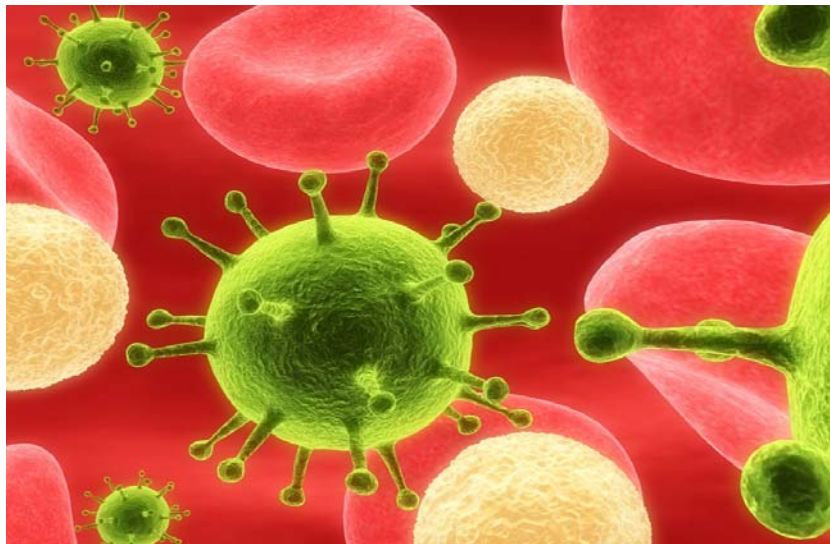


# OUTCOME ANALYSIS

2008

## LEUKEMIA



Written By: Aaron P. Scholnik, MD, FACP

## Outcome Analysis – 2008 - Leukemia

Leukemia is a group of diseases which, taken together, account for the sixth most common cause of cancer death in men and the seventh most common cause of cancer death in women.

Leukemia, while a relatively infrequent type of malignancy, is nonetheless a major cause of cancer illness and death at the Marquette General Cancer Center as well as throughout the world.

Leukemia is a somewhat archaic term meaning “white [leuk] blood [emia]”. The earliest description of leukemia was made through the observation that blood of some patients contained many times the normal white blood cells making the blood plasma appear milky instead of clear. At the time of this description however, it was not realized that there were multiple types of white cells and therefore multiple types of leukemia.

Leukemia can be divided into four general types depending both on how mature the proliferating white cells are and on the type of white blood cell that is proliferating. The leukemias in which the main component is mature appearing cells are termed “chronic.” These chronic leukemias tend to progress more slowly, tend to require treatment later in their course, and patients usually live longer than patients with the other type of leukemia called “acute” leukemia. In acute leukemias the cells are often “poorly differentiated” and seem to be primitive cells which are sometimes very difficult to recognize and type specifically. Patients with acute leukemia tend to have more aggressive disease, which requires early and very aggressive treatment and unfortunately, in many cases, the patients do not live as long as those with chronic leukemias. In addition, leukemias can be classified as either “lymphocytic” or “myelocytic.” Lymphocytic leukemias are derived from cells that form lymphocytes, which help maintain the immune system. The myelocytic leukemias are derived from the cells which form the bacteria fighting granulocyte and monocyte cells as well as the cells that form blood platelets and red cells. There are also some leukemias derived from other cells such as “hairy cell leukemia” a special type of lymphoma.

There are an estimated 231,500 people in the United States living with leukemia and an estimated 44,300 new cases of leukemia will be diagnosed in the United States in 2008.

Nationwide chronic leukemias account for about 7% more cases than acute leukemias; however in the Marquette General Cancer Center registry the chronic leukemias outnumber the acute leukemias by 57% to 38%. This is partly explained by the fact that chronic leukemias tend to occur in older populations and the age of the residents of the Upper Peninsula is significantly

older on average than that of the United States as a whole. For instance, the average age at diagnosis of patients with chronic lymphocytic leukemia nationwide is 67. Conversely the most common form of leukemia among children under 20 is acute lymphoblastic leukemia and it is the most common cancer in children 1-7 years old.

\*\*age table 0-20, 20-40, 40-60 and 60+ each of the five kinds of leukemia

AGE AT DIAGNOSIS OF PATIENTS DIAGNOSED AT MARQUETTE GENERAL HOSPITAL WITH LEUKEMIA 1997 – 2007					
AGE AT DIAGNOSIS	ACUTE MYELOCYTIC LEUKEMIA	CHRONIC LYMPHOCYTIC LEUKEMIA	CHRONIC MYELOCYTIC LEUKEMIA	ACUTE LYMPHOCYTIC LEUKEMIA	HAIRY CELL LEUKEMIA
<b>0 – 20 YEARS OLD</b>	0 PATIENTS	0 PATIENTS	1 PATIENTS	5 PATIENTS	0 PATIENTS
<b>21 – 40 YEARS OLD</b>	9 PATIENTS	0 PATIENTS	5 PATIENTS	2 PATIENTS	2 PATIENTS
<b>40 – 60 YEARS OLD</b>	16 PATIENTS	20 PATIENTS	10 PATIENTS	5 PATIENTS	4 PATIENTS
<b>61 YEARS AND OLDER</b>	39 PATIENTS	75 PATIENTS	15 PATIENTS	4 PATIENTS	5 PATIENTS

Table 1.

The most common types of leukemias in adults are chronic lymphocytic leukemia with 15,100 new cases for 2008 followed by acute myelocytic leukemia at an estimated 13,300 new cases, acute lymphocytic leukemia with approximately 5,400 cases and finally chronic myelocytic leukemia with approximately 4,800 cases.

