Leukemia

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ACUTE MYELOID LEUKEMIA

- Acute myeloid leukemia (AML) consists of a group of relatively well-defined hematopoietic neoplasms involving precursor cells committed to the myeloid line of cellular development.

- AML is the most common acute leukemia in adults and accounts for approximately 80% of cases in this group of neoplasms.
- In contrast, AML accounts for less than 10% of acute leukemias in children younger than 10 years of age

- In adults, the median age at diagnosis is approximately 67 years.
- The male-to-female ratio is approximately 5:3.

- AML is characterized by a clonal proliferation of myeloid precursors with a reduced capacity to differentiate into mature myeloid cells.
- As a result, there is an accumulation of leukemic blasts in the bone marrow, peripheral blood, and occasionally in other tissues, with a variable reduction in the production of normal red blood cells, platelets, and mature granulocytes.

- The proliferation of malignant cells, along with a reduction in normal hematopoietic cells, results in a variety of systemic consequences including anemia, bleeding, and an increased risk of infection.

- Based on karyotype status (characterization of the chromosome such as shape, type, or number), two major groups of AML can be identified:
- (a) those with an abnormal karyotype, which accounts for approximately 50% to 60% of patients, and (b) those that demonstrate a normal karyotype by conventional cytogenetic testing, which accounts for the remainder of AML patients.

- Eight major variants of AML are defined by the French– American–British (FAB) classification system based on morphologic characteristics.
- More recently, the World Health Organization (WHO) has developed a classification system that expands the number of AML subtypes and better incorporates genotypic information, which is important in determining prognosis.

- Cells of myeloid origin commonly contain myeloperoxidase enzymes and express surface markers CD13, CD33, CD14, and CD15.

- Specific clonal chromosomal abnormalities are associated with several AML subtypes.

- These aberrations include gains or losses of whole chromosomes on the long (q) or short (p) arms, as well as a variety of structural rearrangements (e.g., translocations, inversions, insertions).

- The translocation t(15;17) is the cytogenetic hallmark of acute promyelocytic leukemia (APL or AMLM3).

- Patients with AML generally present with symptoms related to complications of pancytopenia (e.g., anemia, neutropenia, and thrombocytopenia), including weakness and easy fatigability, infections of variable severity, and hemorrhagic findings such as gingival bleeding, ecchymosis, epistaxis, or menorrhagia.

- Although a presumptive diagnosis of AML can be made by examination of the peripheral blood smear when there are circulating leukemic blasts, a definitive diagnosis usually requires a bone marrow aspiration and biopsy.

- The goal of the initial chemotherapy is to clear the bone marrow and peripheral blood of all blast cells in the hope that normal blood cell components can regenerate.

- CR: Criteria for this are platelet count higher than 100,000 cells/µL,
- neutrophil count higher than 1,000 cells/µL, and bone marrow specimen with less than 5% blasts

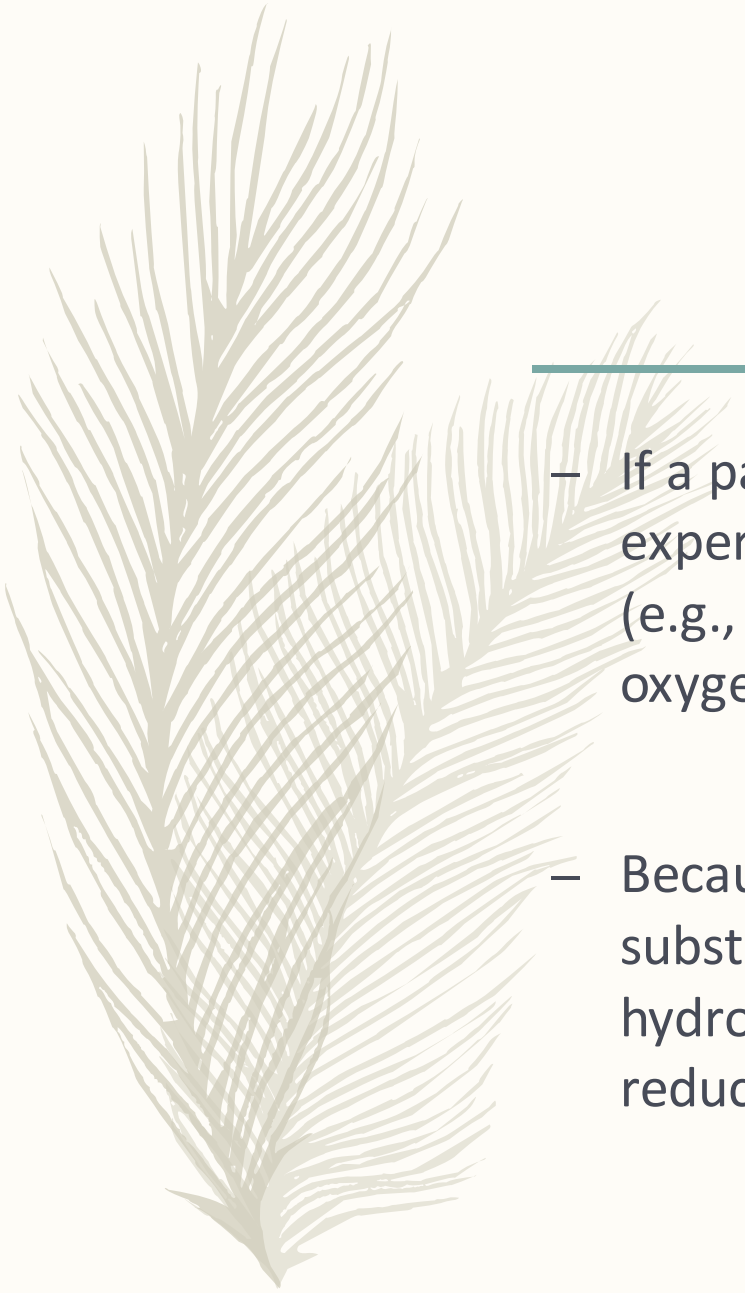
- The most commonly used induction regimens for AML are the “7+3” regimens, which combine a 7-day continuous intravenous (IV) infusion of cytarabine (100 or 200 mg/m2/day) with a short infusion or bolus of an anthracycline given on days 1 through 3.

