Summary

IN BRIEF Treatment of AML is usually divided into 2 chemotherapy phases:

- remission induction
- post-remission therapy (consolidation)

1-Remission Induction

This first part of treatment is aimed at getting rid of all visible leukemia. It usually involves treatment with 2 chemotherapy drugs, cytarabine (ara-C) and an anthracycline drug such as daunorubicin (Daunomycin) or idarubicin (Idamycin). Sometimes a third drug, 6-thioguanine, is added. This intensive therapy, which usually takes place in the hospital, typically lasts one week. How intense the treatment is may depend on the person's age and on other prognostic factors**.**

In rare cases where the leukemia has spread to the brain or spinal cord, chemotherapy may be given into the cerebrospinal fluid (CSF) as well.

Most of the normal bone marrow cells as well as the leukemia cells will be destroyed by the treatment. During chemotherapy and the following couple of weeks, the patient's blood cell counts will probably be dangerously low, and drugs to raise white blood cell counts, antibiotics, and blood product transfusions may be used to help protect against complications. Usually, the patient stays in the hospital during this time. If induction is successful, no leukemia cells will be found in the blood, and the number of blast cells in the bone marrow will be less than 5% within a week or two. Normal bone marrow cells will return in a couple of weeks and start making new blood cells.

If one week of treatment does not induce remission, the process may be repeated. Induction is successful in about 40% to 80% of all AML patients. This depends to a large part on a person's specific prognostic factors. For instance, older people are more likely to have unfavorable cytogenetic test results, are more likely to have a pre-existing blood disorder, and are less likely to be able to tolerate intensive therapy than younger patients, so generally they don't respond as well.

Remission induction usually does not destroy all the leukemia cells and a small number often persist. Without more treatment, called consolidation, the leukemia is likely to return within several months.

2-Consolidation (Post-remission) Therapy

If remission induction is successful, further treatment may be given to try to destroy any remaining leukemia cells and help prevent a relapse. The options for AML consolidation therapy are:

- several courses of high-dose cytarabine (ara-C) chemotherapy
- allogeneic (donor) stem cell transplant
- autologous stem cell transplant

High-dose consolidation chemotherapy differs from induction therapy in that usually only cytarabine (ara-C) is used. The drug is given at very high doses, typically over 5 days. This process is repeated once or twice. When examined four years after this treatment, about 40% of young patients (younger than 60 years) will not show any signs of leukemia. In older adults, this number is around 15%.

Another approach after successful induction therapy is a stem cell transplant. Patients first receive very high doses of chemotherapy to destroy all bone marrow cells. This is followed by either an allogeneic (from a donor) or autologous (patient's own) stem cell transplant to restore blood cell production.

It is not clear which of the 3 treatment options (high-dose chemotherapy, allogeneic transplant, or autologous transplant) is best for consolidation. They each have their pros and cons. Doctors look at several different factors when recommending what type of post-remission therapy a patient should receive.

Stem cell transplants are intensive treatments with real risks of serious complications, including death, and their exact role in treating AML is not clear. Some doctors feel that if the patient is healthy enough to withstand the procedure and a compatible donor is available, an allogeneic transplant offers the best chance for survival. Others feel that studies have not yet shown this conclusively, and that in some cases a transplant should be reserved in case the leukemia comes back after standard treatment. Because most studies of stem cell transplants have involved patients who tend to be younger and in better health, their improved survival might not be due to the procedure. That is, they might chemotherapy 0

The following represent some of the recent advances in the management of AML:

1. Monoclonal antibodies are proteins that target specific markers on the tumor cells and destroy them.These agents have the advantage of sparing many of the normal cells and therefore have less side effects.

2. Infliximab (Remicade) is another monoclonal antibody which works against a cytokine called Tumor Necrosis Factor Alpha (TNF –alpha) which is involved in leukemic cell growth.

3. Thalidomide is an orally administered drug that has been found to slow the growth and even lead to complete remission in AML in some patients.

4. Farnesyl Transferase Inhibitors ("FTI"s) are a group of compounds that have the ability to inhibit the activation of the cancer-related gene called Ras oncogene that is present in a third of the patients with AML.

5. A new drug called Clofarabine is being tried in patients with AML at selected institutions in the country in clinical trials. This drug is given as an intravenous infusion in the out patient clinic. This drug is tolerated by patients well and is showing a lot of promise in the treatment of AML.

6. In patients who are eligible **for bone marrow or stem cell tnsplantation,** newer modalities of therapy include "**mini**" transplants or **"non-myeloablative stem cell transplantation**". These modalities utilize less intensive "conditioning" therapy prior to transplantation.

There are many exciting new agents for testing in AML, but we remain near the bottom of a very large and imposing mountain of disease. Progress in the coming decade will be built on dedication to improving molecular understanding of the basis of AML.

We advocate the introduction of novel agents earlier into the ourse of treatment, including first line therapy. Outcomes with standard therapies are poor, and even those patients in the favorable risk categories are at high risk for relapse and death.

In addition to therapeutic efforts, it is crucial to assemble large cohorts of patients with banked materials for micro array or other hypothesis-testing molecular analyses to facilitate meaningful progress in our long the climb to mountaintop .