MULTIPLE MYELOMA TREATMENT: A POPULATION-BASED STUDY ON SURVIVAL RATE IN USA FOR YEAR 2014-2019

Dissertation Submitted to

The IIHMR University, Jaipur

for the partial fulfillment for the award of the degree of

Master of Business Administration (MBA)

in

Hospital and Health Management

By

Dr Mahek Jain

Under the supervision and Guidance of

Dr Sheenu Jain

2022

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DECLARATION BY STUDENT

I hereby declare that this dissertation **Multiple Myeloma Treatment: A Population-Based Study on survival rate in USA for year 2014-2018** is the Bonafide record of my original research work. I declare that it has not been submitted to any other university or institution for the award of any degree or diploma. Information derived from the published or unpublished work of others has been duly acknowledged in the text.

Name: Dr
Mahek Jain

Date:
23/06/2022

CERTIFICATE OF INTERNSHIP

PharmaACE
Analytics Center of Excellence

Date: 30/06/2022

TO WHOMSOEVER IT MAY CONCERN

This is to certify that **Mahek Jain,** student of IIHMR University, Jaipur has completed her internship with **PharmaACE Analytics LLP** during the period of **March 22, 2022 to June 19, 2022.** During her internship she worked with the Advanced Analytics department and has successfully worked on the project; **Multiple Myeloma Treatment: A population Based Study on Survival Rate in USA between year 2014-2019.**

We wish her every success in life.

Gargi Agrawal
Executive – Corporate Communications
PharmaACE

PharmaACE Innovations LLP, Blueridge Qubix, SEZ, IT-5, Ground Floor, Phase 1, Hinjewadi, Pune – 411057
Email: info@pharmaace.com, www.PharmaACE.com

Appendix F: Certificate from Faculty Guide and School Dean

CERTIFICATE

This is to certify that dissertation titled..... is a record of the research work undertaken by (Name of Student) in partial fulfillment of the requirements for the award of the degree of MBA (Hospital and Health Management)/MBA (Pharmaceutical Management)/MBA (Rural Management) from the IIHMR University, Jaipur under my guidance and supervision and his/her approach to the research study has been sincere, scientific, and analytical.

Faculty Guide
IIHMR University, Jaipur

Date

School Dean
IIHMR University, Jaipur

Date

ABSTRACT

Treatment options in multiple myeloma (MM) are increasing with the introduction of complex multi-novel-agent-based regimens investigated in randomized clinical trials. However, application in the real-world setting, including feasibility of and adherence to these regimens, may be limited due to varying patient-, treatment-, and disease-related factors. Therefore, treatment decisions must be tailored based on additional considerations beyond clinical trial efficacy and safety, such as treatment feasibility (including frequency of clinic/hospital attendance), tolerability, effects on quality of life (QoL), and impact of comorbidities. There are multiple factors of importance to real-world MM patients, including disease symptoms, treatment burden and toxicities, ability to participate in daily activities, financial burden, access to treatment and treatment centers, and convenience of treatment. All of these factors are drivers of QoL and treatment satisfaction/compliance which also leads to the increase or decrease in the survival rate of the patients. Importantly, given the heterogeneity of MM, individual patients may have different perspectives regarding the most relevant considerations and goals of their treatment. Patient perspectives/goals may also change as they move through their treatment course. Thus, the 'efficacy' of treatment means different things to different patients, and treatment decision-making in the context of personalized medicine must be guided by an individual's composite definition of what constitutes the best treatment choice. This review summarizes the various factors of importance and practical issues that must be considered when determining real-world treatment choices. The study also shows about the growth in the number of MM patients in the recent years i.e from year 2018-2022. The average new patients and the total new patients. It assesses the current instruments, methodologies, and recent initiatives for analyzing the MM patient experience. Finally, it suggests options for enhancing data collection on patients and treatments to provide a more holistic definition of the effectiveness of a regimen in the real-world setting by showing example of drug Kyprolis manufactured by Amgen. We can conclude that with the advancement in therapies we can seen improvement in the overall survival rate over years. The 5-year survival rate has also increased in the recent years.

Multiple Myeloma (MM), Treatment, Quality of Life (QoL), Efficacy, Survival Rate, New Patients, Total Patients

ACKNOWLEDGEMENT

I owe a great debt to all professionals at **PharmaACE Analytics Pvt Ltd, Pune India** for efficiently sharing their knowledge and time, which encouraged me to do best in this project report.

My sincere gratitude to **Mr. Anubrato Mitra** (Senior Consultant- Advanced Analytics), for showing his keen interest in the study and for sharing their opinions in the face of his very busy schedule. It has been my privilege to work under their zestful supervision.

I am extremely thankful to **Ms. Gargi Agrawal** (HR Manager) for the constant support and encouragement. This study would not have been possible without her support.

I express my warm veneration towards my mentor **Dr. Sheenu Jain** for her valuable guidance throughout the entire course of study to its completion.

I would like to express my heartless thanks to my parents for their moral support, which always motivates me to preform my best. And finally credit goes to all my friends, colleagues who helped me out in this study.

Sincerely,

Dr. Mahek Jain

HHM Batch 2020-2022

(IIHMR University, Jaipur)

TABLE OF CONTENTS

LIST OF FIGURES

LIST OF TABLES

ABBREVIATIONS

MM- Multiple Myeloma

QoL- Quality of life

CNS- Central Nervous System

OS- Overall Survival

PFS- Progression Free Survival

SMM- Smoldering Multiple Myeloma

IV- Intra Venous

FDA- Food and Drug Administration

RSR- Relative Survival Rate

CHAPTER

1. INTRODUCTION:

1.1 About Organization

PharmaACE is a US-headquartered life sciences focused company with offices across the globe including Germany, Canada and India. The company provides consulting and data analytics solutions for the efficient commercialization and development of pharmaceutical/portfolio. PharmaACE operates at the intersection of science, data, technology and business strategy. They have selective and elite client base which includes established, multinational bio-pharmaceutical leaders and innovators, as well as entrepreneurial firms on the cutting edge of science. Their expertise spans across multiple therapy areas: Oncology, Immuno-science, CNS, Cardiovascular and Metabolic diseases, Rare Diseases and many others.