- The most commonly used anthracycline in this regimen is daunorubicin, but idarubicin may be used instead.

- Sixty to 80% of adult patients with newly diagnosed AML will attain a complete remission with intensive induction chemotherapy.
- However, without additional cytotoxic therapy, virtually all of these patients will relapse within a median of 4 to 8 months.
- In contrast, patients who receive postremission therapy may expect 4-year survival rates as high as 40% in young and middle-aged adults with good-risk disease.

- High-dose cytarabine (HiDAC) has been the consolidation chemotherapy of choice for more than a decade for younger patients with good- or intermediate-risk disease.

- For patients with an abnormal karyotype or with adverse molecular mutations, consolidation with HiDAC followed by an allogeneic hematopoietic cell transplantation (HCT) with a suitably matched donor is the treatment of choice whenever possible



- If a patient presents with a very high WBC count, he or she may experience complications associated with hyperviscosity of the blood (e.g., ringing ears, stroke, blindness, or headache as a result of impaired oxygen delivery to the central nervous system, pulmonary infarction).

- Because it may take several days for cytarabine and idarubicin to substantially decrease the WBC count, the patient may receive hydroxyurea 2 to 4 grams orally or undergo leukapheresis to rapidly reduce the WBC count

- Leukapheresis is not routinely done unless the patient is experiencing symptoms of hyperviscosity or has a WBC 100,000 cells/µL or greater on diagnosis.

- APL:

Induction therapy with 7 + 3 is standard for all types of AML, with one exception:

- APL (also called AML-M3).
- APL is uniquely characterized by the t(15;17) translocation that fuses the PML gene on chromosome 15 to the retinoic acid receptor-alpha (RAR-α) gene on chromosome 17.
- In clinical trials, tretinoin (ATRA) has induced complete remission in approximately 90% of patients with APL

- Unfortunately, tretinoin typically induces brief remissions.
- A number of trials have investigated combination treatment with chemotherapy and tretinoin.

- Current evidence supports the use of concurrent tretinoin with arsenic trioxide or an anthracycline with or without cytarabine for induction in the treatment of low-risk APL.
- For high-risk APL, conventional chemotherapy remains the standard of care.

- In addition, postremission therapy should include at least two cycles of an anthracycline-based regimen.
- Maintenance herapy with intermittent tretinoin has been shown to decrease the relapse rate

- retinoic acid syndrome:
- fever, weight gain, respiratory distress, lung infiltrates, pleural or pericardial effusion, hypotension, and acute renal failure.

- If this syndrome develops, corticosteroid therapy (dexamethasone 10 mg twice a day for 3 to 5 days with a taper over 2 weeks) should be initiated.

- Other:
- Tretinoin also causes dryness of the lining of the mouth, rectum, and skin; hair loss; skin rash; blepharoconjunctivitis; corneal erosions; muscle weakness; nail changes; depression; elevated liver enzymes; and high cholesterol

- TLS:
- On administration of chemotherapy, patients with a hypercellular bone marrow and high number of blast cells can have a rapid lysis of the blast cells and the release of cellular contents.

- hyperuricemia, hyperphosphatemia, hypocalcemia, and uremia.

These disturbances may lead to arrhythmias and acute renal failure.

In most cases, TLS occurs 12 to 24 hours after chemotherapy is initiated.

- Patients should receive IV hydration (3–4 L/day) beginning 24 to 48 hours before chemotherapy to maintain renal perfusion, optimize the solubility of tumor lysis products, and compensate for fluid losses caused by fever or vomiting.

- Alkalinization of the urine with the addition of sodium bicarbonate to the IV fluids may also reduce or prevent uric acid from precipitating in the renal tubules and collection ducts by maintaining the urate in its ionized state, but is not currently recommended for all patients.

- This is because the increased pH may increase the risk of precipitating calcium phosphate in both soft tissue and kidney tubules, and it may aggravate hypocalcemia.

