making, as MRD negativity is the strongest predictor of favorable outcomes. 2. Reducing treatment-related toxicity, particularly in elderly or frail patients, by minimizing intensive chemotherapy and incorporating TKIs with immunotherapy. 3. Individualizing the role of allo-HSCT, reserving it primarily for patients with persistent MRD, high-risk features, or early relapse. 4. Integrating novel agents such as blinatumomab, inotuzumab, and CAR-T therapies earlier in the treatment course to improve long-term survival and potentially reduce the need for transplantation. In summary, modern management of Ph+ ALL emphasizes TKI-based regimens, MRD-guided therapeutic decisions, and the incorporation of targeted immunotherapies. While allo-HSCT remains relevant for selected patients, emerging evidence suggests that long-term remission may increasingly be achievable without transplantation, especially when potent TKIs and immunotherapies are combined. This evolving paradigm reflects a shift toward personalized, less toxic, and more effective treatment strategies for Ph+ ALL.

https://doi.org/10.1016/j.htct.2025.106206

Abstract 030

CRS AND ICANS MANAGEMENT

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CRS (Cytokine Release Syndrome) CRS is an exaggerated systemic inflammatory response triggered by treatments such as Bispecific Antibodies (BsAb), which activate T cells and cause the release of inflammatory cytokines. CRS symptoms range from mild flu-like symptoms to severe multiorgan failure. Symptoms: Fever, hypotension, hypoxia, tachycardia, organ dysfunction. Physical Examination - Temperature, blood pressure, pulse oximetry or arterial blood gas (or mixed venous blood gas/O2 saturation), skin, heart, and lung examination Laboratory Tests - Complete blood count with differential diagnosis; Coagulation (PT/PTT, fibrinogen, fibrin D-dimer); Chemistry (serum electrolytes, kidney and liver function, uric acid, lactate, LDH; C-reactive protein and ferritin (inflammation); Microbiological tests, especially in neutropenic patients (blood and urine cultures); cardiac markers are clinically indicated. Do not await laboratory results. Laboratory findings: Cytopenias, elevated creatinine, elevated liver enzymes, irregular coagulation parameters, elevated C-Reactive Protein • Management of CRS (see Management Section below) does not require laboratory testing and should not be delayed pending laboratory results. **Management by grade:** • Grade 1: Support only (antipyretic, fluid support, close monitoring). • Grade 2: Low-dose oxygen, IV fluids, low-dose vasopressors if necessary. Tocilizumab may be initiated. • Grade ≥3: High-dose oxygen, intensive care support, vasopressor requirement. **Medical Treatment:** • First choice: Tocilizumab (anti-IL-6 monoclonal antibody) • If no response: Corticosteroids (e.g., dexamethasone, methylprednisolone) are added. • Other support: Antibiotic prophylaxis/treatment, electrolyte balance, close monitoring of organ functions. **Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS):** Neurological toxicity caused by the inflammatory effects of cytokines released after BsAb treatment results in disruption of the blood-brain barrier and accumulation of inflammatory cytokines in the central nervous system. ICANS is a diagnosis of exclusion after other possibilities have been excluded. Neurological toxicity develops after immune activation. Flu-like symptoms: Fever (≥38.0°C/<100.4°F) (unattributable to another cause); nausea; fatigue; headache; rash; diarrhea, arthralgia, myalgia Hypotension Systemic inflammatory response syndrome (circulatory collapse; vascular leakage; peripheral and/or pulmonary edema; renal failure; cardiac dysfunction; multiorgan failure) Respiratory symptoms: cough; tachypnea; hypoxia, ARDS Rash and Urticaria (allergic reaction) Low-grade CRS is common and high-grade is rare **Diagnosis:** • ICANS should be suspected if there are new or worsening neurological symptoms following recent immune effector cell (IEC) therapy, such as CAR-T cell therapy or BsAb therapy. • Initial symptoms may be mild, such as loss of attention and/or slurred speech or tremors. • Further evaluation to investigate other possible causes should include review of concomitant medications or recent use of CNS-active drugs (e.g., opiates, benzodiazepines). Investigation may include a head CT or brain MRI, and a lumbar puncture to investigate infectious causes. Management: It may occur with or without CRS. **Treatment:** • Grade 1 (mild): Close neurological monitoring, supportive care. • Grade ≥2: Corticosteroids (Dexamethasone or Methylprednisolone) are initiated. • Tocilizumab is generally not effective for ICANS (because the IL-6 antibody does not cross the blood-brain barrier well). • Seizure prophylaxis/treatment: Levetiracetam is preferred. • Intensive care support in severe cases.

