al. Monoclonal B-cell lymphocytosis (MBL): biology, natural history and clinical management. *Leukemia*. 2010; 24: 512-520. doi: 10.1038/leu.2009.287

Swerdlow SH, et al. WHO classification of Tumours of Haematopoietic and Lymphoid Tissues. 4th ed. Lyon: IARC; 2008, page 180.

Thomas X. Acute Promyelocytic Leukemia: A History over 60 Years-From the Most Malignant to the most Curable Form of Acute Leukemia. *Oncol Ther*. 2019; 7 :33-65. doi: 10.1007/s40487-018-0091-5

Vaughan A, et al. Surviving apoptosis: a possible mechanism of benzene-induced leukemia. *Chem Biol Interact.* 2005; 153-154:179-185. doi: 10.1016/j.cbi.2005.03.022

Wingard JR, et al. Long-term survival and late deaths after allogeneic hematopoietic cell transplantation. *J Clin Oncol*. 2011; 29: 2230. doi: 10.1200/JCO.2010.33.7212

Woyach JA, et al. Ibrutinib Regimens versus Chemoimmunotherapy in Older Patients with Untreated CLL. *N Engl J Med*. 2018; 379: 2517. doi: 10.1056/NEJMoa1812836

Yadlapati S, Efthimiou P. Autoimmune/Inflammatory Arthritis Associated Lymphomas: Who Is at Risk? *Biomed Res Int*. 2016; 2016:8631061. doi: 10.1155/2016/8631061

Zhang L, et al. Aberrations in chromosomes associated with lymphoma and therapy-related leukemia in benzene-exposed workers. *Environ Mol Mutagen*. 2007; 48(6): 467-74. doi: 10.1002/em.20306

B. Materials Considered

General Materials

- Expert Report of John C. Lipscomb, Ph.D., DABT (February 7, 2025)
- Expert Report of Julie E. Goodman, Ph.D., DABT, FACE, ATS – Trichloroethylene, Perchloroethylene, Benzene, Vinyl Chloride, and trans-1, 2-Dichloroethylene Exposure and NHL Risk (February 7, 2025)
- Expert Report of Julie E. Goodman, Ph.D., DABT, FACE, ATS – Trichloroethylene, Perchloroethylene, Benzene, Vinyl Chloride, and trans-1, 2-Dichloroethylene Exposure and Leukemia Risk (February 7, 2025)
- Expert Report of Michael J. McCabe, Jr., Ph.D. – Camp Lejeune Water Volatile Organic Chemicals and Non-Hodgkin's Lymphoma and Leukemia (February 7, 2025)
- Expert Report of Peter G. Shields, MD (February 7, 2025)
- Expert Report of Jay L. Brigham, Ph.D. (December 9, 2024)
- Expert Report of Dean W. Felsher, M.D., Ph.D. – Leukemia & Non-Hodgkin Lymphoma (December 9, 2024)
- Expert Report of Howard Hu, M.D., M.P.H., Sc.D. (December 9, 2024)

- Expert Report of Kathleen M. Gilbert, PhD – TCE, Non-Hodgkin Lymphoma, and Leukemia (December 9, 2024)
- Expert Report of Lukasz Gondek, MD, PhD – Leukemia (December 9, 2024)
- Expert Report of Steven B. Bird, MD – Hematopoietic Cancers: Leukemia & Non-Hodgkin's Lymphoma (December 9, 2024)
- Expert Report of Timothy M. Mallon, M.D., M.P.H, MS. – Leukemia (December 9, 2024)