- Allopurinol, a xanthine oxidase inhibitor that blocks the production of uric acid,
- should be started before chemotherapy to prevent or minimize the complications of TLS.
- The recommended adult dosage is 300 to 600 mg/day.
- Allopurinol may be discontinued if the serum uric acid is within normal limits, the LDH has normalized, and the WBC count is low.

- Rasburicase, a recombinant urate oxidase product, can also be used as prophylaxis in patients who are at high risk of developing TLS or for the treatment of patients who present with or develop TLS.
- Rasburicase acts as a catalyst in the enzymatic oxidation of uric acid to allantoin, which is 5 to 10 times more soluble than uric acid and undergoes rapid renal excretion.
- The recommended dose of rasburicase for both prevention and treatment of TLS is 0.2 mg/kg/dose IV.
- Rasburicase results in a rapid reduction in serum uric acid (within 4 hours of administration) and is generally well tolerated

Chronic myeloid leukemia

- Chronic myeloid leukemia is a myeloproliferative disorder characterized by unregulated stem cell proliferation in the bone marrow and an increase in mature granulocytes in the peripheral blood.

- The disease is relatively rare, representing only 0.4% of all cancer cases and 12% of new leukemia cases.
- The median age of diagnosis is 64 years and the current estimated 10-year survival rate is 80% to 90%.

- Approximately 30% to 50% of patients are asymptomatic at presentation with the most common physical finding of splenomegaly occurring in 50% to 60% of patients.

- Additional symptoms may include fatigue, abdominal fullness, fever, anorexia, and weight loss.

- For many patients, the suspicion for CML is based solely on an abnormal CBC with a confirmatory bone marrow biopsy revealing the hallmark of CML, the Philadelphia (Ph) chromosome

- Cytogenetic analysis reveals the presence of the Ph chromosome which is a translocation of chromosomes 9 and 22 t(9;22)(q34;q11).

- This translocation creates a new protein (BCR-ABL) that has unregulated tyrosine kinase (TK) activity.
- The three major mechanisms that have been implicated in the malignant transformation by unregulated TK include abnormal cell cycling, inhibition of apoptosis, and increased proliferation of cells.

- The natural history of CML can be divided into three distinct phases: chronic phase, accelerated phase, and blast phase.

- The greatest number of patients is diagnosed in chronic phase, which is the earliest phase of the disease.

- Less than 10% of blasts in the bone marrow and less than 20% of basophils in the peripheral blood space place patient in chronic phase using the WHO Criteria for CML Staging

Table 96-4

World Health Organization Criteria for CML staging

Chronic phase	■ None of the criteria for blast or accelerated phase
Accelerated phase	■ Blasts 10%–19% of peripheral white blood cells or nucleated bone marrow cells ■ Peripheral blood basophils >20% ■ Persistent thrombocytopenia ($<100 \times 10^9$/L) not related to therapy or persistent thrombocytosis ($>1{,}000 \times 10^9$/L) unresponsive to therapy ■ Increasing spleen size and increasing WBC count, unresponsive to therapy ■ Cytogenetic evidence of clonal evolution
Blast phase	■ Blasts >20% of peripheral white blood cells or nucleated bone marrow cells. ■ Extramedullary blast proliferation ■ Large foci or clusters of blasts in the bone marrow biopsy

Adapted from Vardiman JW et al. The World Health Organization (WHO) classification of myeloid neoplasms. Blood. 2002;100:2292.; Cortes J, Kantarjian H. How I treat newly diagnosed chronic-phase CML. Blood. 2012;120:1390.

- Hematopoietic stem cell transplant (HCT) remains the only curative therapy for CML.
- However, due to its substantial risks of morbidity and mortality, TK inhibitors have become first-line therapy in most patients.
- Patients in accelerated or blast phase at presentation or those progressing during TK inhibitor therapy are generally referred for HCT.

- The primary goals of the TK inhibitors are to prevent progression from chronic phase to accelerated or blast phase while achieving a complete cytogenetic response (CCyR) within 12 to 18 months of therapy initiation.

- Assessment of response to TK inhibitors is based on hematologic, cytogenetic, and molecular responses

Table 96-2

Definition of Hematologic Response in Chronic Myelogenous Leukemia

	Partial Response	Complete Response (CR)
Peripheral leukocyte count	$<10 \times 10^9$/L	$<10 \times 10^9$/L
Platelet count	<50% pretreatment count (but $>450 \times 10^9$/L)	$<450 \times 10^9$/L
Immature cells	Present	Absent
Splenomegaly	Present (but <50% pretreatment extent)	Absent

Adapted with permission from NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines). Chronic myelogenous leukemia. 2015;V1.2015. Available at: http://www.nccn.org/professionals/physician_gls/f_guidelines.asp. Accessed May 17, 2015.

Table 96-3

Definition of Cytogenetic Response in Chronic Myelogenous Leukemia

Cytogenetic Response	Philadelphia (Ph) Chromosome-Positive Metaphase Cells (%)
Complete	0
Partial	1–35
Major (includes complete and partial responses)	0–35
Minor	>35

Adapted with permission from NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines). Chronic myelogenous leukemia. 2015; V1.2015. Available at: http://www.nccn.org/professionals/physician_gls/f_guidelines.asp. Accessed May 17, 2015.