Cases Diagnosed at Marquette General Hospital		
1997 - 2007		
31	Chronic Myelocytic Leukemia	13%
95	Chronic Lymphocytic Leukemia	44%
11	Hairy Cell Leukemia	5%
16	Acute Lymphocytic Leukemia	8%
64	Acute Myelocytic Leukemia	30%
<b>217</b>		<b>100%</b>

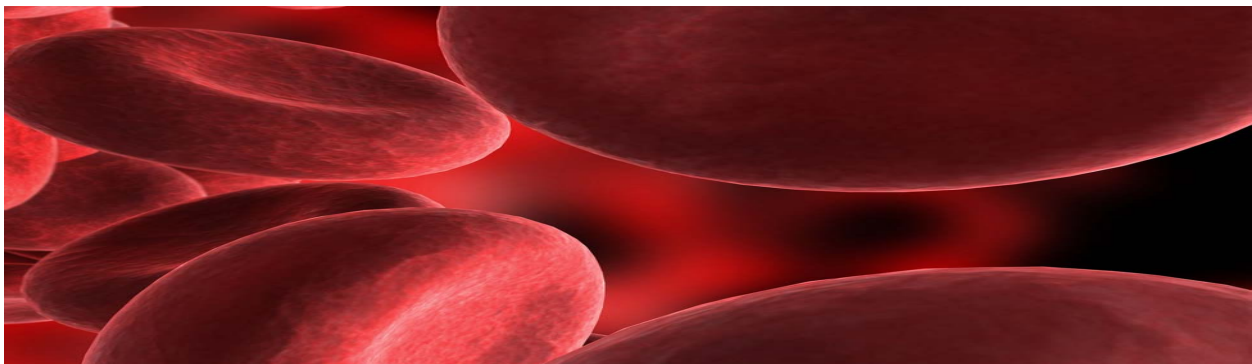
Table 2.

The Leukemia and Lymphoma Society estimates that in 2008 there are 231,461 people in the United States living with leukemia and that an estimated 44,270 new cases of leukemia will be diagnosed. Unfortunately the Leukemia and Lymphoma Society also estimates that approximately 21,710 deaths in the United States will be caused by leukemia in 2008. Many

patients have lived with their leukemia for many years before succumbing to it and treatments for leukemia are continuously improving.

The five-year relative survival rate of leukemia patients has nearly quadrupled in the past 48 years. (Relative survival rate is the survival rate of leukemia patients compared to a similar group of patients who do not have leukemia, since in all groups of people there are other causes of death including accidents, myocardial infarctions, infections, kidney disease, strokes etc.) This is a point to keep in mind when you look at the Marquette General Cancer Center survival rates. Since the U.P. has an older than average population, patients with leukemia also tend to be older and thus some of those patients, especially those with chronic lymphocytic leukemia, may die with their disease as opposed to because their disease.

Leukemia is often diagnosed either during a routine examination or when the patient presents because of rather vague and nonspecific illness complaints. By far the most frequent abnormality to call attention to the possibility of leukemia is an abnormal CBC (complete blood count). Other frequent findings which raise the suspicion for leukemia are easy bruising or bleeding, the finding of an enlarged liver or spleen, a patient having unexplained shortness of breath, night sweats, fever or weight loss. While many leukemias can be suspected and sometimes initially diagnosed through studies of the peripheral blood, in many cases an examination of the bone marrow (a bone marrow biopsy and/or aspirate) is necessary to confirm the diagnosis and to gather baseline information before treatment. In some cases no abnormal blood cells are seen in the blood count and a bone marrow examination is the only way of making a diagnosis. The procedure of performing a bone marrow biopsy is a simple outpatient procedure, which generally requires only local anesthesia as one might have for a dental procedure. Occasionally some patients may require or request sedation, however the need for true anesthesia is a rarity.



<b>Leukemia – Presenting Signs &amp; Symptoms 1997 – 2007 217 Total Cases</b>	
<b>SYMPTOMS</b>	<b>PERCENT OF TOTAL CASES</b>
Bone pain	0.4%
Pruritus	0.4%
Nausea	1.4%
Chest Discomfort	1.4%
Vomiting	1.8%
Change in Bowel Habits	2.3%
Persistent Cough	3.2%
Lump of Thickening	4.6%
Loss of Appetite	6.8%
No Symptoms	7.3%
Weight Loss	7.3%
Unexplained Fever	9.1%
Night Sweats	9.1%
Dyspnea	11.0%
Physical Findings (splenomegaly, hepatomegaly, bleeding, etc.)	21.9%
Abnormal CBC	92.2%

Table 3.

The most frequent type of leukemia diagnosed at Marquette General Cancer Center is chronic lymphocytic leukemia (CLL). We have diagnosed and treated 95 patients over the last ten years with this diagnosis. Nationwide the average age at diagnosis of chronic lymphocytic leukemia is 67 years old. At the Marquette General Cancer Center the average age at diagnosis is 68. Because chronic lymphocytic leukemia is often picked up at an early asymptomatic stage and progresses only very slowly it is common to follow many patients without treatment until it is clear that their disease is progressing and is causing or is about to cause other problems. Of the 95 patients diagnosed with chronic lymphocytic leukemia over the last ten years at Marquette General Cancer Center only 20 required immediate treatment. The other 75 required no initial treatment and underwent periodic observation only until their leukemia was deemed to be progressing fast enough that it was either about to cause or already causing problems for the patient. The average time from first diagnosis of chronic lymphocytic leukemia until first treatment in these patients was 44 months and some patients went 6-9 years with their disease being observed before they required active treatment.

Over the last 10-15 years the treatment of chronic lymphocytic leukemia has continued to improve as new types of chemotherapy and chemotherapy combinations have been introduced.

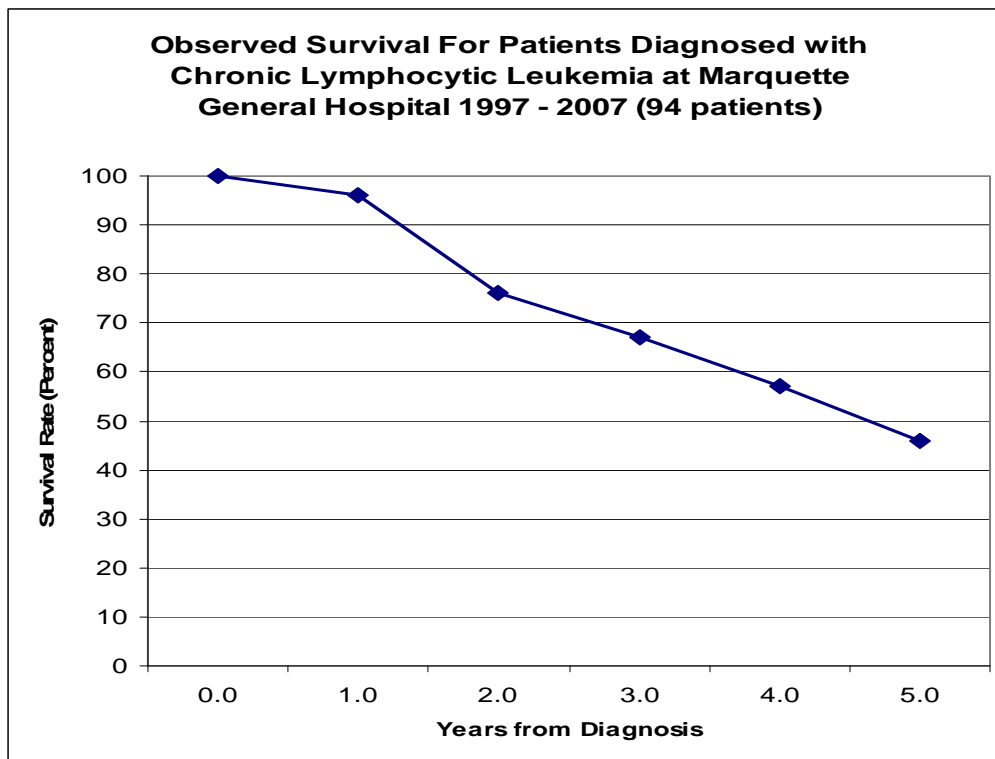
More recently the monoclonal antibodies, which attack various components of the leukemia cell, have come into practice to be used either by themselves or along with chemotherapy, which has significantly increased the effectiveness and lowered the toxicity of our treatment.