Case-Specific Materials

Amsler v. United States

- Amsler Complaint (March 4, 2023)
- Amsler Short-Form Complaint (November 5, 2023)
- Amsler Discovery Pool Profile Form [00284_AMSLER_DPPF_0000000001-17]
- Amsler Track 1 Trial Plaintiff Damages Assessment [00284_AMSLER_0000011143-11145]
- Deposition Testimony and Exhibits of Dr. Jenniffer Yannucci (June 3, 2024)
- Deposition Testimony and Exhibits of Dr. John Moore (August 7, 2024)
- Deposition Testimony and Exhibits of Dr. Praneeth Baratam (June 6, 2024)
- Deposition Testimony and Exhibits of Karen Amsler (April 16, 2024)
- Deposition Testimony and Exhibits of Michael Wukitch (August 8, 2024)
- Expert Report of Judy S. LaKind, Ph.D., *Amsler v. United States* (April 8, 2025)
- Expert Report of Lisa A. Bailey, Ph.D., *Amsler v. United States* (April 8, 2025)
- Expert Report of Lukasz P. Gondek, MD, PhD, *Amsler v. United States* (February 7, 2025)
- Expert Report of Dubravka Tosic, Ph.D., *Estimated Economic Loss of Mrs. Karen Marie Amsler* (April 8, 2025)
- Report by The Center for Forensic Economic Studies, Chad L. Staller & Stephen M. Dripps, *Amsler v. United States* (February 7, 2025)
- Medical Records and other documents produced by Plaintiff [00284_AMSLER_0000000043-523, 00284_AMSLER_0000000654-7913, 00284_AMSLER_0000007923-7961, 00284_AMSLER_0000008029-8038, 00284_AMSLER_0000008047-9894, 00284_AMSLER_0000009907-9938, 00284_AMSLER_0000010300-10476, 00284_AMSLER_0000010492-10998]
- Medical Records from Adult Primary Care Waters [00284_AMSLER_APCW_0000000001-358]
- Medical Records from Lehigh Valley Health Network [00284_AMSLER_LVH_0000000001-70]
- Medical Records from Low Country Cancer Care Clinics [00284_AMSLER_AON_0000000001-272]
- Medical Records from MUSC Health [00284_AMSLER_MUSC_0000000001-777, 00284_AMSLER_MEDRECS_0000000002-2187]
- Medical Records from the Office of Dr. John Moore [00284_AMSLER_JM_0000000002-359]

Connard v. United States

- Connard Short-Form Complaint (November 11, 2023)
- Connard 1st Amended Short-Form Complaint (February 14, 2024)
- Connard 2nd Amended Short-Form Complaint (July 19, 2024)
- Connard Discovery Pool Profile Form [01557_CONNARD_DPPF_0000000001-14]
- Connard Track 1 Trial Plaintiff Damages Assessment [01557_CONNARD_DPPF_0000001670-73]
- Deposition Testimony and Exhibits of Vivian Connard (February 26, 2024)
- Deposition Testimony of Dr. Aaron Rapoport (May 7, 2024)
- Deposition Testimony of Dr. Gorgun Akpek (July 19, 2024)
- Expert Report of Judy S. LaKind, Ph.D., *Connard v. United States* (April 8, 2025)
- Expert Report of Lisa A. Bailey, Ph.D., *Connard v. United States* (April 8, 2025)
- Expert Report of Lukasz P. Gondek, MD, PhD, *Connard v. United States* (February 7, 2025)
- Expert Report of Dubravka Tosic, Ph.D., *Estimated Economic Loss of Stephen M. Connard* (April 8, 2025)
- Report by The Center for Forensic Economic Studies, Chad L. Staller & Stephen M. Dripps, *Connard v. United States* (February 4, 2025)
- Medical Records from UMMS [01557_CONNARD_UMMS_0000000001-3351]
- Medical Records produced by Plaintiff, including records from University of Maryland Greenebaum Comprehensive Cancer Center, University of Maryland Medical System, and Washington Medical Center [01557_CONNARD_0000000001-1673]

Fiolek v. United States

- Fiolek Complaint (March 31, 2023)
- Fiolek Short-Form Complaint (November 6, 2023)
- Fiolek 1st Amended Short-Form Complaint (March 15, 2024)
- Fiolek 2nd Amended Short-Form Complaint (January 28, 2025)
- Fiolek Discovery Pool Profile Form [00062_FIOLEK_DPPF_0000000001-14]
- Fiolek 1st Amended Track 1 Trial Plaintiff Damages Assessment (September 19, 2024)
- Fiolek 2nd Amended Track 1 Trial Plaintiff Damages Assessment (December 27, 2024)
- Deposition Testimony and Exhibits of Robert J. Fiolek (Vols. I and II)
- Deposition Testimony of Jeraldine Fiolek (April 25, 2024)
- Deposition Testimony and Exhibits of Dr. John Cho (May 3, 2024)
- Deposition Testimony and Exhibits of Dr. Walter Wardell (August 13, 2024)
- Deposition Testimony and Exhibits of Dr. Jeffrey Goodwin (January 8, 2025)
- Expert Report of Judy S. LaKind, Ph.D., *Fiolek v. United States* (April 8, 2025)
- Expert Report of Lisa A. Bailey, Ph.D., *Fiolek v. United States* (April 8, 2025)
- Expert Report of Max Kates, M.D., *Fiolek v. United States* (April 8, 2025)
- Expert Report of Dubravka Tosic, Ph.D., *Estimated Potential Offsets of Mr. Robert J. Fiolek* (April 8, 2025)