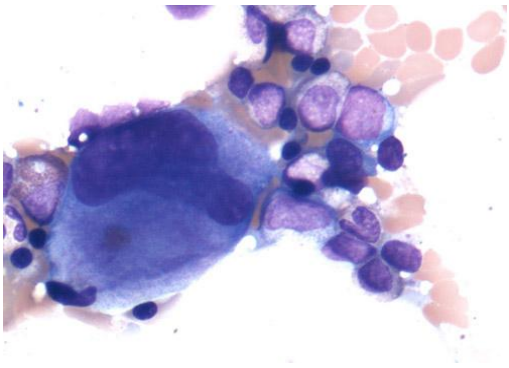
1.2 About Disease Area

Myeloma is a cancer of blood in which cells found in the bone marrow, specifically the so-called “plasma cells.” The bone marrow is the spongy tissue inside your bones that normally creates the different parts of your blood. Plasma cells are a key part of the . They produce antibodies that help the body fight infection. Myeloma begins when active plasma cells change and grow out of control. This may result in multiple bone lesions that increase the risk of bone fractures. That is where the phrase "multiple myeloma" comes from.

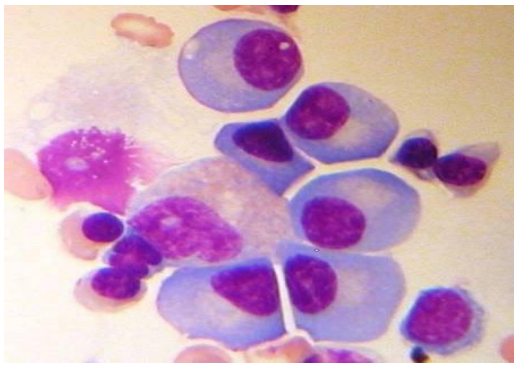
Multiple Myeloma is a cancer of plasma cells. The plasma cells are a type of white blood cell in the bone marrow. With this condition, a group of plasma cells becomes cancerous and multiplies. The disease can damage the bones, immune system, kidneys and red blood cell count. Myeloma causes structural bone damage, which can result in weakened bones and leads to painful fractures or bone breaks over time. Myeloma is usually called multiple myeloma because most people (90% or more) have more than 1 bone lesion when they are diagnosed or lesions develop over the course of the illness. Solitary plasmacytoma is a mass, or tumor, of myeloma cells that involves only 1 site in the bone or, less commonly, in other organs, such as those in the upper respiratory tract, including the nose and throat, or the gastrointestinal system.

Extramedullary plasmacytoma describes myeloma that started outside the bone marrow in locations such as the lymph glands, sinuses, throat, liver, digestive tract, or under the skin.

Figure 1.1



Normal Bone Marrow



Multiple Myeloma

Symptoms may not be present or may be non-specific such as loss of appetite, bone pain and fever. Treatments include medication, chemotherapy, corticosteroids, radiation or a stem-cell transplant.

Multiple Myeloma Features:

- Low blood counts
- Bone and Calcium problems
- Infections
- Kidney Problems

Multiple myeloma is a relatively uncommon cancer. In the United States, the lifetime risk of getting multiple myeloma is 1 in 132 (0.76%).

The American Cancer Society's estimates for multiple myeloma in the United States for 2022 are:

- About 34,470 new cases will be diagnosed (19,100 in men and 15,370 in women).
- About 12,640 deaths are expected to occur (7,090 in men and 5,550 in women).

Our study has several strengths, including the large population-based design with high-quality data.

1.3 Purpose of research

The incidence of multiple myeloma (MM) is rising and there are fewer studies; a comprehensive research of MM patients' survival data in a real-world population is needed. This study aims to analyze the survival status of MM patients in USA. This is a detailed study on Multiple Myeloma. This study will revolve around the various treatment options/therapies available for MM in USA. We will also study about the growth in MM patient volume in the recent years i.e between year 2018-2022. The purpose of this research is to study the MM market in the USA considering the treatment options, 5-year survival rate of patients and the MM patient volume growth rate (i.e average new patients and the total patients).

The availability of new medications has given new hope for better treatments and better results and thus affecting the growth of the market as well. However, the survival of patients with a limited response while receiving treatment with primary immunodeficiency therapy remains poor and is one of the major challenges.

1.4 Aims:

The aim of the study is to highlight the MM market in USA considering the treatments options, growth rate and 5-year relative survival rate of rare disease like Multiple Myeloma.

1.5 Objectives:

- To study the various treatment options available for management of Multiple Myeloma in USA.

- To study the 5-year survival rate of Multiple Myeloma in USA between year 2015-2019
- To study the growth rate in patient volume of Multiple Myeloma cases in USA in the recent years i.e 2018-2022
- To study the number of patients opting for drug Kyprolis between year 2018-2022 when compared with other drug regimens.

CHAPTER 2

2.LITERATURE REVIEW:

In cancer care, different types of doctors often work together to create a patient's overall treatment plan that combines different types of treatments. This is called a multidisciplinary team . Cancer care teams also include a variety of other health care professionals, including physician assistants, nurse practitioners, oncology nurses, oncology social workers, pharmacists, counselors, dietitians, and others.

The treatment of multiple myeloma depends on whether the patient is experiencing symptoms and the patient's overall health. In many cases, a team of doctors will work with the patient to determine the best treatment plan. The goals of treatment are to eliminate myeloma cells, control tumor growth, control pain, and allow patients to have an active life. While there is no cure for multiple myeloma, the cancer can be managed successfully in many patients for years.