- Complete molecular response is defined quantitatively by polymerase chain reaction assay with no detectable BCR-ABL mRNA identified to 4.5 logs below the standard baseline

- Imatinib, a first-generation TK inhibitor, inhibits BCR-ABL kinase, which prevents phosphorylation of substrates that are involved in regulating the cell cycle.

- The most common toxicities reported with imatinib are superficial edema, nausea, muscle cramps, and rashes.

- Dasatinib is a second-generation TK inhibitor that binds the BCR-ABL protein in the active confirmation, making it 325 times more potent than imatinib.

- Dasatinib demonstrates a similar safety profile compared with imatinib but with a higher incidence of pleural effusion, pulmonary hypertension, and thrombocytopenia as well as a lower incidence of rash and diarrhea.

- Nilotinib is a second-generation TK inhibitor which is structurally similar to imatinib but 30 times more potent as a result of an improved structural fit in the receptor pocket.

- Nilotinib demonstrates a similar safety profile compared with the other TK inhibitors, with a higher incidence of rash, headache, pruritus, and alopecia and a lower incidence of nausea, diarrhea, vomiting, edema, and muscle spasm

- dasatinib,
- nilotinib,
- bosutinib,
- ponatinib,
- and omacetaxine

Chronic Lymphocytic Leukemia

- Chronic lymphocytic leukemia (CLL) is a disorder of mature but functionally incompetent lymphocytes.
- CLL is the most common type of leukemia in adults, with approximately 15,000 new cases annually and 4,700 deaths.
- It is a disease of the older population, and the median age at diagnosis is 65 years, with 90% of patients older than age 50 at diagnosis

- This disease is characterized by overproduction of functionally incompetent B-cell lymphocytes derived from a single stem cell clone in the bone marrow.
- These lymphocytes accumulate in the blood, bone marrow, lymph nodes, and spleen.
- Approximately 40% of patients are asymptomatic at presentation and are diagnosed by routine CBC (lymphocytosis, anemia, or thrombocytopenia).
- Symptomatic patients commonly experience night sweats, fatigue, weight loss, fever, and painful lymphadenopathy.
- Patients often seek medical attention for infection caused by immune suppression or bleeding caused by thrombocytopenia.

- Predicting the clinical course of CLL remains a challenge because some patients experience an indolent course and maintain a good quality of life, whereas others experience more aggressive disease and debilitation.

- Therefore, survival is variable and depends on the stage of disease at diagnosis. CLL is staged based on peripheral lymphocyte counts; enlargement of lymph nodes, liver, and spleen; and the presence of anemia or thrombocytopenia.

- Selection of therapy is in part determined by the presence or absence of cytogenetic abnormalities such as del(11q) or del(17p) which are unfavorable, comorbidities, and age.

- Common first-line therapies include targeted monoclonal antibodies in combination with chlorambucil, bendamustine, fludarabine, or cyclophosphamide.

- Relapsed disease is often treated with combinations of the same drugs used for initial treatment

- CLL is usually included in the differential diagnosis of any adult with persistent lymphocytosis (>5,000 lymphocytes/µL in peripheral blood).

- Additional causes of lymphocytosis include transient reactions to acute infections such as influenza or mononucleosis, as well as other hematologic malignancies.

- To differentiate between benign and malignant lymphocytosis, examination of the peripheral blood or bone marrow morphology may be required.

- Patients with CLL commonly have lymphocytosis in both the peripheral blood and bone marrow, whereas patients with other disorders have a high percentage of atypical lymphocytes in the peripheral blood alone.

- Bone marrow biopsy with aspirate may be useful to determine the definitive diagnosis.

- An accepted treatment modality for early-stage disease includes a conservative,
- watchful waiting approach.
- No clear advantage has been demonstrated in treating asymptomatic patients in early-stage disease with alkylator-based chemotherapy as compared with deferred treatment.
- The survival of patients with smoldering CLL is similar to an age- and sex-matched normal population

- Indications for treatment initiation in CLL include significant anemia or thrombocytopenia, progressive disease demonstrated by lymphadenopathy, hepatomegaly, splenomegaly, a lymphocyte doubling time of less than 6 months, persistent B symptoms (fever, night sweats, and weight loss), threatened end-organ function, and recurrent infection.

- Patient performance status, comorbid conditions, pharmacoeconomic variables, and social support should all be taken into consideration when selecting treatment.
- Cytogenetic results will also be considered

- Chlorambucil
- Therapy for CLL has historically included use of an alkylating agent, most often oral chlorambucil or cyclophosphamide, with or without prednisone.

- The overall response (OR) rate to chlorambucil was approximately 40% to 60%, but only 3% to 5% achieved a CR.

- Chlorambucil use has diminished, and the use of purine analogs, such as fludarabine, is more common in clinical practice; however, chlorambucil is recommended for patients older than or equal to 70 years, or in younger patients if they have significant comorbidities.
- Chlorambucil is often used in combination with monoclonal antibodies

- **Fludarabine**
- Fludarabine is an active agent in the treatment of CLL. Fludarabine monotherapy at a dose range of 25 to 30 mg/m2/dose IV × 5 days has shown a 70% to 80% OR rate, and CR rates of 20% to 30% with increased progression-free survival (PFS).