<b>PATIENTS DIAGNOSED WITH CHRONIC LYMPHOCYTIC LEUKEMIA AT MARQUETTE GENERAL HOSPITAL 1997 – 2007 TREATMENT &amp; LENGTH OF TIME TO RECURRENCE (95 PATIENTS)</b>						
<b>TREATMENT TYPE</b>	<b>NUMBER OF CASES</b>	<b>RECURRENCE</b>				<b>TOTAL (%)</b>
		<b>NO RECURRENCE</b>	<b>RECURRED</b>	<b>NEVER DISEASE FREE</b>	<b>UNKNOWN IF RECURRED</b>	
<b>CHEMO NOS</b>	7	0(0%)	0(0%)	7(100%)	0(0%)	7(7.4%)
<b>CHEMO (LEUKERAN)</b>	2	0(0%)	1(50%) 1- 37 months	1(50%)	0(0%)	2(2.1%)
<b>CHEMO (RITUXAN, FLUDARABINE)</b>	1	0(0%)	0(0%)	1(100%)	0(0%)	1(1.0%)
<b>CHEMO (FLUDARABINE)</b>	2	2(100%)	0(0%)	0(0%)	0(0%)	2(2.1%)
<b>CHEMO (FLUDARABINE, CYTOXAN)</b>	2	2(100%)	0(0%)	0(0%)	0(0%)	2(2.1%)
<b>CHEMO (LEUKERAN,COP)</b>	1	1(100%)	0(0%)	0(0%)	0(0%)	1(1.1%)
<b>CHEMO (RITUXAN)</b>	1	1(50%)	0(0%)	0(0%)	0(0%)	1(1.1%)
<b>CHEMO (REVLIMID) DECADRON</b>	1	0(0%)	0(0%)	1(100%)	0(0%)	1(1.1%)
<b>CHEMO (FLUDARABINE, CYTOXAN, RITUXAN)</b>	1	0(0%)	0(0%)	1(100%)	0(0%)	1(1.1%)
<b>CHEMO (MINI-CHOP, RITUXAN)</b>	1	1(100%)	0(0%)	0(0%)	0(0%)	1(1.1%)
<b>CHEMO (LEUKERAN, PCR,CpG PROTOCOL, ALEMTUZIMAB, RITUXIMAB,CFAR)</b>	1	1(100%)	0(0%)	0(0%)	0(0%)	1(1.1%)
<b>NO TREATMENT/OBSERVATION ONLY AS 1<sup>ST</sup> COURSE OF TREATMENT</b>	75	0(0%)	1(1.3%) 1-53 months	72(96%)	2(2.6%)	75(78.9%)
<b>LENGTH OF TIME UNTIL CHEMOTHERAPY BEGAN</b>  <b>1 YEAR OR LESS – 2 PATIENTS</b> <b>1 – 2 YEARS – 6 PATIENTS</b> <b>2 – 3 YEARS – 4 PATIENTS</b> <b>3 – 4 YEARS – 1 PATIENT</b> <b>4 – 5 YEARS – 3 PATIENTS</b> <b>5 – 6 YEARS – 2 PATIENTS</b> <b>6 – 7 YEARS – 1 PATIENTS</b> <b>7 – 8 YEARS – NO PATIENTS</b> <b>8 – 9 YEARS – 1 PATIENT</b>  <b>NO TREATMENT/OBSERVATION ONLY OR PATIENT EXPIRED BEFORE FURTHER TREATMENT GIVEN – 55 PATIENTS</b>						

Table 4.

New techniques such as flow cytometry and cytogenetics are now helping us to decide on which kind of treatment is most appropriate for the patients and in recent years these studies are being done here in Marquette, either at MGH or as a joint venture with MGH and Northern Michigan University. This gives us a much more rapid access to results and allows us to use these results in “real time”. We have come to see flow cytometry and cytogenetics as invaluable for helping us treat other types of leukemias as well.

As can be seen from this graph almost 50% of patients diagnosed with chronic lymphocytic leukemia are still alive after 5 years even though many of these patients have advanced age and other significant health problems.



Graph 1.

There were 31 patients with chronic myelocytic leukemia diagnosed at Marquette General Cancer Center between 1997 and 2007. This type of cancer involves proliferation of many mature appearing cells in the bone marrow, especially the granulocytes. It was found in the 1960's that there was a frequent chromosome abnormality in patients with chronic myelocytic leukemia called the Philadelphia chromosome. In this abnormality a piece of chromosome 9 and