Treatment overview

People with early-stage myeloma and no symptoms, called **smoldering multiple myeloma or SMM** may simply be closely monitored by the doctor through checkups. This approach is called active surveillance or watchful waiting. As noted previously, if there is evidence of bone thinning, or osteoporosis, periodic infusions of bisphosphonates to reverse this process may be recommended. There are also clinical protocols, or processes, used to evaluate whether using medications called **targeted therapy or immunotherapy** can prevent or delay myeloma from developing into a disease that requires treatment. If symptoms appear, then active treatment

starts. Two clinical trials in high-risk SMM have shown that early treatment can slow the progression to myeloma with symptoms for some patients, but whether this helps people live longer is not known.

Treatment overview for patients with symptoms

Treatment for people with symptomatic myeloma includes both treatment to control the disease as well as supportive care to improve quality of life, such as by relieving symptoms and maintaining good nutrition. Disease-directed treatment typically includes therapy using medications, such as targeted therapy and/or chemotherapy, with or without steroids. Bone marrow/stem cell transplantation may be an option. Other types of treatments, such as radiation therapy and surgery, are used in specific circumstances. Each type of treatment is described below.

The treatment plan includes different phases:

- **Induction therapy** for rapid control of cancer and to help relieve symptoms.
- **Consolidation** with more chemotherapy or a bone marrow/stem cell transplant.
- **Maintenance therapy** over a prolonged period to prevent cancer recurrence.

Therapies using medications

Treatments using medication are used to destroy cancer cells. Medication may be given through the bloodstream to reach cancer cells throughout the body. When a drug is given this way, it is called systemic therapy. Medication may also be given locally, which is when the medication is applied directly to the cancer or kept in a single part of the body.

This type of medication is generally prescribed by a medical oncologist, a doctor who specializes in treating cancer with medication.

Medications are often given through an intravenous (IV) tube placed into a vein using a needle or as a pill or capsule that is swallowed (orally). If you are given oral medications, be sure to ask your health care team about how to safely store and handle it.

The types of medications used for multiple myeloma include:

- Chemotherapy
- Targeted therapy
- Immunomodulatory drugs
- Steroids
- Bone-modifying drugs
- Immunotherapy

A person usually receives a combination of medications given at the same time. They can also be given as part of a treatment plan that includes surgery and/or radiation therapy. Combination regimens are an important part of the treatment of multiple myeloma. Combining different treatment effects from different types of drugs—such as a combination of an immunomodulatory drug, a proteasome inhibitor, and a steroid—can be an effective way of managing the disease. In addition, other targeted treatments may be added, depending on the individual's specific situation.

Chemotherapy

Chemotherapy is the use of drugs to destroy cancer cells, usually by keeping the cancer cells from growing, dividing, and making more cells.

A chemotherapy regimen, or schedule, usually consists of a specific number of cycles given over a set period of time. A patient usually receives combinations of different drugs at the same time.

Combination chemotherapy has been used successfully for the treatment of myeloma. These drugs include cyclophosphamide (available as a generic drug), doxorubicin (available as a generic drug), melphalan (Alkeran, Evomela), etoposide (available as a generic drug), cisplatin (available as a generic drug), carmustine, and bendamustine (Bendeka). Chemotherapy drugs like these may be used in certain situations. For example, melphalan is most commonly used when a bone marrow transplantation is part of the treatment plan. A high dose of melphalan is used to

suppress the myeloma for a long time, and the patient's own bone marrow cells are used to recover from this treatment.

It may also be recommended to combine chemotherapy with other types of treatment, including targeted therapies or steroids. For instance, the combination of melphalan, the steroid prednisone (multiple brand names), and a targeted therapy called bortezomib (Velcade) is approved by the U.S. Food and Drug Administration (FDA) for the initial treatment of multiple myeloma. This is because this combination often helps people live longer when compared with the combination of melphalan and prednisone. A targeted version of melphalan called melphalan flufenamide (Pepaxto) combined with dexamethasone may be used to treat multiple myeloma that has not been stopped by 4 or more previous treatments.

The side effects of chemotherapy depend on the individual and the dose used, but they can include fatigue, risk of infection, nausea and vomiting, hair loss, loss of appetite, and diarrhea or constipation. Other side effects include peripheral neuropathy (tingling or numbness in feet or hands), blood clotting problems, and low blood counts. These side effects usually go away once treatment is finished. Occasionally an allergic reaction such as skin rash may occur and the drug may have to be stopped.
The length of chemotherapy treatment varies from patient to patient and is usually given until the myeloma is well controlled.

Targeted therapy

Targeted therapy is a treatment that targets the cancer's specific genes, proteins, or the tissue environment that contributes to cancer growth and survival. This type of treatment blocks the growth and spread of cancer cells and limits damage to healthy cells. In recent years, targeted treatment, sometimes called novel therapy, has proven to be increasingly successful at controlling myeloma and improving prognosis. Researchers continue to investigate new and evolving drugs for this disease in clinical trials.

Not all tumors have the same targets. To find the most effective treatment, your doctor may run tests on cancer cells to identify genes, proteins, and other factors. This helps doctors better match each patient with the most effective treatment whenever possible. In addition, research studies

continue to find out more about specific molecular targets and new treatments directed at them. Learn more about the basics of **targeted treatments**.