- Toxicities associated with fludarabine are typically mild and include fever and immunosuppression.
- Increased incidence of infection and autoimmune hemolytic anemia are also associated with fludarabine therapy.
- Infection prophylaxis should be considered in elderly patients and patients with advanced disease or renal dysfunction

- Fludarabine has been combined with other chemotherapy and monoclonal antibodies, including cyclophosphamide and rituximab, in an effort to prevent multidrug resistance and increase response.

- Bendamustine
- Bendamustine, a nitrogen mustard/alkylating agent, was approved in 2008 for the treatment of CLL.
- In clinical studies, it has been shown to be superior to chlorambucil with OR and CR rates of 68% and 31%, respectively.
- A typical dose and schedule is 100 mg/m2 IV on days 1 and 2.
- Toxicities include infusion reactions and myelosuppression.
- It is often used in combination with rituximab and primarily in patients older than or equal to 70 years or those with comorbidities

- Rituximab
- Rituximab is a chimeric human–murine anti-CD20 monoclonal antibody. The CD20 surface antigen is expressed on a high percentage of CLL cells.
- Rituximab monotherapy as initial therapy for untreated patients at a dose of 375 mg/m2 weekly for four doses yielded OR rates of 58% and CR rates of 9%; these are lower than those seen with cytotoxic therapy, with a disappointing duration of response.
- Therefore, rituximab monotherapy is reserved for patients with significant comorbidity.
- Generally, it is used in combination therapy with cytotoxic agents.

- A regimen for initial treatment is the combination of FCR.
- In a study of first-line treatment of CLL, patients were treated with fludarabine 25 mg/m2 IV on days 1 to 3, cyclophosphamide 250 mg/m2 IV on days 1 to 3, and rituximab 375 mg/m2 IV on day 1 of cycle 1, escalated to 500 mg/m2 in subsequent cycles.
- OR rate was 96%.
- Toxicity of this regimen included infusion-related reactions, nausea, vomiting, and
- myelosuppression.
- Grade 3 or 4 neutropenia was frequently noted with an infection rate of 20%.The FCR regimen is recommended in patients younger than 70 years without significant comorbidities or older patients without comorbidities, and in any patient with the unfavorable del(17p) cytogenetic abnormality

- Infections contribute significantly to morbidity and mortality in patients with CLL.
- The immune compromise of CLL is attributable to immunoglobulin deficiency, abnormal T-cell function, neutropenia, and chemotherapy, which contribute to the increased rate of both common and opportunistic infections
- Up to 80% of patients will develop an infectious complication; therefore, the use of IV immune globulin, antibacterials (trimethoprim–sulfamethoxazole), and antivirals (acyclovir for herpes simplex virus), and vaccinations (influenza, pneumococcal) are common.
- Opportunistic infections are particularly common in patients receiving a purine analog.
- The use of supplemental IV immune globulin for prophylaxis of future infection is often used in patients with low immunoglobulin levels (IgG <500 mg/dL) and recurrent infections requiring hospitalization

Multiple Myeloma

- Multiple myeloma (MM) is defined as a malignancy of "plasma cells," terminally differentiated B lymphocytes responsible for the production of antibodies and for the rapid immune response to antigen exposure.

- MM occurs nearly twice as often in African-Americans compared to whites, is slightly more common in males than in females, and is diagnosed at a median age of 65 years

- monoclonal gammopathy of undetermined significance (MGUS):

- It is characterized by the accumulation of abnormal clonal plasma cells and may be differentiated from MM by the serum concentration of M-protein (<3 g/dL) and the lack of clinical manifestations typically associated with MM (osteolytic bone lesions, hypercalcemia, renal dysfunction, etc.)

- Smoldering myeloma:

- Smoldering myeloma represents an indolent form of the disease in which patients produce M-protein ≥3 g/dL and/or have 10% to 60% plasma cells in the bone marrow, but remain asymptomatic.

- Smoldering myeloma progresses to MM at a rate of 10%/year for the first 5 years after diagnosis, 3%/year for the next 5 years, and 1%/year for the next 10 years

- Patients presenting initially with symptomatic MM frequently complain of bone pain, fatigue, and recurrent infections.

- **CRAB:**
- Hypercalcemia
- Renal failure
- Anemia
- Bone lesion

- Because MM is not generally considered to be a curable malignancy, the goal of treatment is to achieve and maintain a clinical response through the combination of induction therapy, hematopoietic stem cell transplant (HCT), and maintenance therapy.

- Patients presents with a number of the classic features of MM. Bone pain and skeletal disease are common and occur when plasma cells infiltrate the bone marrow and secrete osteoclast-activating factors.

- Excessive immunoglobulin production may also cause hyperviscosity syndrome, which may lead to CNS, renal, cardiac, or pulmonary symptoms. Plasmapheresis may be used to alleviate life-threatening cases.

