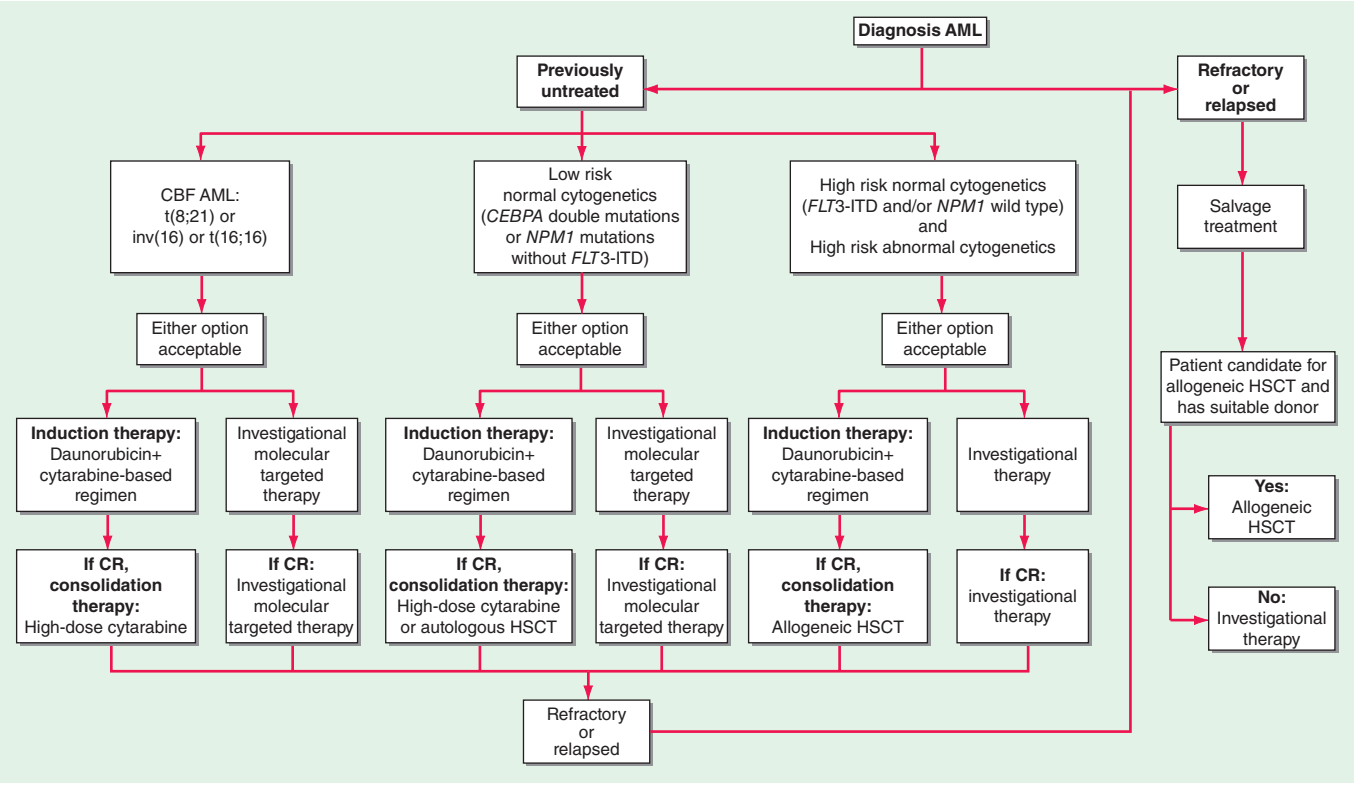

FIGURE 132-2 Flow chart for the therapy of newly diagnosed acute myeloid leukemia (AML). For all forms of AML except acute promyelocytic leukemia (APL), standard therapy includes a regimen based on a 7-day continuous infusion of cytarabine (100–200 mg/m^2 per day) and a 3-day course of daunorubicin (60–90 mg/m^2 per day) with or without additional drugs. Idarubicin (12–13 mg/m^2 per day) could be used in place of daunorubicin (not shown). Patients who achieve complete remission (CR) undergo postremission consolidation therapy, including sequential courses of high-dose cytarabine, autologous hematopoietic stem cell transplantation (HSCT), allogeneic HSCT, or novel therapies, based on their predicted risk of relapse (i.e., risk-stratified therapy). Patients with APL (see text for treatment) usually receive tretinoin and arsenic trioxide–based regimens with or without anthracycline-based chemotherapy and possibly maintenance with tretinoin. CBF, core binding factor; ITD, internal tandem duplication.

