Multiple Myeloma Therapies

Chemotherapy

IMiDs (Immunomodulatory Drugs)

Agents that affects, enhances or suppresses the immune system.

Thalomid (Thalidomide) Celgene

Side Effects: Embryofetal toxicity, low white blood cell counts, low platelet counts, venous and arterial thromboembolism, diarrhea, fatigue, anemia, constipation, rash

Revlimid (Lenalidomide) Celgene

Side Effects: Embryofetal toxicity, low white blood cell counts, low platelet counts, venous and arterial thromboembolism, diarrhea, fatigue, anemia, constipation, rash

Polamyst (Pomalidomide) Celgene

Side Effects: Embryofetal toxicity, low white blood cell counts, low red blood cell counts, low platlet counts, venous and arterial thromboembolism, fatigue, weakness, dizziness and confusion, constipation, nausea, diarrhea, neuropathy

Proteasome Inhibitors

A drug that interferes with the normal function of the proteasome, an enzyme complex responsible for breaking down and recycling unwanted proteins in both normal and cancer cells. This "recycling" of protein is important to maintain balance within the cell and helps regulate several functions including cell growth. These drugs seem to affect tumor cells more than normal cells.

Velcade (Bortezomib) Takeda

Side Effects: Peripheral neuropathy (subcutaneous administration preferred), fatigue, nausea, diarrhea, thrombocytopenia, low blood pressure; more rarely headache, insomnia, fever, back pain, muscle cramps

Kyprolis (Carfibzomib) Amgen

Side Effects: Fatigue, anemia, thrombocytopenia, shortness of breath, diarrhea, fever, low blood pressure, cardiac failure and other cardiac events, infusion reactions, embryofetal toxicity

Ninlaro (Ixazomib) Takeda

Side Effects: Thrombocytopenia, neutropenia, diarrhea, constipation, nausea, vomiting, peripheral neuropathy, peripheral edema (swelling of the feet) rash, liver toxicity, back pain, upper respiratory tract infection

Histone Deacatylase (HDAC) Inhibitor

HDAC inhibitors induce cancer cell cycle arrest, differentiation and cell death, reduce angiogenesis and modulate immune response. They do this by interacting with proteins in the chromosomes called histones.

Farydak (Panibinostat) Novartis

Side Effects: Low blood counts, diarrhea, nausea or vomiting, cardiac toxicity, hemorrhage (due to low platelets), infections, liver toxicity, embryo-fetal toxicity, fatigue

Monoclonal Antibodies

An artificially manufactured antibody that is specifically designed to find and bind to cancer cells or immune system cells for diagnostic or treatment purposes. Monoclonal antibodies can be used alone or with can be used to deliver drugs, toxins or radioactive materials directly to tumor cells. The act of binding to the cancer cells is thought to both kill the cell directly as well as to help the immune system attack these cells.

Darzalex (Daratumumab) Janssen

Side Effects: IV: Infusion reactions, fatigue, nausea, back pain, fever, cough, low blood cell counts

Dara FasPro (subcutaneous injection)

Side Effects: Injection: Serious allergic reactions and other severe systemic administration related reactions, injection site reactions, decreases in blood cell counts, changes in blood tests, upper respiratory infection, fatigue, nausea, diarrhea, shortness of breath, trouble sleeping, fever, cough, muscle spasms, back pain, vomiting, cold-like symptoms, peripheral neuropathy, constipation, pneumonia

Empliciti (Elotuzumab) BMS

Side Effects:Infusion reactions, low blood counts, infections, fatigue, diarrhea, fever, constipation, muscle spasms, decreased appetite

Isatuximab (Sarclisa)

Side Effects: Neutropenia, infection, infusion reaction, diarrhea

Alkylators/Alkylating Agent

A chemotheraputic agent that cross-links with the DNA of myeloma cells to block cell division and growth.