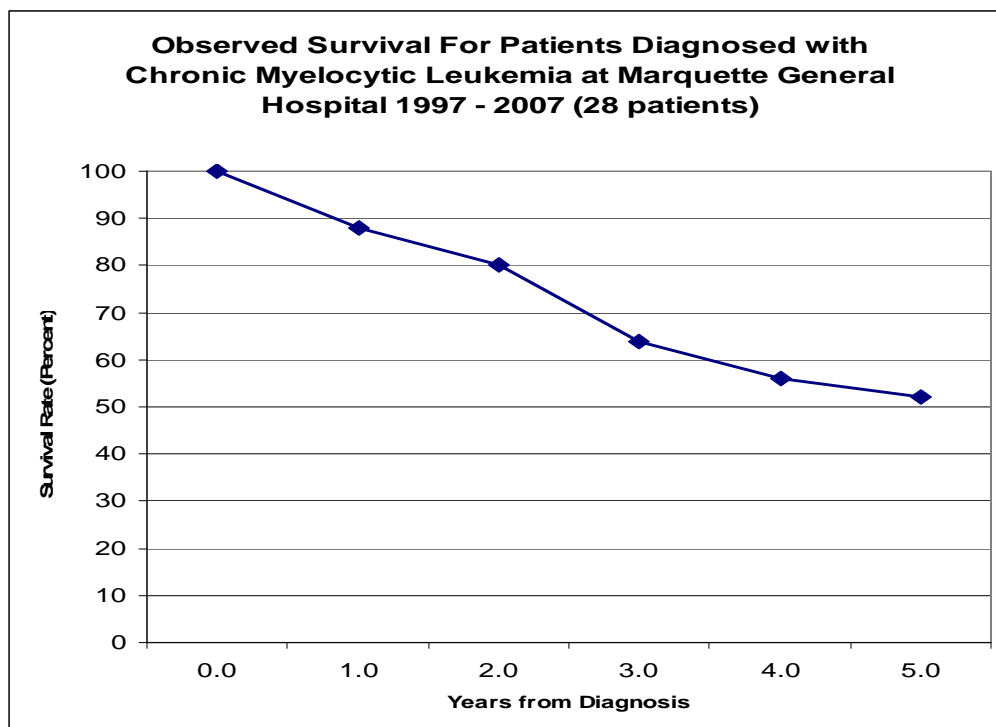
a piece of chromosome 22 break off and switch places. This puts the genes from one chromosome next to those of a completely different chromosome so that they form a brand new gene called BCR-ABL. This new gene causes production of an abnormal protein, which causes the myeloid bone marrow cells to divide rapidly and essentially uncontrolled. For many years our treatments consisted of using drugs that slowed down the growth of bone marrow cells in general but did not treat the specific abnormality. We found that without a bone marrow transplant patients eventually converted to an acute leukemia which was extremely difficult to treat, and died within a few years. In the late 1990's the structure of the abnormal protein was able to be studied and a new drug called Imatinib or Gleevec was developed which could inactivate this abnormal protein that caused chronic myelocytic leukemia. In 2001 this drug became commercially available and has probably changed the natural history of chronic myelocytic leukemia. Many people with CML on Gleevec have all evidence of the disease disappear, and many have undetectable amounts of the BCR-ABL gene. These patients can live essentially normal lives for more than 5 years. Additional Tyrosine Kinase Inhibitor drugs, which are also oral as is Gleevec, had been developed for those patients who do not tolerate or cease to respond to Gleevec. Thus we do not yet know the full extent or duration for which chronic myelocytic leukemia may be controlled by these breakthrough drugs. This principle of "targeted therapy" using a molecule which is targeted at the active site of an abnormal gene or abnormal protein that causes the leukemia to develop is now being applied to the other leukemias as well, although not yet with the success seen with CML. The success of these Tyrosine Kinase Inhibitors has led to a continual reevaluation of the need for bone marrow transplants in patients who have complete responses.

Of the 31 patients with CML who were diagnosed and treated at Marquette General Cancer Center from 1997 to 2007, four underwent bone marrow transplant. Prior to the availability of Gleevec, chemotherapy with oral drugs such as busulfan, phenylalanine mustard, and hydroxyurea were used. Some people who were either early in the illness or were elderly and had many other health complications were not treated at all. Since 2001, 12 patients have been treated with Gleevec and most have done quite well with very acceptable minimal side effects and excellent control of their disease.

PATIENTS DIAGNOSED WITH CHRONIC MYELOCYTIC LEUKEMIA AT MARQUETTE GENERAL HOSPITAL 1997 – 2007 TREATMENT & LENGTH OF TIME TO RECURRENCE (31 PATIENTS)						
TREATMENT TYPE	NUMBER OF CASES	RECURRENCE				TOTAL(%)
		NO RECURRENCE	RECURRED	NEVER DISEASE FREE	UNKNOWN WHEN OR IF RECURRED	
CHEMOTHERAPY NOS	2	0 (0%)	0 (0%)	2 (100%)	0 (0%)	2 (3.6%)
CHEMO NOS, BONE MARROW TRANSPLANT	4	3 (75%)	0 (0%)	0 (0%)	1 (25%)	4 (14.3%)
CHEMO (GLEEVEC)	13	8 (61.5%)	2 (7.1%) 1-37 months	1 (3.6%)	2 (7.1%)	13 (46.4%)
PRIOR TO 2001	1	1 (100%)	0 (0%)	0 (0%)	0 (0%)	1(4%)
AFTER 2001	12	5 (42%)	1 (8%) 1-37 months	3 (25%)	3 (25%)	12 (42%)
NO TREATMENT	12	0 (0%)	0 (0%)	12 (100%)	0 (0%)	12 (39%)
AGE AT DIAGNOSIS 0-20 YEARS 21-40 YEARS 41-60 YEARS 61 YEARS & OLDER	ALL PATIENTS WHO HAVE RECEIVED NO TREATMENT WERE DIAGNOSED AT AGE 63 AND OLDER					

Table5.

As can be seen in Graph 2, over 50% of the patients with chronic myelocytic leukemia are alive at five years despite many of them having advanced age and/or coexistent significant health problems.