After one cycle of the 7 and 3 chemotherapy induction regimen, if persistence of leukemia is documented, the patient is usually retreated with the same agents (cytarabine and the anthracycline) for 5 and 2 days, respectively. Our recommendation, however, is to consider changing therapy in this setting.

POSTREMISSION THERAPY

Induction of a durable first CR is critical to long-term disease-free survival in AML. However, without further therapy, virtually all patients experience relapse. Thus, postremission therapy is designed to eradicate residual leukemic cells to prevent relapse and prolong survival. The type of postremission therapy in AML is often based on age and cytogenetic and molecular risk.

For younger patients, most studies include intensive chemotherapy and allogeneic or autologous hematopoietic stem cell transplantation (HSCT). In the postremission setting, high-dose cytarabine for three to four cycles is more effective than standard-dose cytarabine. The Cancer and Leukemia Group B (CALGB), for example, compared the duration of CR in patients randomly assigned after remission to four cycles of high (3 g/m^2, every 12 h on days 1, 3, and 5), intermediate (400 mg/m^2 for 5 days by continuous infusion), or standard (100 mg/m^2 per day for 5 days by continuous infusion) doses of cytarabine. A dose-response effect for cytarabine in patients with AML who were age ≤60 years was demonstrated. High-dose cytarabine significantly prolonged CR and increased the fraction cured in patients with favorable [t(8;21) and inv(16)] and normal cytogenetics, but it had no significant effect on patients with other abnormal karyotypes. As discussed, high-dose cytarabine has increased toxicity in older patients. Therefore, in this age group, for patients without CBF AML, exploration of attenuated chemotherapy regimens has been pursued. However, because the outcome of older patients is poor, allogeneic HSCT, when feasible, should be strongly considered. Postremission therapy is also a setting for introduction of new agents **(Table 132-5)**.

Autologous HSCT preceded by one to two cycles of high-dose cytarabine is also an option for intensive consolidation therapy. Autologous HSCT has been generally applied to AML patients in the context of a clinical trial or when the risk of repetitive intensive chemotherapy represents a higher risk than the autologous HSCT (e.g., in patients with severe platelet alloimmunization) or when other factors including patient age, comorbid conditions, and fertility are considered.

Allogeneic HSCT is used in patients age <70–75 years with a human leukocyte antigen (HLA)-compatible donor who have high-risk cytogenetics. Selected high-risk patients are also considered for alternative donor transplants (e.g., mismatched unrelated, haploidentical related, and unrelated umbilical cord donors). In patients with CN-AML and high-risk molecular features such as *FLT3*-ITD, allogeneic HSCT is best applied in the context of clinical trials because the impact of aggressive therapy on outcome is unknown. For older patients, exploration of reduced-intensity allogeneic HSCT has been pursued.

Trials comparing intensive chemotherapy and autologous and allogeneic HSCT have shown improved duration of remission with allogeneic HSCT compared to autologous HSCT or chemotherapy alone. However, overall survival is generally not different; the improved disease control with allogeneic HSCT is erased by the increase in fatal toxicity. In fact, relapse following allogeneic HSCT occurs in only a small fraction of patients, but treatment-related toxicity is relatively high; complications include venoocclusive disease, graft-versus-host disease (GVHD), and infections. Autologous HSCT can be administered in young and older patients and uses the same preparative regimens. Patients subsequently receive their own stem cells collected while in remission. The toxicity is relatively low with