Targeted therapy for multiple myeloma includes:

- **Proteasome inhibitors.** Bortezomib (Velcade), carfilzomib (Kyprolis), and ixazomib (Ninlaro) are classified as proteasome inhibitors. They target specific enzymes called proteasomes that digest proteins in the cells. Because myeloma cells produce a lot of proteins , they are particularly vulnerable to this type of drug. These drugs may be used to treat newly diagnosed myeloma and recurrent myeloma.
- **Histone deacetylase inhibitors.** Panobinostat (Farydak), an inhibitor of the enzyme histone deacetylase (HDAC), also treats recurrent myeloma. HDACs help keep the DNA tightly coiled, while panobinostat helps uncoil the DNA and activate genes that stop or slow the growth of cancer cells.
- **Monoclonal antibodies** Elotuzumab (Empliciti) and daratumumab (Darzalex) are monoclonal antibodies that bind to myeloma cells and label them for removal by the person's own immune system. Daratumumab may be given to treat newly diagnosed multiple myeloma. A drug combination of daratumumab and hyaluronidase-fihj (Darzalex Faspro) with or without pomalidomide (Pomalyst) and dexamethasone (multiple brand names) may also be used to treat multiple myeloma. This combination is given under the skin of the abdomen and is quicker than when it is given by injection through a vein. Daratumumab with or without hyaluronidase-fihj combined with carfilzomib and dexamethasone may be used to treat multiple myeloma that has stopped responding to 1 to 3 previous treatments. Isatuximab-irfc (Sarclisa) is a monoclonal antibody approved by the FDA for the treatment of adults with multiple myeloma who have received 1 to 3 previous treatments. Isatuximab-irfc may be given in combination with pomalidomide and dexamethasone or carfilzomib and dexamethasone.
- **Nuclear export inhibitors.** Selinexor (Xpovio) is a targeted therapy that is given in combination with dexamethasone, a steroid available as a generic drug. This combination is used to treat adults with multiple myeloma that has come back

after 4 or more previous treatments. It may also be given in combination with bortezomib and dexamethasone to people who have received at least 1 previous treatment.

- **B-cell maturation antigen (BCMA) targeting agent.** Belantamab mafodotin-blmf (Blenrep) is an antibody-drug conjugate approved by the FDA to treat adults with recurrent or refractory multiple myeloma who have received at least 4 previous treatments. Belantamab mafodotin-blmf uses an antibody to bind to BCMA and delivers chemotherapy to the myeloma cell. BCMA is a protein on the surface of myeloma cells.

Targeted therapies may also be used in combination with chemotherapy, immunomodulatory drugs, or steroid medications , because certain combinations of drugs can sometimes have a better effect than a single drug. For example, the drugs lenalidomide, bortezomib, and dexamethasone, as well as bortezomib, cyclophosphamide, and dexamethasone, are offered in combination as initial treatment. Clinical trials are exploring whether the combination of lenalidomide, bortezomib, and dexamethasone may be as effective as lenalidomide, bortezomib, and dexamethasone followed by a bone marrow/stem cell transplant .

Thalidomide (Synovir, Thalomid), lenalidomide, and bortezomib can also be effectively used as maintenance therapy to extend the disease's response to the initial therapy or after a bone marrow/stem cell transplant. However, the decision to undergo a transplant is complex and should be discussed carefully with your doctor.

Research has shown that maintenance therapy with lenalidomide and/or bortezomib increases how long patients survive and extends how long they live without active myeloma. Maintenance therapy has to be used with some caution, although recent studies have shown significant improvement with survival using this approach. therapy has to be used with some caution, although recent studies have shown significant improvement with survival using this approach.

Immunomodulatory drugs

Thalidomide, lenalidomide (Revlimid), and pomalidomide (Pomalyst) are classified as immunomodulatory drugs, which stimulate the immune system. These drugs also keep new blood vessels from forming and feeding myeloma cells. Thalidomide and lenalidomide are

approved to treat newly diagnosed patients. Lenalidomide and pomalidomide are also effective for treating recurrent myeloma.

Steroids

Steroids, such as prednisone and dexamethasone, may be given alone or at the same time as other drug therapy, such as with targeted therapy or chemotherapy (see above). Steroids are very effective at reducing the burden of plasma cells, but this effect is only temporary.

For example, lenalidomide and dexamethasone as induction and maintenance therapy is recommended for those who are not able to have bone marrow/stem cell transplantation. Adding bortezomib to this combination has recently been shown to be effective in a clinical trial.

Bone-modifying drugs

Most people with myeloma receive treatment with bone-modifying drugs. These drugs help strengthen the bone and reduce bone pain and the risk of fractures.

There are 2 types of bone-modifying drugs available for treating bone loss from multiple myeloma. The choice of drugs depends on your overall health and your individual risk of side effects.

- Bisphosphonates, such as zoledronic acid (Zometa) and pamidronate (Aredia), block the cells that dissolve bone, called osteoclasts. For multiple myeloma, either pamidronate or zoledronic acid is given by IV every 3 to 4 weeks. Each treatment of pamidronate lasts at least 2 hours, and each treatment of zoledronic acid lasts at least 15 minutes. Patients with existing severe kidney problems usually receive lower doses of pamidronate given over a longer time (such as 4 to 6 hours instead of 2 hours). Zoledronic acid is generally not recommended for people with severe kidney problems.

- Denosumab (Xgeva) is an osteoclast-targeted therapy called a RANK ligand inhibitor. It is approved to treat multiple myeloma and may be a better option for people with severe kidney problems. Denosumab can be more expensive than

bisphosphonates. It has been shown to have similar effectiveness to bisphosphonates.

Treatment with a bone-modifying drug is recommended for up to 2 years. At 2 years, treatment may be stopped if it is working. If the myeloma comes back and new bone problems develop, treatment with a bone-modifying drug is usually started again. Talk with your doctor for more information about stopping and restarting treatment with these drugs.

Side effects of bisphosphonates may include flu-like symptoms, anemia, joint and muscle pain, and kidney problems. If you are taking pamidronate or zoledronic acid, you should have a blood test to check how well the kidneys are working before each time you receive the drug. Side effects of denosumab may include diarrhea, nausea, anemia, and back pain.

Osteonecrosis of the jaw is an uncommon but potentially serious side effect of both types of bone-modifying drugs. The symptoms may include pain, swelling, and infection of the jaw; loose teeth; and exposed bone. Before treatment, patients should receive a thorough dental examination, and any tooth or mouth infections should be treated. While receiving treatment with a bone-modifying drug, patients should avoid having any invasive dental work done, such as dental surgery. Take care of your teeth, gums, and tongue with regular brushing and flossing.