- Expert Report of Damian A. Laber, M.D., F.A.C.P., *Fiolek v. United States* (February 7, 2025)
- Medical Records and other documents produced by Plaintiff [00062_FIOLEK_0000000001-11678]
- Medical Records from VBA [00062_FIOLEK_VBA_0000000001-2689]
- Medical Records from VHA [00062_FIOLEK_VHA_0000000001-82]
- Medical Records from Coastal Carolina Health Care [00062_FIOLEK_CCHC_0000000001-915]
- Medical Records from CarolinaEast Medical Center [00062_FIOLEK_CEMC_0000000001-842, 00062_FIOLEK_CEMC_000000942-4436, 00062_FIOLEK_CEMC_0000004538-10874]
- Medical Records from UNC Hospitals [00062_FIOLEK_UNC_0000000001-324]

Gleesing v. United States

- Gleesing Short-Form Complaint (November 3, 2023)
- Amended Short-Form Complaint (June 18, 2024)
- Gleesing Discovery Pool Profile Form [01486_GLEESING_DPPF_0000000055-76]
- Deposition Testimony of Joseph Gleesing (April 12, 2024)
- Deposition Testimony of Charlene Gleesing (June 4, 2024)
- Deposition Testimony of Dr. Min Luo (July 22, 2024)
- Deposition Testimony of Dr. Muhammad Usman (September 26, 2024)
- Expert Report of Judy S. LaKind, Ph.D., *Gleesing v. United States* (April 8, 2025)
- Expert Report of Lisa A. Bailey, Ph.D., *Gleesing v. United States* (April 8, 2025)
- Expert Report of Damian A. Laber, M.D., F.A.C.P., *Gleesing v. United* States (February 7, 2025)
- Expert Report of Dubravka Tosic, Ph.D., *Estimated Economic Loss of Joseph M. Gleesing* (April 8, 2025)
- Report by The Center for Forensic Economic Studies, Chad L. Staller & Stephen M. Dripps, *Gleesing v. United States* (February 7, 2025)
- Medical Records from [01486_GLEESING_BMH0000000001-2395]
- Medical Records produced by Plaintiff, including records from Borgess Medical Center, Bronson Healthcare Group, University of Michigan Cancer Center (UMCC), and Ann Arbor VA Hospital [01486_GLEESING_0000000001-7186]

Hill v. United States

- Hill Complaint (November 20, 2023)
- Hill 3rd Amended Short-Form Complaint (August 16, 2024)
- Hill Discovery Pool Profile Form [00028_HILL_DPPF_0000000001-23]
- Deposition Testimony and Exhibits of Bruce Hill (April 9, 2024)
- Deposition Testimony of Kristie Hill (June 14, 2024)
- Deposition Testimony and Exhibits of Dr. Maxim Norkin (June 6, 2024)

- Deposition Testimony and Exhibits of Dr. Bradley Fletcher (June 13, 2024)
- Deposition Testimony and Exhibits of Dr. Jessica Schmit (July 15, 2024)
- Deposition Testimony and Exhibits of Stephen McCready, PA-C (May 8, 2024)
- Expert Report of Judy S. LaKind, Ph.D., *Hill v. United States* (April 8, 2025)
- Expert Report of Lisa A. Bailey, Ph.D., *Hill v. United States* (April 8, 2025)
- Expert Report of Deborah A. Navarro, MA, *Rehabilitation Evaluation and Life Care Plan of Bruce Hill* (April 8, 2025)
- Expert Report of Dubravka Tosic, Ph.D., *Estimated Economic Loss of Bruce Hill* (April 8, 2025)
- Expert Report of Dean W. Felsher, M.D., Ph.D., *Hill v. United States* (February 7, 2025)
- Report by The Center for Forensic Economic Studies, Chad L. Staller & Stephen M. Dripps, *Hill v. United States* (February 7, 2025)
- Medical Records from VBA [00028_HILL_VBA_0000000024-9561]
- Medical Records from VHA [00028_HILL_VHA_0000000001-1411]
- Medical Records from University of Florida Health Shands Cancer Hospital [00028_HILL_MEDRECS_0000000015-71]
- Medical Records and other documents produced by Plaintiff [00028_HILL_0000000005-15, 00028_HILL_0000004844-64]