- Plasmapheresis may be used to alleviate life-threatening cases

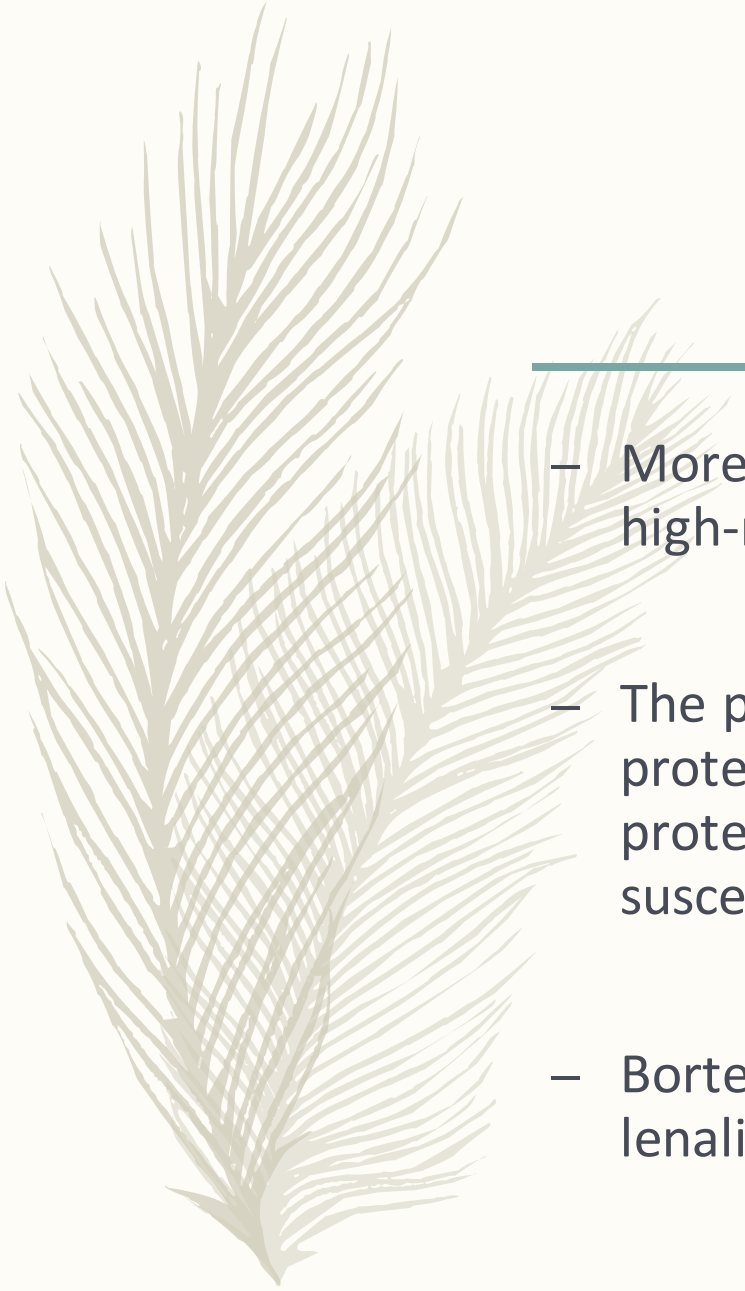
- Two staging systems have been used for patients with MM:
- the older Durie–Salmon system, developed in 1975,
- and the newer international staging system (ISS).

- The ISS was validated in a large international study
- demonstrating that prognosis can be predicted reliably from serum β2 macroglobulin (a light chain protein expressed on all nucleated cells) and albumin

- The most effective treatment is induction followed by autologous HCT; therefore, eligibility for HCT helps determine the most appropriate treatment option.

- Determination of HCT eligibility includes consideration of patient age (typically 65 years of age or younger) and comorbidities.