Immunotherapy

Immunotherapy, also called biologic therapy, is designed to boost the body's natural defenses to fight the cancer. It uses materials made either by the body or in a laboratory to improve, target, or restore immune system function.

The cellular immunotherapies approved to treat multiple myeloma are idecabtagene vicleucel (Abecma) and ciltacabtagene autoleucel (Carvykti). These are chimeric antigen receptor (CAR) T-cell therapies that target BCMA (see "Targeted therapy," above). They may be used to treat multiple myeloma that has not been stopped by 4 or more treatments.

In CAR T-cell therapy, some cells are removed from a patient’s blood. Then, the T cells are changed in a laboratory so they have specific proteins called receptors. These receptors allow the changed T cells to recognize the cancer cells. In the case of idecabtagene vicleucel and ciltacabtagene autoleucel, the cells recognize a protein called BCMA on the myeloma cells. The

changed T cells are grown in large numbers in the laboratory and returned to the patient's body. Once there, they seek out and destroy cancer cells.

Different types of immunotherapies can cause different side effects. Common side effects include skin reactions, flu-like symptoms, diarrhea, and weight changes. Talk with your doctor about possible side effects for the immunotherapy recommended for you. Learn more about the basics of immunotherapy.

Bone marrow/stem cell transplantation

A bone marrow transplant is a medical procedure in which bone marrow that contains cancer is replaced by highly specialized cells. These cells, called hematopoietic stem cells, develop into healthy red blood cells, white blood cells, and platelets in the bone marrow. Hematopoietic stem cells are blood-forming cells found both in the bloodstream and in the bone marrow. This procedure is also called a stem cell transplant.

Before recommending transplantation, doctors will talk with the patient about the risks of this treatment. They will also consider several other factors, such as the type of cancer, results of any previous treatment, and the patient's age and general health.

There are 2 types of hematopoietic stem cell transplantation depending on the source of the replacement blood stem cells: allogeneic (ALLO) and autologous (AUTO). ALLO uses donated stem cells, while AUTO uses the patient's own stem cells. For multiple myeloma, AUTO is more commonly used. ALLO is being studied in clinical trials. In both types, the goal is to destroy all of the cancer cells in the marrow, blood, and other parts of the body using high doses of chemotherapy (usually melphalan) and then allow replacement blood stem cells to create healthy bone marrow and restore the body's immune response.

Side effects depend on the type of transplant, your general health, and other factors.

Radiation therapy

Radiation therapy is the use of high-energy x-rays or other particles to destroy cancer cells. A doctor who specializes in giving radiation therapy to treat cancer is called a radiation oncologist. The most common type of radiation treatment is called external-beam radiation therapy, which is

radiation given from a machine outside the body. A radiation therapy regimen, or schedule, usually consists of a specific number of treatments given over a set period of time.

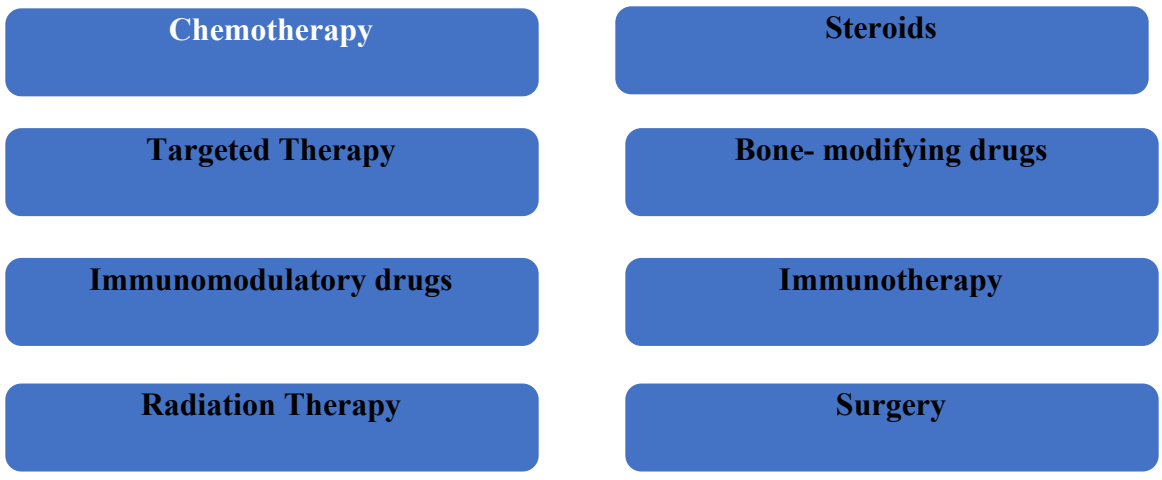
Doctors may recommend radiation therapy for patients with bone pain when chemotherapy is not effective or in order to control pain. However, using radiation therapy is not an easy decision. In many instances, pain (especially back pain) is due to structural damage to the bone. Radiation therapy may not help relieve this type of pain and may affect the bone marrow's response to future treatment.

Side effects of radiation therapy may include fatigue, mild skin reactions, upset stomach, and loose bowel movements. Most side effects go away soon after treatment is finished.

Surgery

Surgery is not usually a disease-directed treatment option for multiple myeloma, but it may be used to relieve specific symptoms (see below). Surgery is used to treat bone disease, especially if there are fractures, and recent plasmacytomas, especially if they occur outside the bone. If surgery is recommended for you, talk with your health care team about the details of the surgery, including the recovery period.

Figure 2.1 Treatment options for Multiple Myeloma:



Multiple myeloma (MM) is generally considered an incurable disease. In recent decades, new treatment alternatives have changed both the clinical course of the disease and improved

survival. Subsequently, clinical trials have shown that using novel agents as first-line treatment can further improve survival in MM. Real-world data, such as population-based studies, are very important tools to evaluate this, since the included participants in clinical trials, for the most part, are generally not representative of the whole MM patient group, which compromises their generalizability. A **relativ survival rate** compares people with the same type and stage of cancer to people in the overall population. For example, if the **5-yea relative survival rate** for a specific stage of multiple myeloma is 60%, it means that people who have that cancer are, on average, about 60% as likely as people who don't have that cancer to live for at least 5 years after being diagnosed.

