Supportive Care for NHL
Tumor Lysis Syndrome (TLS)

- Laboratory hallmarks of TLS:
  - High potassium
  - High uric acid
  - High phosphorous
  - Low calcium

- Symptoms of TLS:
  - Nausea and vomiting, shortness of breath, irregular heartbeat, clounding of urine, lethargy, and/or joint discomfort.

- High-risk features
  - Histologies of Burkitt Lymphoma and Lymphoblastic Lymphoma; occasionally patients with DLBCL and CLL
  - Spontaneous TLS
  - Elevated WBC
  - Bone marrow involvement
  - Pre-existing elevated uric acid
  - Ineffectiveness of allopurinol
  - Renal disease or renal involvement by tumor

Treatment of TLS:

- TLS is best managed if anticipated and treatment is started prior to chemotherapy.
- Centerpiece of treatment includes
  - Rigorous hydration
  - Management of hyperuricemia
  - Frequent monitoring of electrolytes and aggressive correction is essential
- First-line and at retreatment
  - Allopurinol beginning 2–3 days prior to chemotherapy and continued for 10–14 days
  - Rasburicase is indicated for patients with any of the following risk factors:
    - presence of any high-risk feature
    - urgent need to initiate therapy in a high-bulk patient
    - situations where adequate hydration may be difficult or impossible
    - Acute renal failure
  - One dose of rasburicase is frequently adequate. Doses of 3–6 mg are usually effective. Redosing should be individualized.
- If TLS is untreated, its progression may cause acute kidney failure, cardiac arrhythmias, seizures, loss of muscle control, and death.
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For other immunosuppressive situations, see NCCN Guidelines for Prevention and Treatment of Cancer-Related Infections.

Monoclonal Antibody Therapy and Viral Reactivation

Anti-CD20 Antibody Therapy

Hepatitis B virus (HBV):
- Hepatitis B surface antigen (HBsAg) and Hepatitis B core antibody (HBcAb) testing for all patients receiving anti-CD20 antibody therapy
  - Quantitative hepatitis B viral load by PCR and surface antibody only if one of the screening tests is positive
- Note: Patients receiving IV immunoglobulin (IVIG) may be HBcAb-positive as a consequence of IVIG therapy.
- Prophylactic antiviral therapy with entecavir is recommended for any patient who is HBsAg-positive and receiving anti-lymphoma therapy. If there is active disease (PCR+), it is considered treatment/management and not prophylactic therapy. In cases of HBcAb positivity, prophylactic antiviral therapy is preferred; however, if there is a concurrent high-level hepatitis B surface antibody, these patients may be monitored with serial hepatitis B viral load.
  - Avoid lamivudine due to risks of resistance development.
  - Other antivirals including adefovir, telbivudine, and tenofovir are proven active treatments and are acceptable alternatives.
  - Monitor hepatitis B viral load with PCR monthly through treatment and every 3 months thereafter
    - If viral load is consistently undetectable, treatment is considered prophylactic
    - If viral load fails to drop or previously undetectable PCR becomes positive, consult hepatologist and discontinue anti-CD20 antibody therapy
  - Maintain prophylaxis up to 12 mo after oncologic treatment ends
    - Consult with hepatologist for duration of therapy in patient with active HBV

Hepatitis C virus (HCV):
- New evidence from large epidemiology studies, molecular biology research, and clinical observation supports an association of HCV and B-cell NHL. Recently approved direct-acting antiviral agents (DAA) for chronic carriers of HCV with genotype 1 demonstrated a high rate of sustained viral responses.
  - Low-grade B-cell NHL
    - According to the American Association for the Study of Liver Diseases, combined therapy with DAA should be considered in asymptomatic patients with HCV genotype 1 since this therapy can result in regression of lymphoma.
  - Aggressive B-cell NHL
    - Patients should be initially treated with chemoimmunotherapy regimens according to NCCN Guidelines for NHL.
    - Liver functional tests and serum HCV RNA levels should be closely monitored during and after chemoimmunotherapy for development of hepatotoxicity.
    - Antiviral therapy should be considered in patients in complete remission after completion of lymphoma therapy.

Anti-CD20 Antibody Therapy and Brentuximab Vedotin

Progressive multifocal leukoencephalopathy (PML):
- Caused by the JC virus and is usually fatal.
  - Diagnosis made by PCR of CSF and in some cases brain biopsy.
- No known effective treatment.
- Clinical indications may include changes in behavior such as confusion, dizziness or loss of balance, difficulty talking or walking, and vision problems.
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Monoclonal Antibody Therapy and Viral Reactivation (continued)

Anti-CD52 Antibody Therapy: Alemtuzumab
Cytomegalovirus (CMV) reactivation:
• The current appropriate management is controversial; some NCCN Member Institutions use ganciclovir (oral or IV) preemptively if viremia is present, others only if viral load is rising.
• CMV viremia should be measured by quantitative PCR at least every 2 to 3 weeks.
• Consultation with an infectious disease expert may be necessary. See NCCN Guidelines for Prevention and Treatment of Cancer-Related Infections.

Rituximab Rapid Infusion
• If no infusion reactions were experienced with prior cycle of rituximab, a rapid infusion over 90 minutes can be used.

Methotrexate and Glucarpidase
• Consider use of glucarpidase if significant renal dysfunction and methotrexate levels are >10 microM beyond 42 to 48 hours.
  Leucovorin remains a component in the treatment of methotrexate toxicity and should be continued for at least 2 days following glucarpidase administration. However, be aware that leucovorin is a substrate for glucarpidase, and therefore should not be administered within two hours prior to or following glucarpidase.