IJCRT.ORG ISSN : 2320-2882

INTERNATIONAL JOURNAL OF CREATIVE RESEARCH THOUGHTS (IJCRT)

An International Open Access, Peer-reviewed, Refereed Journal

Remidies Of Chronic Myeloid Leukemia Disease

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ABSTRACT

The Philadelphia chromosome and the bcr-abl fusion gene cause aberrant myeloid cell proliferation, which is the hallmark of chronic myeloid leukemia (cml), a Myeloproliferative disease. Patient outcomes have significantly improved over the past 20 years due to considerable breakthroughs in treatment, especially with the development of tyrosine kinase inhibitors (tkis) like Imatinib. Tkis are now the mainstay of cml treatment, allowing 85–95% of patients to survive during the chronic periods while achieving a long-term remission. Patients who do not respond to first-generation tkis are treated with second- and third-generation tkis, such as dasatinib, nilotinib, andponatinib. For individuals who do not react to tkis, stem cell transplantation is still a curative option, albeit with increased risks. Leukapheresis, chemotherapy, and interferon-alpha are further treatments that are generally saved for particular situations or crises. It is essential to regularly assess hematologic, cytogenetic, and molecular responses in order to modify treatment and sustain remission. With improved survival rates and quality of life, cml is no longer a fatal disease for the majority of patients, thanks to treatment advancements.

Keywords -

LEUKEMIA DISEASE, TREATMENT, SYMPTOMS, MONITORING.

INTRODUCTION

One of the essential components of blood, myeloid cells, are overproduced in chronic myeloid leukaemia (cml), a disease that affects the bone marrow and blood. This particular kind of leukaemia advances more slowly than acute variants and is usually linked to a particular genetic mutation called the philadelphia chromosome. This mutation arises from a translocation of chromosomes 9 and 22, which forms the bcr-abl fusion gene and causes myeloid cells to

Proliferate uncontrollably. [2]
Three stages of cml are distinguished: blast crisis, accelerated, and chronic. Tyrosine kinase inhibitors (tkis) and other targeted medicines are commonly used to effectively manage the most stable period of the disease, which is the chronic phase. The illness may worsen and become more aggressive. Phases if left untreated .[3]

Fatigue, nocturnal sweats, inexplicable weight loss, and splenomegaly-an enlargement of the spleen are possible symptoms. Genetic testing, bone marrow biopsy, and blood tests are commonly used in the diagnosis process.

The prognosis for those with cml has generally improved dramatically due to medical advancements, turning the formerly lethal illness into a chronic illness that many patients can now manage

Several epidemiological features associated with chronic myeloid leukaemia (cml) [4]

INCIDENCE : in comparison to other forms of leukaemia, cml is comparatively uncommon. There are one to two cases per 100,000 people on an annual basis. [5]

AGE: adults are the main target population for cml, with most instances occurring in those between the ages of 50 and 70. In kids, it's not common. [5]

GENDER: with a male-to-female ratio of roughly 1.5:1, cml is slightly more frequent in males than in women.

ETHNICITY: although cml can affect people of any ethnicity, some research indicates that incidence rates vary depending on the population, with higher rates seen in particular ethnic groups.

RISK FACTORS: although the precise origin of chronic myeloid leukemia (cml) is unknown, exposure to ionizing radiation and specific chemicals, such as benzene, has been linked to a higher
Additionally, genetic predispositions might be involved.

GEOGRAPHIC VARIABILITY: access to healthcare and environmental factors can have an impact on the occurrence of cml in different geographic regions.
Although cml is still a serious health risk overall, patient outcomes have significantly improved thanks to medical advancements.[5]

OBJECTIVE

The following important aims are part of the core objective of controlling chronic myeloid leukemia (cml): [6]

REACHING REMISSION :- hematologic, cytogenetic, and molecular remission are the main objectives, and they will be attained by minimizing or eliminating the leukemic cells. This entails limiting the bcr-abl gene mutation, lowering the philadelphia chromosome level—a marker of chronic myeloid leukemia—and managing the white blood cell count.

STOPING THE DISEASE'S ADVANCEMENT: cml has the potential to go from a chronic phase into an accelerated phase, also known as a blast crisis, which is more aggressive and challenging to treat. Maintaining the chronic phase and delaying or stopping development are the objectives.

INCREASING SURVIVAL RATES: the goal of treatment is to increase the patient's overall survival and make sure they stay in a stable state for as long as possible. Ideally, this results in atypical lifespan.

REDUCING SIDE EFFECTS: in order to preserve the patient's quality of life, therapies like tyrosine kinase inhibitors (tkis) work to control the disease while reducing harmful side effects.

ESTABLISHING LONG-TERM REMISSION: maintaining long-term illness control is crucial. Some patients may experience deep molecular remission, which allows for the possible reduction or cessation of medication while being closely monitored.

MONITORING AND MANAGING TREATMENT: to keep treatment effective, it is important to continuously monitor the patient's reaction to therapy (via regular blood tests and molecular evaluations). Improving prognoses for cml patients needs early detection and timely, efficacious therapy.

TREATMENTS

Chronic myeloid leukaemia (cml) is typically managed through various methods and treatments that focus on controlling the abnormal growth of white blood cells, achieving remission, and preventing disease progression. Below are the primary methods and treatments used in cml:

1. TYROSINE KINASE INHIBITORS (TKIS)

Tyrosine kinase inhibitors (tkis) are the standard treatment for cml. They target the bcr-abl protein, which is produced by the philadelphia chromosome (a genetic abnormality in cml) and is responsible for uncontrolled cell growth.[7]

- **First-generation tki**:
  imatinib (gleevec): this was the first tki introduced and revolutionized cml treatment. It works by blocking the bcr-abl enzyme.