Table 2.1 Literature Review

S. No	Authors	Study Location	Sample Size	Sampling Technique	Salient Features
1.	Shaji K. Kumar, S. Vincent Rajkumar, Angela Dispenzieri, Martha Q. Lacy, Suzanne R. Hayman, Francis K. Buadi, Steven R. Zeldenrust, David Dingli, Stephen J. Russell,	USA	387 Patients 2981 Patients	Convenience Sampling	In conclusion we demonstrate a clear-cut improvement in the outcome of patient with myeloma in last decade. In our study we believe that HDT and supportive care were responsible for the trends along with the novel drugs contributed to the striking improvement. Analysis of the survival trends among the patients with newly diagnosed MM in a large cohort of patients demonstrate a significant

	John A. Lust, Philip R. Greipp, Robert A. Kyle, Morie A. Gertz March 2008				improvement in survival during the last decade compared the previous two decades.
2.	Sigrun Thorsteinsdottir, Paul Dickman, Ola Landgren, Ingemar Turesson, Magnus Björkholm, and Sigurdur Y. Kristinsson. 2019	Sweden	21,502	Population Based Study, Convenience Sampling	Survival in MM diagnosed patients was found to be improved over time in all age groups. We believe this progress is due to the revolutionary change in the therapeutic arsenal and supportive care in MM. Limitations of the study herein include lack of clinical data for individual patients including clinical stage of disease or the treatment each patient receive. This

					could improve to lead time bias if MM is detected at an earlier stage.
3.	Andrew J. Cowman. Damian J. Green. Mary Kwok; et al Feb 2022	USA	34,920	Convenience Sampling	Approximately 34,920 people in the US and 156888 people worldwide are diagnosed with Multiple Myeloma each year. Induction therapy with an injectable protease inhibitor or an oral immunomodulator are standard care for eligible patients.
4.	Terpos, E., Mikhael, J., Hajek, R. *et al* *Blood Cancer J.* **11,** 40 (2021).	USA		Population Based Study	It is important to emphasize that selection of treatment options requires a review of individual patient's characteristics along with careful understanding of the difference between efficacy and effectiveness, and open honest communication with patients to appropriately define their

					preferences. A broader scope of additional endpoints and patient related factors must be considered due to their critical impact on the effectiveness of the treatment in the real world.
5.	María-Victoria Mateos, Jesús F. San Miguel, *Hematology Am Soc Hematol Educ Program* (2017) 2017 (1): 498–507.	USA		Convenience Sampling Descriptive Study	The optimal treatment approach for young and elderly newly diagnosed MM patients should provide a good balance of efficacy and safety against costs. The novel agent-based combinations producing deeper and longer remissions. The use of optimized tools to monitor our patients alongside the development of new drugs will help us offer our patients a personalized and optimized treatment in

					the future.
6.	Hemminki, K., Försti, A. & Hansson, *Sci* *Rep* 11, 17272 (2021)	Sweden	91,444	Systematic Sampling	Progress in cancer control is measured by improvements in survival but to properly interpret this measure it is important and to do it in context of the other related epidemiological measures of incidence and mortality. Limitations of the study are that we have no individual data on such factors or treatment. The challenges in MM care are old patients and patients at any stage beyond year 1 and after diagnosis including those with refractory disease and co-morbidities.
7.	Gulla A, Anderson KC. *Hematologica l.* 2020;105(10): 2358-2367.	USA	32,020	Convenience Sampling	Over the past decades a deeper understanding of the complex of MM pathobiology has informed drug development and clinical

	Published 2020 Oct 1. 10.3324/Hematol. 2020.247015				practice resulting in significant improvements in patient outcome. Ultimately the future use of novel targeted and immune therapies will be defined by vulnerability within individual patients.

CHAPTER 3

3. METHODOLOGY:

The study was conducted between March 21 to June 1, 2022, in which we studied in detail about the Multiple Myeloma, various therapies available for its treatment and the survival rate of Multiple Myeloma in US population.

3.1 Research Question:

- What is the growth rate of MM patient volume and 5-year survival rate of patients diagnosed with Multiple Myeloma undergoing treatment in USA?

3.2 Research Design:

A population-based study was conducted to analyze the extent of survival rate of patients over a period in USA. Real-time data recorded for Multiple Myeloma patients has been used in the survival rate study.

3.3 Study type- The study done is of descriptive type in which we are referring to the real-time data to have better correlation between the findings and the results.

3.4 Study area- The study area chosen is USA as USA have an emerging market for Multiple Myeloma and patient data available is more reliable than other countries.

3.5 Study Period- Study is done between 21st March 2022 to 19th June 2022 during which we studied about the Multiple Myeloma in detail.

3.6 Sample Technique- The sampling technique is Convenience Sampling. Although secondary data, you calculate the needed sample, and if the available data meet the minimum required by power calculation, then you are fine. To do power analysis to estimate your sample size, you must write your hypothesis, and based on that you decide what statistical test you will use.

3.7 Data Type- The data gathered is through Secondary Research (procurement of data from datasets)

3.8 Study Respondents- The participants of the study do not belong to any specific age group. All age groups have been included in the study.

Inclusion Criteria: Patients diagnosed with MM in USA or undergoing treatment for MM in USA.

Exclusion Criteria: Does not include the patient diagnosed with cancer other than MM or patients who have recently died of MM in USA.

3.9 Objectives:

- To study the survival rate of people diagnosed with Multiple Myeloma undergoing treatment is USA between year 2017-2021.
- To study various therapies used in the management of Multiple Myeloma.
- To study the growth rate in MM Patient volume between year 2018-2022.