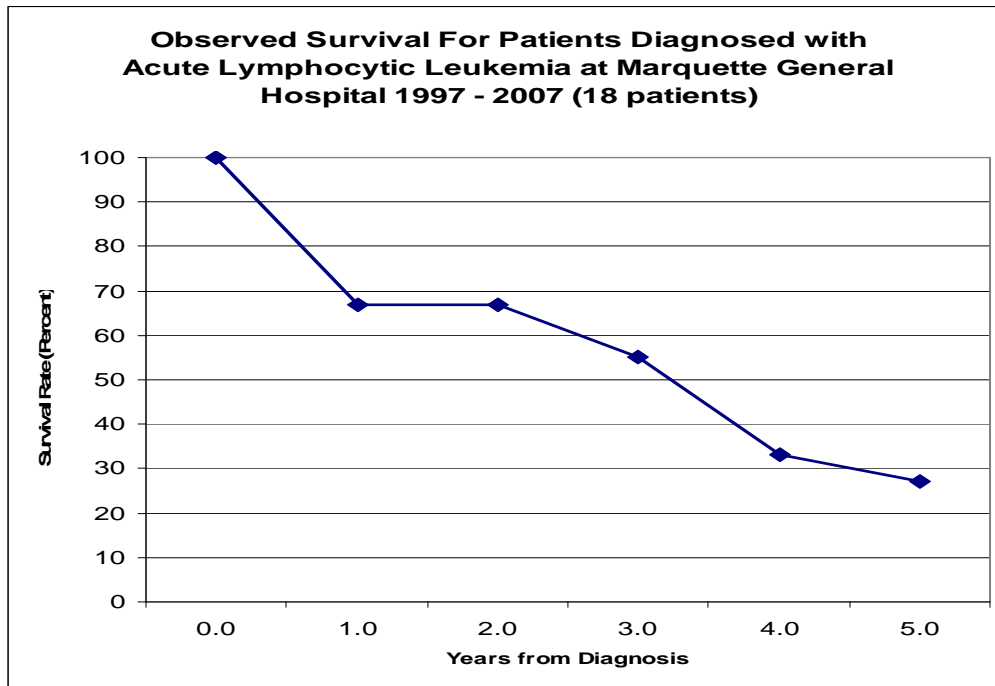


Graph 2.

Acute lymphoblastic leukemia is the least frequent acute leukemia in adults although it is the most frequent acute leukemia in children. In children, great advances have been made in the treatment of acute lymphoblastic leukemia and the majority of children are cured with modern techniques of chemotherapy and occasional bone marrow transplant. In adults, unfortunately, acute lymphoblastic leukemia acts like a different disease and seems to be much more resistant to treatment. While cures still occur, they are infrequent and often require a complete remission with chemotherapy followed by a bone marrow transplant to prevent relapse. Possibly because of the older population in the Upper Peninsula, patients with acute lymphoblastic leukemia comprise only 8% of the leukemias seen at Marquette General Cancer Center. Our three-year survival is 55% but our five-year survival is 27%.

<b>PATIENTS DIAGNOSED WITH ACUTE LYMPHOCYTIC LEUKEMIA AT MARQUETTE GENERAL HOSPITAL 1997 – 2007 TREATMENT &amp; LENGTH OF TIME TO RECURRENCE (16 PATIENTS)</b>						
<b>TREATMENT TYPE</b>	<b>NUMBER OF CASES</b>	<b>RECURRENCE</b>				<b>TOTAL(%)</b>
		<b>NO RECURRENCE</b>	<b>RECURRED</b>	<b>NEVER DISEASE FREE</b>	<b>UNKNOWN IF RECURRED</b>	
<b>CHEMO NOS</b>	5	2(40%)	1(20%) <b>1- 57 months</b>	1(20%)	1(20%)	5(29%)
<b>CHEMO, RT</b>	1	1(100%)	0(0%)	0(0%)	0(0%)	1(6%)
<b>CHEMO (CVAD)</b>	2	0(0%)	2(100%) <b>1 - 9 months 1 – 27 months</b>	0(0%)	0(0%)	2(12%)
<b>CHEMO (VCR, PDN, ARA-C, MTX, L- ASPARIGNASE, DAUNORUBICIN)</b>	1	1(100%)	0(0%)	0(0%)	0(0%)	1(6%)
<b>CHEMO (CTX, DAUNORUBICIN, L- ASPARIGINASE)</b>	1	0(0%)	0(0%)	1(100%)	0(0%)	1(6%)
<b>CHEMO (VCR, ARA-C, MTX, CcG PROTOCOL – AALL01P2) BONE MARROW TRANSPLANT</b>	1	1(100%)	0(0%)	0(0%)	0(0%)	1(6%)
<b>CHEMO (CYCLOSPHAMIDE, VCR, DAUNORUBICIN, L-AASPARIGNASE, LARSON PROTOCOL, GLEEVAC, VCR, 6MP, MTX)</b>	1	0(0%)	1(100%) <b>1 – 4 months</b>	0(0%)	0(0%)	1(6%)
<b>CHEMO (VCR, ARA-C, MTX, 6MP)</b>	1	1(100%)	0(0%)	0(0%)	0(0%)	1(6%)
<b>NO TREATMENT</b>	3	0(0%)	0(0%)	4(100%)	0(0%)	4(23%)

Table 6.



Graph 3.

Table 7 shows the details of MGCC patients with acute myelocytic leukemia. Between 1997 and 2007, 64 patients with acute myelocytic leukemia were diagnosed and treated at Marquette General Cancer Center. Acute myelocytic leukemia is the most frequent acute leukemia found in adults and, while it is not infrequent in young adults, it peaks dramatically after age 60. Just as acute lymphoblastic leukemia is a broad category for what are probably several different diseases, so acute myelocytic leukemia is also a general category for multiple different diseases. Some acute myelocytic leukemias develop suddenly and seemingly have no precursor illness or exposure to toxins or radiation. On the other hand, some cases of acute myelocytic leukemia seem to be related to radiation or toxin exposure including treatment of prior malignancies with chemotherapy and/or radiation. These latter cases of acute myelocytic leukemia often occur after a progressive degenerative disease of the bone marrow (usually referred to as Myelodysplastic Syndrome) and are called Secondary Leukemias. Secondary Leukemias are often much more difficult to treat.

Chemotherapy for acute myelocytic leukemia involves intense doses of medications that kill the leukemia cells but in doing so temporarily severely suppress the normal cells as well. Because the bone marrow is often severely damaged by the leukemia to begin with, the induction of a remission (disappearance of leukemia cells and reappearance of a normal marrow after chemotherapy) is often accompanied by a major risk of infections and a need for transfusions, antibiotics and other supportive measures.