- **Second-generation tkis**: these are more potent and often used in cases of imatinib resistance or intolerance.
  Dasatinib (sprycel)
  Nilotinib (tasigna)

TKI TYPE	COMMON DRUG NAMES	USES	APPROXIMATE EFFICACY RATE
First generation	Imatinib (gleevec)	First-line therapy for most patients	85-90% long-term survival rate
Second generation	Dasatinib (sprycel), nilotinib (tasigna)	Used in patients resistant/intolerant to imatinib or as frontline treatment	90-95% remission rates
Third generation	Ponatinib (iclusig)	For t315i mutation or multi-drug resistance	70-80% remission in resistant cases

- **Third-generation tki**:
  Ponatinib (iclusig): used in cases where cml is resistant to first- and second-generation tkis, particularly in patients with the t315i mutation.[8]

2. STEM CELL (BONE MARROW) TRANSPLANTATION

Allogeneic stem cell transplantation (sct) is the only known curative treatment for cml, but it carries significant risks and is usually reserved for patients who:[9]

- Do not respond to tkis.
- Progress to an accelerated phase or blast crisis.
- Have a suitable donor available.

It involves replacing the patient's diseased bone marrow with healthy marrow from a donor.[10]

Type of transplant	Usage	Approximate efficacy rate	Key considerations
Allogeneic sct	Reserved for patients resistant to tkis or in advanced phases (accelerated/blast phase)	60-80% long-term survival, depending on disease phase	High risk of complications (gvhd), only curative treatment but not first-line due to risks

3. INTERFERON-ALPHA

Interferon-alpha is an older treatment used prior to tkis but is sometimes still used in specific cases, such as during pregnancy when tkis cannot be used. It works by stimulating the immune system to attack leukemic cells and slow their growth.[11]

- It may be combined with tkis for better control of the disease in some cases.

Type	Usage	Approximate efficacy rate	Key considerations
Interferon-alpha	Used in specific cases (e.g., pregnancy) or intolerance to tkis	15-25% cytogenetic response	Considered outdated, mostly replaced by tkis, side effects include flu-like symptoms

[12]

4. CHEMOTHERAPY

Although not as commonly used as tkis, chemotherapy may be considered in cases where patients do not respond to tki therapy or if the disease progresses to a more aggressive phase (blast crisis).[13]

- Hydroxyurea: this oral chemotherapy drug is sometimes used to temporarily reduce white blood cell counts in patients before initiating tki therapy.
- Cytarabine (ara-c): can be used during the blast crisis phase.[14]

Drug name	Usage	Approximate efficacy rate	Key considerations
Hydroxyurea	Temporary control of high white blood cell counts before tki therapy	Short-term efficacy, used for initial control	Usually a stop-gap therapy, not long-term
Cytarabine (ara-c)	In accelerated/blast phases or in combination with tkis	30-50% remission in blast crisis	High toxicity, used when cml progresses beyond the chronic phase

5. LEUKAPHERESIS

This is a procedure used to rapidly lower very high white blood cell counts (leukostasis), especially in emergency situations before starting tki treatment. Blood is passed through a machine that removes excess white blood cells.[15]

Drug name	Usage	Approximate efficacy rate	Key considerations
Leukapheresis	Used for rapid reduction of high white blood cell counts (leukostasis)	Immediate but temporary effect	Generally used in emergency settings before tki therapy

[16]

6. CLINICAL TRIALS

Participation in clinical trials for new treatments is an option for patients who are not responding well to standard therapies. These trials might involve newer tkis, combination therapies, or immunotherapy approaches.[17]

Trial type	Usage	Approximate efficacy rate	Key considerations
New tkis or combinations	For patients with resistance or intolerances to standard treatments	Varies based on the trial	Patients may benefit from access to new or experimental therapies

7. SYMPTOMS MANAGEMENT AND SUPPORTIVE CARE

In addition to direct treatments for cml, patients may require supportive care to manage symptoms or complications of the disease, including: [18]

- Blood transfusions (if anemia or low platelet counts develop).
- Antibiotics (to manage infections due to immune suppression).
- Growth factors to stimulate blood cell production.[18]

Response type[16]	Monitoring frequency[16]	Treatment adjustment[16]
Hematologic response	Monthly blood counts	Adjust tkis if response is not achieved
Cytogenetic response	Every 3-6 months, bone marrow biopsy	Consider second-line tki or transplant if poor response
Molecular response	Every 3 months, pcr for bcr-abl	Adjust therapy if there is no deep molecular remission

8. MONITORING [19]

Regular monitoring of cml patients is critical to assess treatment response. Monitoring typically involves:

- Hematologic response: measuring blood counts to assess control over white blood cell levels.
- Cytogenetic response: examining bone marrow cells to measure the presence of the philadelphia chromosome.[19]
- Molecular response: using polymerase chain reaction (pcr) tests to detect bcr-abl gene transcripts at a molecular level.

➢ ***Summary of treatment strategy by disease phase:***

- Chronic phase: tkis are typically effective and well tolerated.
- Accelerated phase: more intensive treatment, potentially including a switch to a more potent tki or considering stem cell transplantation.
- Blast crisis: combination of chemotherapy, tkis, and possible stem cell transplantation.

CONCLUSION OF TREATMENTS:-

The treatment landscape for cml has evolved significantly with tkis being the cornerstone of therapy, allowing many patients to achieve long-term remission. For patients who do not respond adequately or develop resistance, other options such as stem cell transplants or newer tkis are available. Regular monitoring ensures the effectiveness of the treatment and early detection of disease progression.

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