3.10 Data Analysis Plan:

- The research will be conducted to study the survival rate and growth in volume of patients (average new patients and total new patients) diagnosed with multiple myeloma in USA and analysis of data gathered will be done using the excel for better interpretation and results.

- It is a quantitative analysis in which for survival rate study we will be using the SEER data 2015-2019 and to study the growth in MM patient volume we will be extracting data using SQL from dataset depository.
- Data will be gathered through different data sets available in dataset depository naming IQVIA data, EDM and Intrinsiq data.
- The data will be extracted using the SQL tool.
- The analysis of data will be done using the excel.

DATASETS

The following datasets have been used for the research purpose:

Figure 3.1 Datasets:

3.11 Ethical Considerations:

- Informed consent must be taken from study participants. Participation in the study was population based.
- All participants were made aware of the purpose of the study.
- Approval was taken from authorized signatory to use the name of the tool in the study.
- Personal data such as name and contact number were not collected from any of the participants. Identity of the participants have been kept anonymous.
- The data used for MM patient volume is confidential and the confidentiality will be kept for client satisfaction.
- The data is not utilized for any other unjustified reason.

- Only the main statistics are being used out of the complete analysis since the data is sensitive.

CHAPTER 4

4. RESULTS AND DISCUSSIONS:

MM treatment utilization was described among the entire newly diagnosed MM population by identifying utilization of novel and non-novel pharmacotherapies. Furthermore, among these newly diagnosed patients who received a MM treatment, patients treated with novel therapies within 1 year of diagnosis showed significantly better survival than those with only non-novel therapies. The survival disparity between MM patients and their matched controls decreased substantially over time. To validate the robustness of the study findings, a subgroup analysis was performed only among newly diagnosed MM patients who received treatment within 1 year after diagnosis.

Statistics At A Glance:

Table 4.1 New Cases

Estimated New Cases in 2022	34,470
% of All New Cancer Cases	1.8%

Table 4.2 Death Rate

Estimated Deaths In 2022	12,640
% of All Cancer Deaths	2.1%

- **Rate of New Cases and Deaths per 100,000:** The rate of new cases of myeloma was 7.1 per 100,000 men and women per year. The death rate was 3.2 per 100,000 men and women per year. These rates are age-adjusted and based on 2015–2019 cases and deaths.

- **Lifetime Risk of Developing Cancer**: Approximately 0.8 percent of men and women will be diagnosed with myeloma at some point during their lifetime, based on 2017–2019 data.

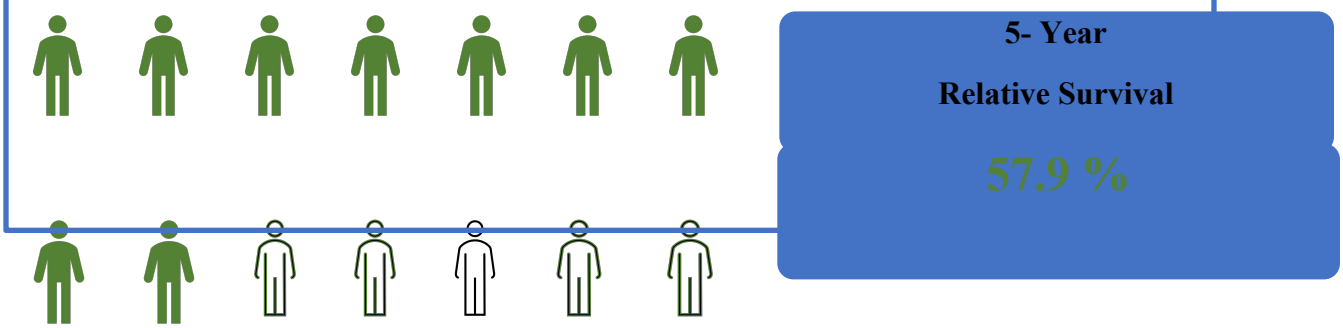
- **Prevalence of This Cancer**: In 2019, there were an estimated 159,787 people living with myeloma in the United States.

Survival Statistics:

1. **How Many People Survive 5 Years Or More after Being Diagnosed with Myeloma?**

Relative survival is an estimate of the percentage of patients who would be expected to survive the effects of their cancer. It excludes the risk of dying from other causes. Because survival statistics are based on large groups of people, they cannot be used to predict exactly what will happen to an individual patient. No two patients are entirely alike, and treatment and responses to treatment can vary greatly.

Figure 4.1 5-Year Relative Survival Rate



- Based on SEER data 2012-2018. White figures represent those who have died of myeloma. Green figures represent those who have survived 5 years or more.

2. **Survival By Stage**

Cancer stage at diagnosis, which refers to extent of a cancer in the body, determines treatment options and has a strong influence on the length of survival. In general, if the

cancer is found only in the part of the body where it started it is *localized* (sometimes referred to as stage 1). If it has spread to a different part of the body, the stage is *regional* or *dista*. For myeloma, 4.1% are diagnosed at the local stage. The 5-year relative survival for localized myeloma is 78.5%.

Percentage of cases & 5-year relative survival by stage at Diagnosis: Myeloma

Table 4.3 Survival Rate by Stage

1.	**Localized** (Confined to primary site)	**4%**
2.	**Regional** (Spread to Regional Lymph nodes)	**0%**
3.	**Distant** (Cancer has metastasized)	**95%**
4.	**Unknown** (Unstaged)	**0%**

Figure 4.2 Percentage of cases by stage

Figure 4.3 Five-Year Relative Survival Rate

3. New Cases and Deaths

How common is this cancer?