<b>PATIENTS DIAGNOSED WITH ACUTE MYELOCYTIC LEUKEMIA AT MARQUETTE GENERAL HOSPITAL 1997 – 2007 BY TREATMENT &amp; LENGTH OF TIME TO RECURRENCE (64 PATIENTS)</b>						
<b>TREATMENT TYPE</b>	<b>NUMBER OF CASES</b>	<b>RECURRENCE</b>				<b>TOTAL(%)</b>
		<b>NO RECURRENCE</b>	<b>RECURRED</b>	<b>NEVER DISEASE FREE</b>	<b>UNKNOWN WHEN OR IF RECURRED</b>	
<b>CHEMOTHERAPY</b>	43	15 (34%)	6 (14%) 1- 6 months 2-7 months 1-13 months 1-34 months 1-11 months	20 (46%)	2 (5%)	43 (67%)
<b>CHEMO (ARA-C) WITH BONE MARROW TRANSPLANT</b>	1	1 (100%)	0 (0%)	0 (0%)	0 (0%)	1 (1.5%)
<b>CHEMO (ARA-C, DAUNORUBICIN) WITH BONE MARROW TRANSPLANT</b>	2	1 (50%)	0 (0%)	1 (50%)	0 (0%)	2 (3%)
<b>CHEMO (IDARUBICIN, ARA-C) WITH BONE MARROW TRANSPLANT</b>	2	2 (100%)	0 (0%)	0 (0%)	0 (0%)	2 (3%)
<b>BONE MARROW TRANSPLANT</b>	1	0 (0%)	0 (0%)	0 (0%)	1 (100%)	1 (1.5%)
<b>NO TREATMENT</b>	15	0 (0%)	0 (0%)	14 (93%)	1 (7%)	15 (24%)
<b>AGE AT DIAGNOSIS</b>  0-20 YEARS 21-40 YEARS 41-60 YEARS 61 YEARS & OLDER	<b>OF THE 15 PATIENTS DIAGNOSED WHO HAVE RECEIVED NO TREATMENT (OBSERVATION ONLY) ALL 15 PATIENTS WERE 61 YEARS AND OLDER AT TIME OF DIAGNOSIS. OF THE 15 PATIENTS, 14 CONTINUED WITH OBSERVATION ONLY, WITH 1 PATIENT RECEIVING CHEMOTHERAPY 1 YEAR AFTER DATE OF DIAGNOSIS. ALL PATIENTS HAVE EXPIRED.</b>					

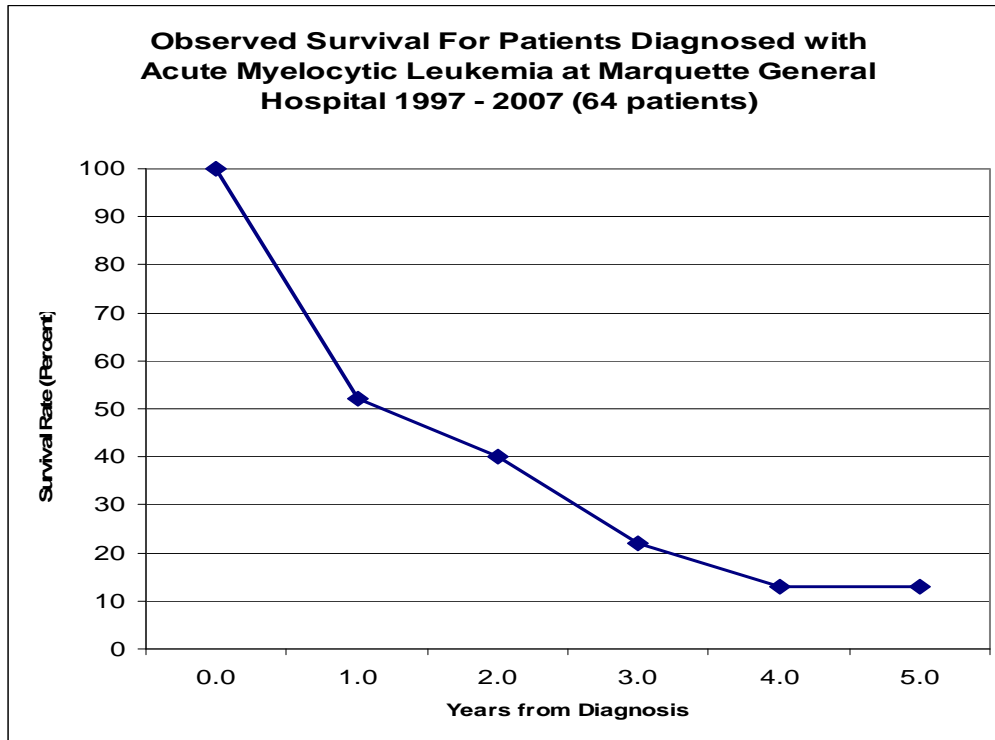
Table 7.

In general, acute myelocytic leukemia is curable by chemotherapy alone in no more than 15% of cases. In patients who are healthy enough to withstand bone marrow transplant and to have a suitable stem cell donor, a stem cell (commonly referred to as bone marrow) transplant can increase the cure rate to almost 50%.

Of the 64 patients with acute myelocytic leukemia treated at the Marquette General Cancer Center over the ten-year span 1997-2007, 48 patients received chemotherapy and 5 received bone marrow transplants in addition. 15 patients did not receive induction chemotherapy because of advanced age and/or severe coexisting medical conditions.

At one year 52% of patients are alive indicating that the Induction period is a dangerous time for all patients but for those that are able to go into remission the majority of them stay in remission

for at least the next year since at 2 years 40% of patients are still alive. Late relapses unfortunately account for most of the patient deaths beyond two years.



Graph 4.

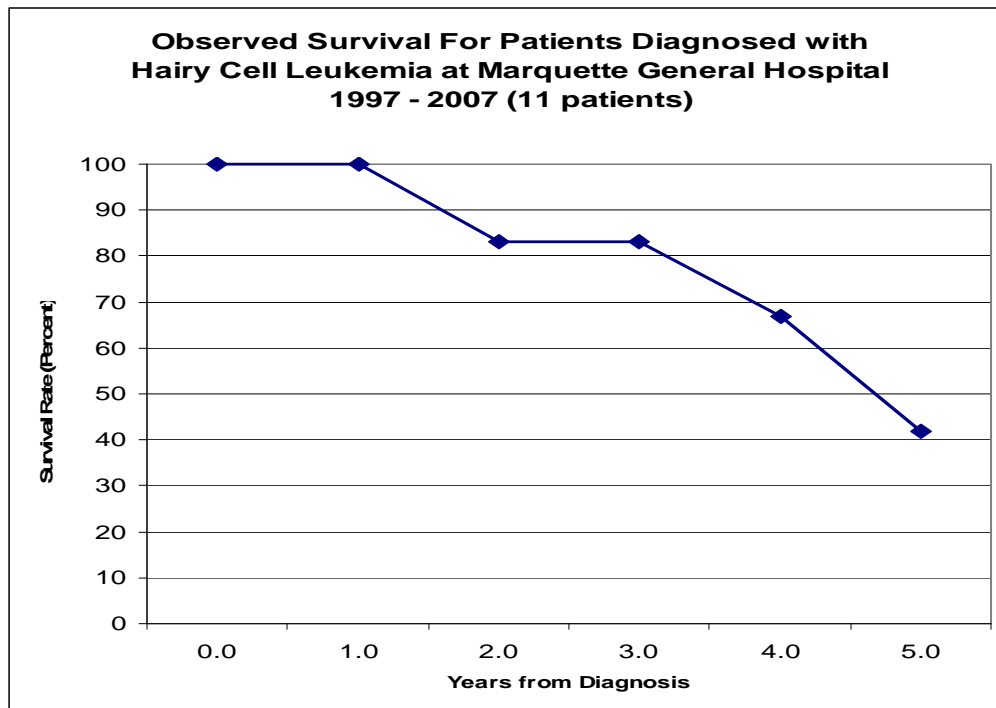
Just as in the other kinds of leukemia, advances in knowledge of the pathology of AML will hopefully lead to further improvement in treatment. Information is now emerging about the importance of chromosomal abnormalities in dictating treatment of AML. The close communication with and the rapid results of bone marrow testing from the Marquette General Hospital pathology department and its flow cytometry and cancer cytogenetics divisions have also improved results.