Keywords: CRS, ICANS, management, treatment.

https://doi.org/10.1016/j.htct.2025.106207

Abstract 031

GRAFT VERSUS HOST DISEASE PROPHYLAXIS

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Graft−versus−host disease (GvHD) is an important complication that can be observed after allogeneic hematopoietic stem cell transplantation (allo-HSCT). The incidence of Acute GvHD (aGvHD) is around 30%-50% in HLA fully matched allo-HSCT. aGvHD is also common in haploidentical and matched unrelated donor transplantation. The mechanism underlying tissue damage in aGvHD is massive inflammatory cytokine secretion. Proinflammatory cytokines [tumor necrosis factor (TNF)-α, interleukin (IL)-1β, and IL-6] are seen, as well as the increased expression of the receptor repertoire (pattern recognition receptors) on antigen-presenting cells. The most important risk factor for GvHD is HLA mismatch. Other risk factors include sex disparity between donor and recipient, the intensity of the conditioning regimen, increased age, multiparous female donors, ineffective GvHD prophylaxis, and the source of the graft. A study showed that aGvHD was

significantly more common with total body irradiation involving a myeloablative regimen and peripheral stem cell transplantation from a fully matched related donor. GvHD can be acute or chronic based on the clinical presentation and its occurrence after or before 100 days after allo-HSCT. aGvHD may occur beyond this arbitrary cut-off of 100 days. The widely accepted National Institutes of Health consensus criteria havebeen used to classify GvHD. GvHD is divided into four subclasses: 1) Classic aGvHD: Diagnostic and distinctive features of chronic GvHD (cGvHD) are absent. Clinical features of aGvHD and present within 100 days of allo-HSCT or donor lymphocyte infusion (DLI). 2) Persistent and/or recurrent late-onset aGvHD: Features of classic aGvHD without diagnostic manifestations of cGvHD occurring beyond 100 days after allo-HSCT or DLI. 3) Classic cGvHD: Present at any time after HSCT. Diagnostic and distinctive features of cGvHD are present without aGvHD. 4) Overlap syndrome; Features of both cGvHD and aGvHD can be seen. The most commonly affected organsa are:Skin,eyes,oral mucosa,liver,GIS tract,genital organs,lungs,joints and fascia. The most important step for the prevention of GvHD is minimizing risk factors with donor selection and a preparative regimen. GvHD prophylaxis is essential for patients undergoing allo-HSCT. Guidelines for GvHD prophylaxis have been proposed by the European Group for Blood and Marrow Transplantation and European LeukemiaNet . The most common form of GvHD prophylaxis has been the combination of cyclosporine and a short course of methotrexate, which demonstrated improved survival compared to either drug alone. Both cyclosporine and tacrolimus decreased the proliferation of T-lymphocytes . Tacrolimus plus methotrexate is better in decreasing the risk for aGvHD than the combination of cyclosporine and methotrexate, particularly in unrelated HSCT. Both regimens are considered as cornerstones for most GvHD prevention strategies for patients receiving allo HSCT. The effects of the addition of corticosteroids to the combination of cyclosporine and a short course of methotrexate have shown conflicting results. Calcineurin inhibitors and Ruxolitinib, a JAK 1/2 inhibitor, are also used as prophylactic treatment. Unfortunately, there is no standard indication or timing for the initiation of therapy for GvHD. Many agents have been tested alone or in combination with corticosteroids. Extracorporeal photopheresis (ECP), mycophenolate mofetil, sirolimus, everolimus, rituximab, and ibrutinib are available options.