Table 4.4 Common Types of Cancer

Common types of cancer	Estimated new cases 2022	Estimated deaths 2022
1. Breast Cancer (Female)	287, 850	43, 250
2. Prostate Cancer	268, 490	34, 500
3. Lung and Bronchus Cancer	236, 490	130, 180
4. Colorectal Cancer	151, 030	52, 580
5. Melanoma of the skin	99, 780	7, 650
6. Bladder Cancer	81, 180	17, 100
7. Non-Hodgkin Lymphoma	80, 470	20,250
8. Kidney and Renal Pelvis Cancer	79, 000	13, 920
9. Uterine Cancer	65, 950	12, 550
10. Pancreatic Cancer	62, 210	49, 830
11. **Myeloma**	**34, 470**	**12, 640**

Figure 4.4 Types of cancer & MM percentage

4. **Who gets this Cancer?**

Although a rare disease, myeloma is more common in men than women and among individuals of African American descent. Risk is higher among those with a history of monoclonal gammopathy of undetermined significance (MGUS). The rate of new cases of myeloma was 7.1 per 100,000 men and women per year based on 2015–2019 cases, age-adjusted.

Percentage of new cases by Age group: Myeloma

Table 4.5 Percentage of new cases

Age	Percentage of new cases
<20	0%
20-34	0.4%
35-40	2.7%
45-54	10.1%
55-64	22.8%
65-74	31.5%
75-84	23.5%
>84	9.0%

Figure 4.5 Percentage of new cases

Median Age at Diagnosis: 69

Inference: Myeloma is most frequently diagnosed among people aged 65-74 years.

Growth in MM Patient Volume between year 2018-2022

Table 4.6 Growth in MM Patient Volume

	Average New Patients	Total New Patients
2018	3,207	27,575
2019	3,306	28,942
2020	3,220	30,262
2021	3,144	30,491
2022	3,182	29,992

Figure 4.6 Graphical Representation of MM Patient Volume

Percentage of deaths by age group: (Table 4.7)

Age	Percentage of Deaths
<20	0%
20-34	0.1%
35-40	0.8%
45-54	4.3%
55-64	14.7%
65-74	28.4%
75-84	32.3%
>84	19.5%

Figure 4.7 Percentage of Deaths by Age

Median Age at Death

75

Inference: The percent of myeloma deaths is highest among people aged 65-74 years.

CHAPTER 5

5. Recommendations:

Keeping track of new cases, deaths, and survival over time (trends) can help scientists understand whether progress is being made and where additional research is needed to address challenges, such as improving screening or finding better treatments.

Using statistical models for analysis, age-adjusted rates for new myeloma cases have been stable over 2010–2019. Age-adjusted death rates have been falling on average 1.0% each year over 2010–2019.

Over the years we have seen advancement in the treatment options for Multiple Myeloma which leads to the better quality of life for patients but on the other hand Multiple Myeloma being a rare disease is complex to understand.

Progress in cancer control is measured by improvements in survival but in order to properly interpret this measure it is important to do it in the context of the other related epidemiological measures of incidence and mortality.

Treatment options should be chosen according to the patient preference so that the patient could respond better for the same.

To study the survival rate and the growth rate gives the better understanding of the Multiple Myeloma market in USA for that time.

MM treatment utilization was described among the entire newly diagnosed MM population by identifying utilization of novel and non-novel pharmacotherapies. Furthermore, among these newly diagnosed patients who received a MM treatment, patients treated with novel therapies within 1 year of diagnosis showed significantly better survival than those with only non-novel therapies. The survival disparity between MM patients and their matched controls decreased substantially over time.

To better study the real-time population data sets are the better options to go ahead with the study as they are updated every week so we can get the accurate and reliable information.

- Extensive research for Multiple Myeloma disease can help in better understanding where the researchers are lacking in developing new and effective therapies.

- A patient should always be preferred to choose its treatment option to properly respond for the same.

- For better research of real-time population, we can refer all these datasets such as EDM, IQVIA and INTRINSIQ as they are updated on weekly basis with all the information.

- All the datasets contain the information collected from the hospital records, claims data, retail and non-retail which are reliable for the research.

- The survival rate and the growth rate help in studying the actual market of the disease multiple myeloma in USA.

- Ideally, discussions around medication value, particularly in oncology, should consider not only medication costs but also other related healthcare costs and outcomes improvement.

- Our analysis quantifies increases in MM treatment-related drug costs alongside a substantial increase in patient survival. Although still present, the survival gap between MM patients and their matched controls shrank considerably over the study period, suggesting that MM patients' life expectancy is close to that of patients with other health problems.

CHAPTER 6

6.Conclusion:

Despite the strength of the real-world data and direct matching, this study had certain general limitations that are associated with such claim based observational studies. First, this study was limited to only those individuals with commercial health coverage or private Medicare supplemental coverage. Consequently, results of this analysis may not be generalizable to patients with other insurance or without health insurance coverage. Second, the identification of MM population relied on diagnosis codes recorded on medical claims and are therefore limited by completeness and accuracy of medical coding.

In conclusion, our large population-based study showed that the survival of Multiple Myeloma patients has been improving dramatically, in particular during the last decade. We believe this progress is due to the revolutionary changes in the therapeutic arsenal and supportive care in MM.

Further efforts are nevertheless needed for the oldest patients, although the impact of newer treatments is spreading to older age groups. Through ongoing research and the introduction of agents with novel mechanisms of action, survival will hopefully continue to improve in the coming years, as we make advances towards changing Multiple Myeloma to a chronic or a curable condition.

However, previous studies have reported variations in survival experience of MM patients by difference races; thereby, it is worthwhile to control this variation in matching. Similarly, this study could not control for MM disease severity, which is unlikely but may have possibly changed over the study period and could impact treatment patterns, costs, and patient survival.

MM treatment utilization was described among the entire newly diagnosed MM population by identifying utilization of novel and non-novel pharmacotherapies. Furthermore, among these

newly diagnosed patients who received a MM treatment, patients treated with novel therapies within 1 year of diagnosis showed significantly better survival than those with only non-novel therapies. The survival disparity between MM patients and their matched controls decreased substantially over time.

The overall 5-year survival rate for people with multiple myeloma in the United States is 55%. For the 4% of people who are diagnosed at an early stage, the 5-year survival rate is over 77%. If the cancer has spread to a distant part of the body, the 5-year survival rate is over 54

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