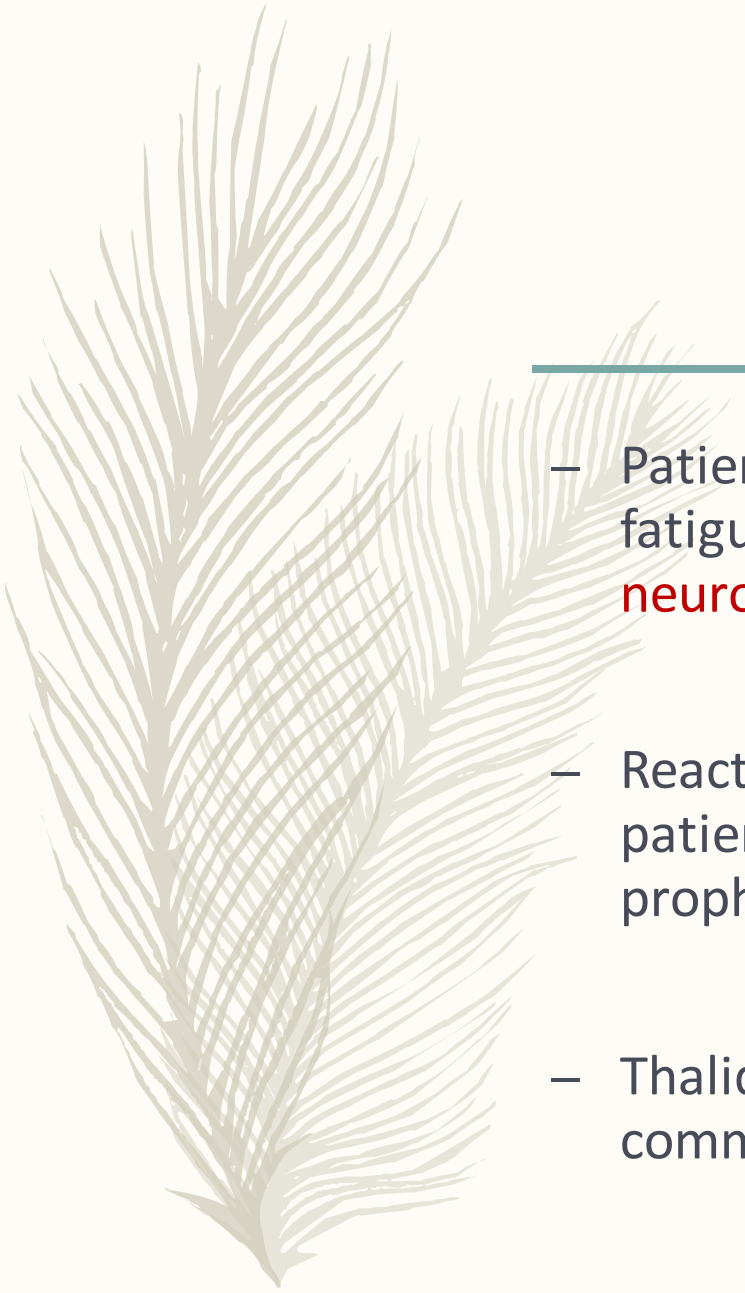
- Those who are eligible for HCT should not be treated with agents such as melphalan, which may compromise the ability to collect a sufficient number of hematopoietic stem cells necessary to perform the autologous HCT



- More aggressive 3 drug combination regimens may be advantageous in high-risk patients to help increase the chance of developing a CR.

- The proteasome inhibitor bortezomib acts by inhibiting the 26S proteasome, a multienzyme complex responsible for regulation of proteins that promote cell survival, stimulate growth, and reduce susceptibility to programmed cell death.

- Bortezomib is commonly used in combination with thalidomide, lenalidomide, cyclophosphamide, and/or dexamethasone



- Patients should be monitored for common adverse events, including fatigue, diarrhea, mild nausea, thrombocytopenia, and peripheral neuropathy.

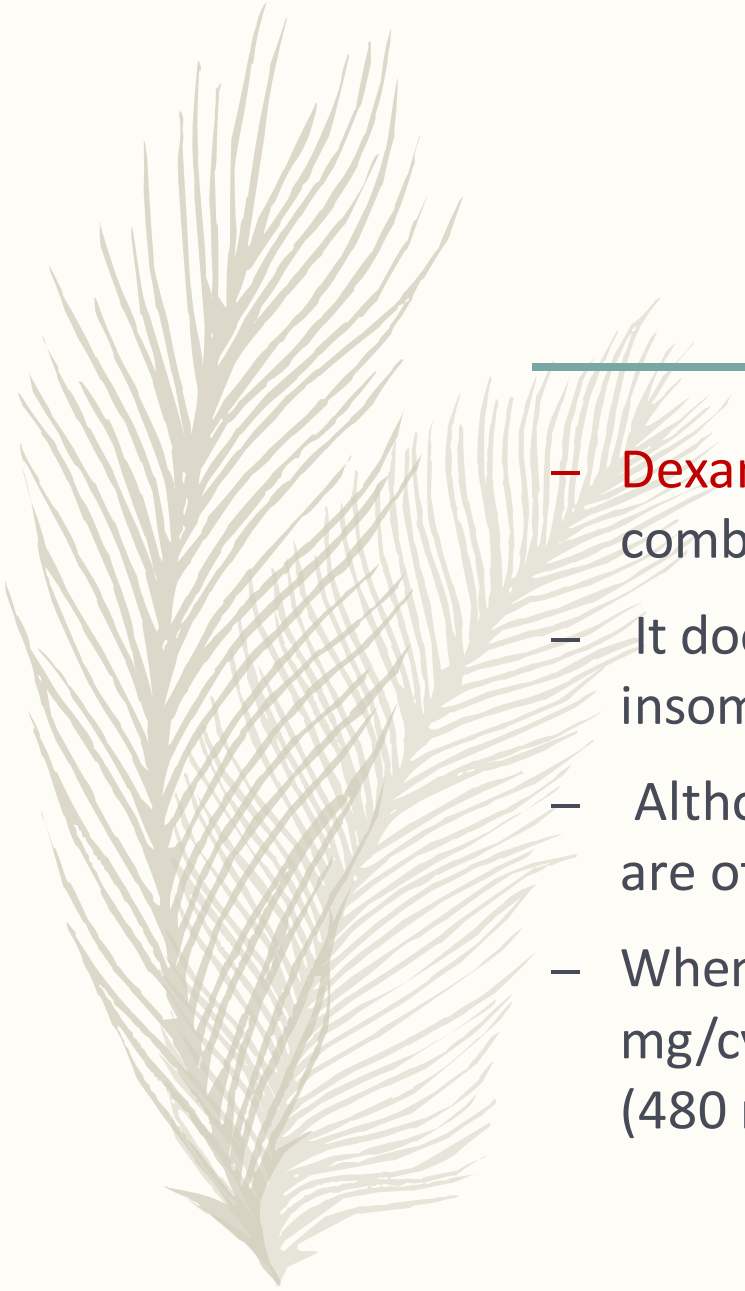
- Reactivation of herpes zoster has been observed in greater than 10% of patients treated with bortezomib; therefore, concomitant antiviral prophylaxis should be utilized.