https://doi.org/10.1016/j.htct.2025.106208

Abstract 032

CHRONİC LYMPHOCYTIC LEUKEMIA (CLL): IMMUNOGENETICS AND DIAGNOSIS

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CLL is a monoclonal proliferation of mature B lymphocytes defined by an absolute clonal count $\geq 5 \times 10^9$/L in blood. CLL is clinically heterogeneous: some patients remain asymptomatic for years, whereas others need multiple lines of therapy. BCR biology and immunogenetics. A central driver of CLL biology is B-cell receptor (BCR) signaling. Compared with normal B cells, CLL cells display low IgM expression, variable responses to antigen, and tonic activation of anti-apoptotic pathways. Gene-expression and tissue array studies show up-regulation of BCR-pathway genes in lymph nodes and marrow versus blood, highlighting microenvironmental homing. The IGHV mutation status is a key immunogenetic marker: about 60% of patients have IGHV mutated ≥2% from germline (typically indolent course), while ∼40% have unmutated IGHV (<2%), associated with faster progression and shorter survival before the era of BCR-targeted therapies. Roughly 30% of cases carry stereotyped BCRs; certain stereotyped subsets (e.g., 1 and 2) predict higher-risk disease. Cytogenetic lesions. Recurrent abnormalities identified by FISH (and, when needed, stimulated metaphase karyotype) include del(13q14.3) (most common; favorable when isolated), trisomy 12 (intermediate risk), del(11q22.3) involving ATM (bulky nodes, aggressive disease in younger patients), and del (17p13.1) affecting TP53 (worst prognosis, poor response to traditional chemotherapy). Complex karyotype (≥3 abnormalities) adversely impacts time to treatment and overall survival. Because clonal evolution can occur even without therapy, FISH (± cytogenetics) should be reassessed before each line of treatment, particularly to detect new del(17p). Gene mutations and microRNAs. CLL genomes are relatively simple (≈20 nonsynonymous changes and ≈5 structural lesions on average) and lack a unifying driver. Recurrently mutated genes include SF3B1, NOTCH1, MYD88, ATM, and TP53. NOTCH1 mutations (∼15%) often co-occur with trisomy 12 and may confer reduced sensitivity to anti-CD20 antibodies and increased risk of Richter transformation; SF3B1 relates to DNA-damage responses; TP53 mutations rise from ∼5% in early untreated disease to ∼40% in advanced disease, frequently coexisting with del(17p). ATM mutations (10–15%) often accompany del(11q). MYD88 mutations are enriched in IGHV-mutated CLL and associate with a more indolent course. Non-coding alterations are also relevant: del(13q14.3) deletes the miR-15/16 cluster, derepressing anti-apoptotic programs (e.g., BCL2); loss of miR-181a and over-expression of miR-155 further support leukemic survival. Immune dysregulation. Beyond the malignant clone, CLL features innate and adaptive immune defects: reduced complement, qualitative neutrophil and NK-cell dysfunction, $CD4^+$ T-cell exhaustion with impaired cytotoxicity, Th1→Th2 polarization, and T-regulatory expansion. Hypogammaglobulinemia is common (≈85% over the disease course), with low IgG/IgA correlating with infections. Diagnosis and differential. CLL is most often detected incidentally via lymphocytosis. Flow cytometry confirms a characteristic phenotype—$CD19^+$, CD20 (dim), $CD22^+$, $CD23^+$, $CD200^+$, $CD5^+$, with dim surface Ig (kappa or lambda). When blood clonal B cells are $\geq 5 \times 10^9$/L, no additional testing is needed to confirm CLL. Take-home. Integrating flow cytometry, cytogenetics (FISH/karyotype), and targeted sequencing with IGHV status and non-coding lesions underpins modern risk stratification and sharpens diagnostic certainty in CLL.

https://doi.org/10.1016/j.htct.2025.106209