The final type of leukemia to be discussed is Hairy Cell Leukemia. Hairy cell leukemia is not truly a leukemia so much as a B-cell lymphoma which often has some cells circulating in the blood stream. It is an unusual type of leukemia/lymphoma as it presents with a large spleen and low blood counts. Treatment 20 years ago was splenectomy however this proved to be a fairly temporary measure for raising the blood counts. Later, Interferon was tried and seemed to work well, however the treatment itself has considerable toxicities. More recently, relatively mild chemotherapy medicines such as cladribine have been used with good affect although they may leave the patient subject to even further temporarily lower blood counts for weeks to months following treatment before full recovery. More recently, the monoclonal antibody Rituximab, which attacks one of the substances on the surface of the hairy cell (as well as on the surface of

other B-cell lymphomas), has been used with excellent effectiveness and lesser toxicity. We have averaged only about one patient with hairy cell leukemia a year over the ten-year period discussed since this is a very infrequent type of leukemia. In the younger and healthier patients survival has been quite good.

PATIENTS DIAGNOSED WITH HAIRY CELL LEUKEMIA AT MARQUETTE GENERAL HOSPITAL 1997 – 2007 TREATMENT & LENGTH OF TIME TO RECURRENCE (11 PATIENTS)						
TREATMENT TYPE	NUMBER OF CASES	RECURRENCE				TOTAL (%)
		NO RECURRENCE	RECURRED	NEVER DISEASE FREE	UNKNOWN IF RECURRED	
CHEMO (CLADRIBINE (2CDA))	6	1(17%)	4(67%) 1 – 4 months 1 – 20 months 1 – 25 months 1 – 62 months	1(17%)	0(0%)	6(55%)
CHEMO (CLADRIBINE (2CDA)) RITUXAN	2	0(0%)	1(50%) 1 – 44 months	1(50%)	0(0%)	2(18%)
NO TREATMENT	3	0(0%)	0(0%)	3(100%)	0(0%)	3(27%)

Table 8.



Graph 5.

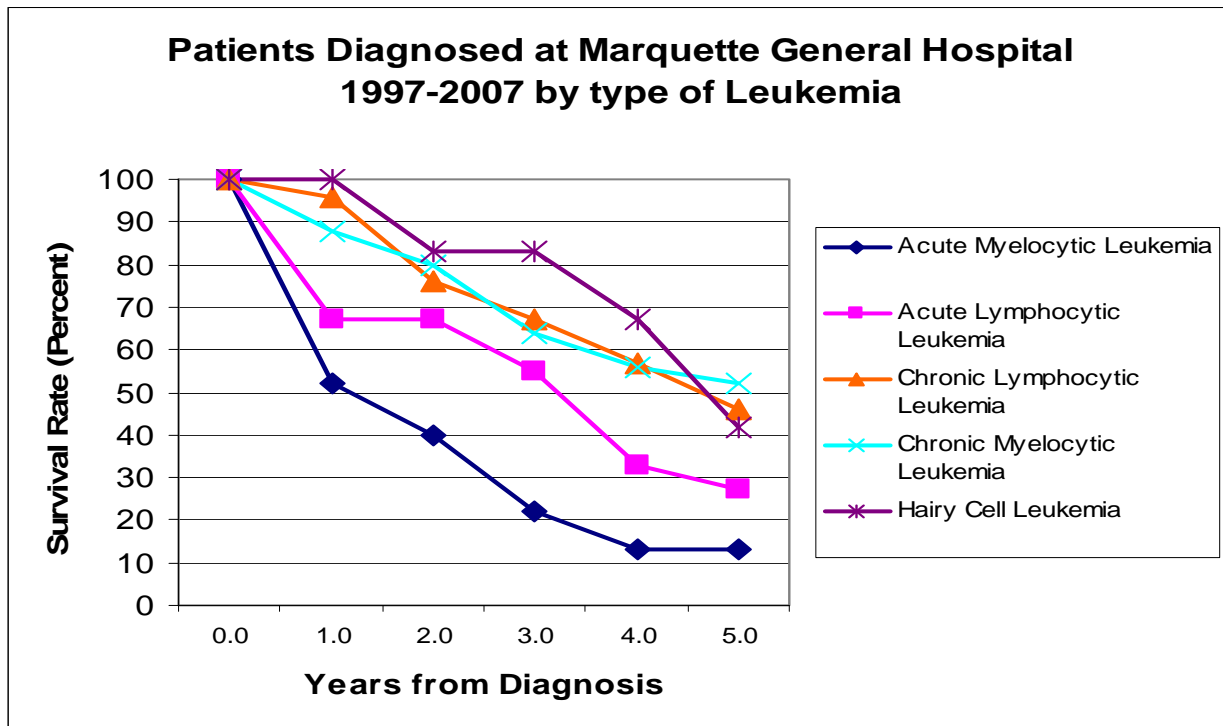
The cause of most leukemias is not known. Some patients have a family history of leukemia or other cancers and perhaps have some genetic instability that makes them more susceptible to the development of leukemia. Some patients may have been exposed to radiation and/or chemotherapy for treatment of prior conditions. Table 5 shows that 36 of the 219 total cases presented in this review (16.4%) have history of previous cancer, but only 1.8% were known to have received chemotherapy or radiation therapy or both for a prior diagnosis. 16 patients (7.3% of the total) had a family history of some type of leukemia and 50.5% of patients in this review had a family history of some type of cancer (which may not be significantly greater than that expected in this general population).