- Thalidomide and lenalidomide are immunomodulatory drugs (IMiDs) commonly used in the initial treatment of MM.

- They possess complex antiangiogenic, antiinflammatory, and immunomodulatory properties that make them active in MM.
- Common adverse effects of lenalidomide include hematologic toxicities, muscle weakness, fatigue, and rash.
- Several studies have also revealed a small but concerning risk of secondary malignancies, which may be associated with combined oral melphalan use

- In comparison with lenalidomide, thalidomide is less potent and has a less favorable toxicity profile with sedation and peripheral neuropathy being common in addition to constipation.

- Both thalidomide and lenalidomide have a risk of thromboembolism, and venous
- thrombotic embolism prophylaxis is recommended.
- Thalidomide and lenalidomide are only available via a restricted access prescription programs due to the risk of teratogenicity



- Dexamethasone is an active treatment option for MM, mostly used in combination regimens.
- It does have significant adverse effects, including hyperglycemia, insomnia, and increased infection risk.
- Although response rates are increased with higher doses, lower doses are often more beneficial.
- When combined with lenalidomide, low-dose dexamethasone (120 mg/cycle) improved 1-year OS compared to high-dose dexamethasone (480 mg/cycle) (96% vs. 87%, p = 0.0002).

- The combination of lenalidomide, bortezomib, and dexamethasone (RVD) has demonstrated response rates up to 100% in patients with newly diagnosed MM and is well tolerated with sensory neuropathy, fatigue, and hematologic toxicities being the most commonly reported

- Osteolytic bone lesions or osteopenia occurs in nearly 80% of all patients with MM and represents one of the most significant challenges to quality of life in this patient population.

- The efficacy of pamidronate and zoledronic acid for the prevention of skeletal related events and improvement in OS has been established in MM patients, irrespective of the presence of osteolytic bone lesions.

- Equivalent efficacy with monthly infusions has been shown with pamidronate and zoledronic acid.
- Because bisphosphonates can negatively affect kidney function, serum creatinine should be monitored monthly and treatment should be held if creatinine increases by more than 0.5 mg/dL above baseline

- Osteonecrosis of the jaw (ONJ) is a rare but serious complication of bisphosphonate therapy.
- Zoledronic acid is associated with a 9.5-fold increased risk of ONJ compared with pamidronate.

- Baseline dental examinations and avoidance of invasive dental procedures during therapy are recommended

- Maintenance:
- Lenalidomide
- bortezomib


Alvocade® 3.5
Bortezomib
Lyophilized Powder For Injection
For Bolus IV or SC Injection Only
3.5 mg
For Hospital Use Only


Rx
100 softgels
All Trans Retinoic Acid
softgel Capsules
CA ATRA-IO
JENOME BIOPHAR
100 softgels
Rx
All Trans Retinoic Acid
softgel Capsules
CA ATRA-IO
JENOME BIOPHAR


100 mg
Bendanit®100
25 mg
Bendanit®25
Bendamustine HCl
Lyophilized Powder For Solution For Infusion
For IV Infusion Only After Dilution


NDC 67457-454-50
Cytarabine
Injection
1000 mg/50 mL
(20 mg/mL)
PHARMACY BULK PACKAGE
Not For Direct Infusion
CYTOTOXIC AGENT
Isotonic
Sterile
For Intravenous and
Subcutaneous Use Only
Mylan
Rx only
Cytarabine


Daunorubicin
Hydrochloride
for Injection USP
Daunotec
20 mg
FOR I.V. USE ONLY
Cipla
Daunotec
Cipla


50 mg
2 ml
Fludarabin-Teva®
Konzentrat für Injektions-/Infusionslösung
50 mg
2 ml
Fludarabini phosphas
25 mg / 1 ml
Zytostatikum
1 Stechampulle
TEVA


Idanthra 5 mg
Idarubicin Hydrochloride
Idanthra 10 mg
Idarubicin Hydrochloride
Idanthra 20 mg
Idarubicin Hydrochloride


10 Capsules
Imatib 100
Imatinib
Do not store above 30°C


100 mg/ 10 ml
Zytux™
Rituximab
Concentrate for solution for infusion
Each box contains 2 vials of 10ml concentrate for solution for infusion.
Each vial of Zytux™ contains 100 mg/ 10 ml Rituximab.
For intravenous use after dilution
زیتاکس
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محلول تغلیظ شده جهت انفوزیون وریدی
برای مصرف وریدی بعد از رقیق شدن
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