Melphalan (Alkeran) now generic

Side Effects: Suppression of blood cell counts, hypersensitivity reactions, gastrointestinal toxicity, pulmonary toxicity, infertility, secondary malignancies (leukemia)

Cyclophosphamide (Cytoxan) now generic

Side Effects: Suppression of blood cell counts, infections, urinary tract and renal toxicity, cardiotoxicity, pulmonary toxicity, secondary malignancies, fever, alopecia (IV), nausea, vomiting, diarrhea

Bendamustine

Melphalan Flufenamide (Melfufen) Oncopeptides AB

Side Effects: Fatigue, nausea, diarrhea, fever, respiratory tract infection

Anti-BMCA Immunoconjugate

Targeting the BCMA (B cell maturation antigen) frequently expressed on the surface myeloma cells. After binding to the BCMA, Blenrep enters the cell, causing cell cycle arrest and apoptosis (programmed cell death).

Belantamab Mafodotin (Blenrep) GlaxoSmithKline

Side Effects: Keratopathy, thrombocytopenia, infusion-related reactions, embryo-fetal toxicity

Selective Inhibitor of Nuclear Export (XPO Inhibitor)

Such drugs works by quasi-irreversibly binding to exportin 1 and thus blocking the transport of several proteins involved in cancer-cell growth from the cell nucleus to the cytoplasm, which ultimately arrests the cell cycle and leads to apoptosis. It is the first Myeloma drug with this type of mechanism.

Selinexor (Xpovio)

Side Effects: Suppression of blood cell counts, diarrhea, constipation, fatigue, nausea and vomiting, shortness of breath, serious infections, tiredness, loss of appetite, low blood sugar

Corticosteroids

Natural and synthetic analogues of the hormones secreted by the pituitary glands. Glucocorticoids (below) have a multiplicative effect, and are used to enhance the actions of many drugs. They also help reduce nausea and vomiting that chemo may cause.

Dexamethasone (Decadron) now generic

Side Effects: Infections, cardiac conditions/ fluid retention, acne, rash, elevated blood glucose, GI disorders, weight gain, coughing, hoarseness, osteoporosis, muscle pain, ophthalmologic disorders, psychiatric effects, sleeplessness

Prednisone

Methylprednisolone

Anthracyclines

A type of antibiotic that comes from certain types of Streptomyces bacteria. Anthracyclines are used to treat many types of cancer. Anthracyclines damage the DNA in cancer cells, causing them to die.

Doxorubicin - now generic **Doxil**

BCL2 Inhibitor

BCL2 is a protein that is present in high amounts in myeloma cells, where it helps the cell survive for longer and makes them more resistant to cancer medications. This drug attaches to the BLC2 in the Myeloma cell, blocking its action and causing the death of the cell. Venetoclax has been found to be especially effective for patients with 11-14 chromosomal translocations.

Venetoclax

Side Effects: thrombocytopenia, anemia, neutropenia, infusion-related reactions, diarrhea, constipation, nausea and vomiting, fatigue, upper respiratory infections

Immunotherapy

This therapy the uses the power of the body's own immune system to locate, attack and destroy cancer cells. Can range from drugs the boost the effectiveness of the body's immune system to re-engineering immune cells to fight cancer.

Cellular Immunotherapy

Involves taking immune cells from your body — sometimes re-engineering them to recognize and fight cancer — and placing them back into your body in large numbers. Many treatments under development focus on using T-cells, the body's anit-infection fighters.

CAR-T Cells – (chimeric antigen receptors T-Cells) – T-cells are taken from the body and re-programmed to recognize certain proteins on the surface of cancer cells through enhanced chimeric antigen receptors, thus enabling them to recognize and attack cancer cells.

Idecabtagene vicleucel (Abecma) BMS and Bluebird Bio

Side Effects: cytokine release syndrome (CRS), neurologic toxicities, fatigue, fever of 100.4°F/38°C or higher, chills or shivering, severe nausea or diarrhea, decreased appetite, headache, dizziness or lightheadedness, confusion, difficulty speaking or slurred speech, cough, difficulty breathing, and fast or irregular heartbeat.