<b>Cancer History of Patients &amp; Family 1997 – 2007 219 Total Cases</b>	
<b>Patients with History of Other Cancer Type with Treatment given for 1<sup>st</sup> Cancer diagnosis (16.4% of Total Patients diagnosed (36 patients) with History of Previous Cancer)</b>	
<b>Type &amp; Treatment Given</b>	<b>% of Total Patients Diagnosed with Previous Malignancy</b>
<b>Leukemia</b> – Unknown Treatment	5.5%
<b>Hodgkins</b> – No treatment	2.8%
<b>Breast</b> – Radiation received	5.5%
Radiation, Chemo, Hormone	2.8%
Unknown treatment	2.8%
<b>Skin</b> – Unknown treatment	8.3%
<b>Female Gynecologic Sites</b> – Unknown treatment	8.3%
<b>Prostate</b> – Surgery only	2.8%
Radiation only	8.3%
Unknown treatment	11.1%
<b>Lip</b> – Surgery only	5.5%
<b>Bladder</b> – Unknown treatment	2.8%
<b>Ovary</b> – Unknown treatment	2.8%
<b>Lymphoma</b> – Chemo received	5.5%
<b>Male Genital</b> – Unknown treatment	2.8%
Surgery, Chemo	2.8%
<b>Lung</b> – Surgery only	2.8%
<b>Rectal</b> – Surgery only	5.5%
<b>Larynx</b> – Unknown treatment	2.8%
<b>Bone, Joints &amp; Cartilage</b> – Unknown treatment	2.8%
<b>Colon</b> – Surgery only	5.5%
<b>All patients known to have received Chemotherapy, Radiation or both for prior Cancer diagnosis</b>	1.8%

Patients with Family History of Leukemia (Histology Type Unknown) (16 pts – 7.3% of total patients diagnosed with Leukemia)	<i>Relative</i>	% of Total Pts. With Family History of Leukemia	Patients with Family History of other Cancer (58.5 % of Total number of patients diagnosed with Leukemia)	<i>Relative</i>	% of Pts with Family History of Other Cancer Type
	Mother	12.5%		Mother	14.2%
	Father	6.0%		Father	11.4%
	Sister	6.0%		Sister	8.2%
	Brother	18.8%		Brother	9.1%
				Daughter	2.3%
	Uncle	18.8%		Aunt	2.7%
	Cousin	6.0%		Uncle	1.0%
Unknown Relative	18.8%	Grandparent	4.1%		
		Unknown Relative	5.5%		
		No Family History of Cancer	41.5%		

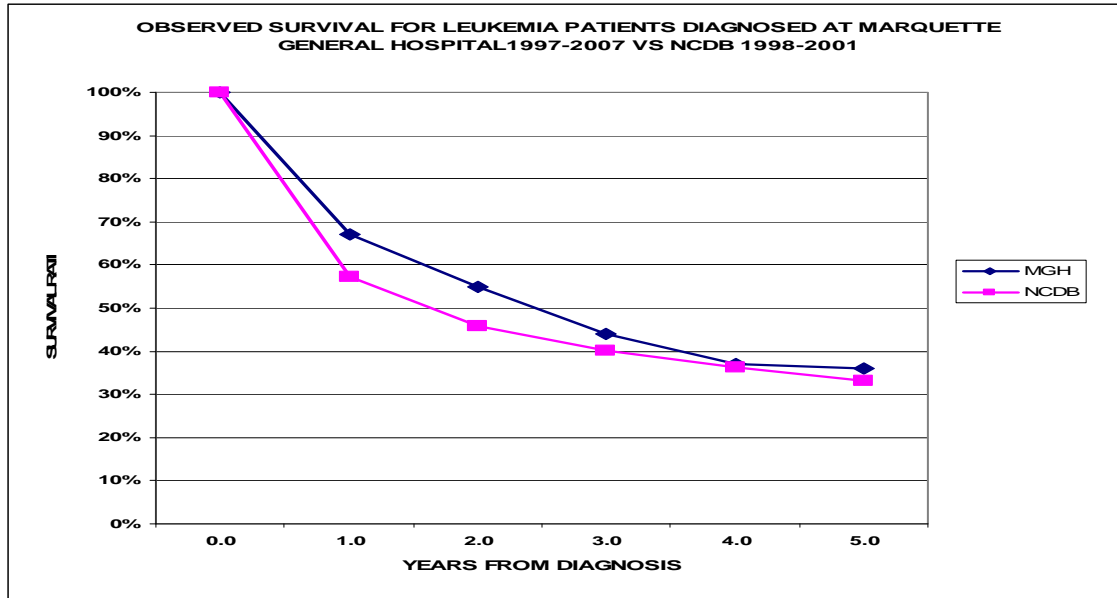
Table 8.

Graph 6 shows the survival of all five of the leukemia types discussed. The combined outcome of all the leukemia patients is also shown as compared to the national cancer database leukemia outcomes for 1990 – 2001. Unfortunately the national cancer database does not break down it's leukemia statistics into the various types of leukemia as we have done with our data, nor does the National Cancer Institute sponsored SEER database nor the State of Michigan cancer registry database.



Graph 6.

Compared to the National Cancer Database (NCDB) our leukemia patients at Marquette General Cancer Center (MGH) are doing quite well with a 2 year survival rate of 55% (NCDA = 45.8%) and a 5 year survival of 36% (NCDB = 33.2%).



Graph 6a. – *To make a comparison, MGH survival data for the year 1997 to 2007 was obtained and compared to NCDB data for the same period.*

The treatment of leukemia is an evolving field and continues to give us hope for improved results. Diagnosis and treatment of leukemia is a cooperative effort between the hematologists, medical oncologists, pathologists, infectious disease specialists and the various other medical and surgical specialists and the diagnostic specialists such as the radiologists who work together to support our patients. The institutional affiliation of the Marquette General Cancer Center with the Karmanos Cancer Institute at Wayne State University in Detroit is especially productive in the field of hemotologic malignancy such as leukemia. Because stem cell (bone marrow) transplantation is such an important part of these treatments, we work closely with the hematology specialists and transplant specialists to generate a plan of action that allows us to consider multiple alternatives.

The greatest thanks of all, however, must go to the nursing staff of the Marquette General Cancer Center Oncology Unit and the U.P. Hematology Oncology Associates offices. Without their caring, skills and diligence we could not have our successes.

Submitted and written by: Aaron P. Scholnik, MD, FACP