Checkpoint Inhibitors

Checkpoint inhibitors work by teaching immune cells to target and attack the pathways where cancer grows. Tumor cells can hide themselves by sending false signals to immune cell "checkpoints" so that they look harmless. Checkpoint inhibitor drugs block these false signals, so the immune system isn't tricked into ignoring tumors.

BiTE (Bispecific T-cell Engager)

These are a class of artificial monoclonal antibodies that direct a host's immune system against cancer cells. BiTEs form a link between the T-cells and the cancer cell, causing the T-cell to exert cytotoxic activity on the tumor cells. This means that the T-cells produce certain proteins that enter the cancer cell and initiate the cell's apoptosis, or cell death.

BONE LOSS

Multiple myeloma can make your bones weaker and more likely to break. Your doctor may give you drugs to help strengthen your bones.

Denosumab (Amgen)

Denosumab is a human monoclonal antibody which works by preventing the development of osteoclasts which are cells that break bone down.

Xgeva

Prolia (brand named when used to treat osteoporosis)

Side Effects: Hypocalcemia, ONJ, atypical femoral fracture, embryofetal toxicity, diarrhea, nausea, anemia, back pain, thrombocytopenia, peripheral edema, hypocalcemia, upper respiratory tract infection, rash, and headache

Bisphosphonates are medications that used to treat bone loss. These drugs can also reduce fracture risk in cases of previous fracture. Bone is constantly undergoing a turnover process in which osteoblasts create bone and osteoclasts destroy it. Bisphosphonates inhibit the actions of osteoclasts by promoting their apoptosis (programmed cell death), which, in turn, slows bone loss.

Zoledronic acid (Zometa) – Novartis

Side Effects: Renal toxicity, fever, vein irritation, general aches and pains, ONJ

Pamironate (Aredia) - Novartis - now generic

(Pamimed) Curacell Biotech

Side Effects: Renal toxicity, fever, vein irritation, general aches and pains, ONJ

Terms Used To Describe Treatment Response

CR: Complete Response (or Remission)

No sign of disease; No sign of M protein in the blood and urine; disappearance of any soft-tissue plasmacytomas, and less than 5% plasma cells in bone marrow aspirates

SCR: Stringent Complete Response

No detectable disease by serum or urine immunofixation, normal kappa/lambda light chain ratio, and no detectable myeloma on bone marrow flow cytometry

VGPR: Very Good Partial Response

A 90% or greater decrease in blood M protein. Urine M protein level <100mg in 24-hour urine collection

PR: Partial Response (or Partial Remission)

More than a 50% decrease in the amount of M protein in the blood and 90% reduction in 24-hour urine collection and 50% or greater reduction in the size of soft tissue plasmacytoma (if present at diagnosis).

MR: Minimal Responses

Reduction between 25-50% in M protein in the blood, reduction between 50-89% in M protein in 24-hour urine collection, and 50% or greater reduction in the size of soft-tissue plasmacytoma (if present at diagnosis).

SD: Stable Disease

Not meeting criteria for complete response , very good partial response, partial response, minimal response or progressive disease

PD: Progressive Disease

At least 25% increase in M protein in the blood and urine, and appearance of new lesions or 50% or greater increase in size of precious lesions.

Refractory Myeloma

Myeloma that does not go into remission or improve substantially after treatment

Relapsed Myeloma

Myeloma that initially responded to therapy but returns after treatment

MRD (Minimum or Measurable Residual Disease) Testing

This test is done through the results of a bone marrow aspiration, and depending upon the test used, can detect Myeloma cells down to one in a million cells. A newer test that shows great promise, but all doctors do not agree on the best use of the results, or what exactly the results mean. However, reaching MRD- has been shown in early trials to indicate longer remissions.