NCCN 11th Annual Congress:
Hematologic Malignancies™

Supportive Care in the Management of T-cell Lymphomas

Erin Kopp, ACNP-BC
City of Hope Comprehensive Cancer Center

National Comprehensive Cancer Network®

NCCN.org – For Clinicians | **NCCN.org/patients** – For Patients

Objectives

- Discuss the role of supportive care in patients with Cutaneous T-Cell Lymphoma
- Review the treatment-related toxicities and the supportive care measures used for their prevention and management in patients with CTCL
- Identify risk factors for tumor lysis syndrome (TLS) in patients undergoing treatment for Peripheral T-Cell Lymphoma (PTCL)
- Develop an effective management strategy for management of TLS in patients with PTCL

Cutaneous T-Cell Lymphoma

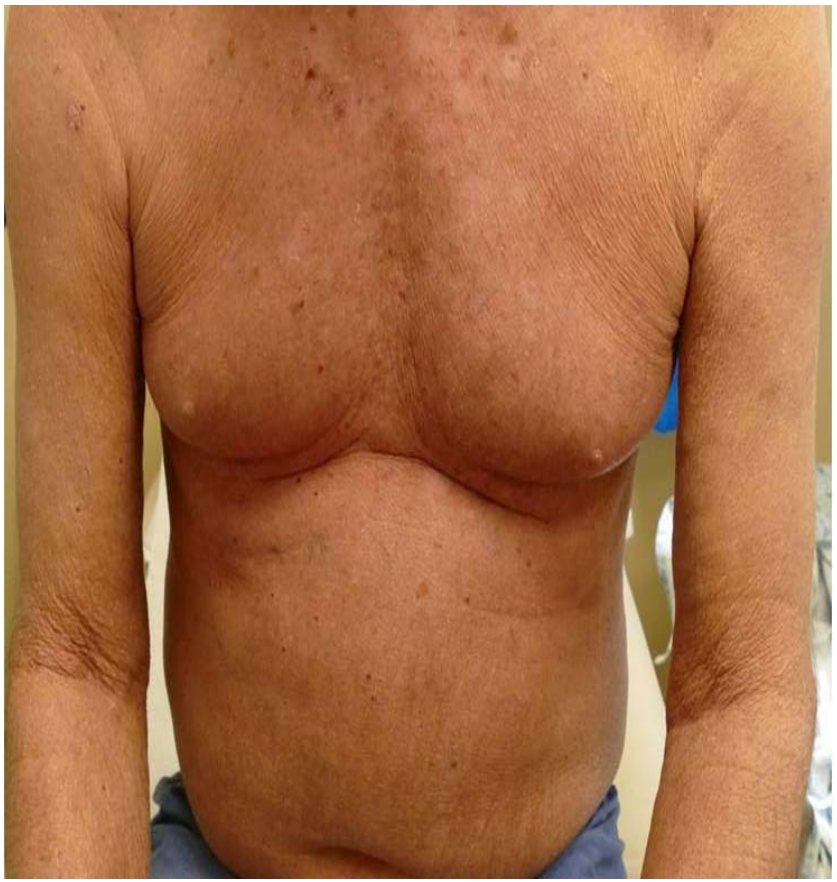
- 70-80% of all cutaneous lymphomas are of T-cell origin
- Mycosis Fungoides is the most common subtype
- Sezary Syndrome is a leukemic variant that is more aggressive
- Treatment approaches are dependent on multiple variables
- Goal of therapy is to achieve remission and optimize quality of life

Benjamin Chase A et al. Clin J Oncol Nurs 2015;19:E131-139.

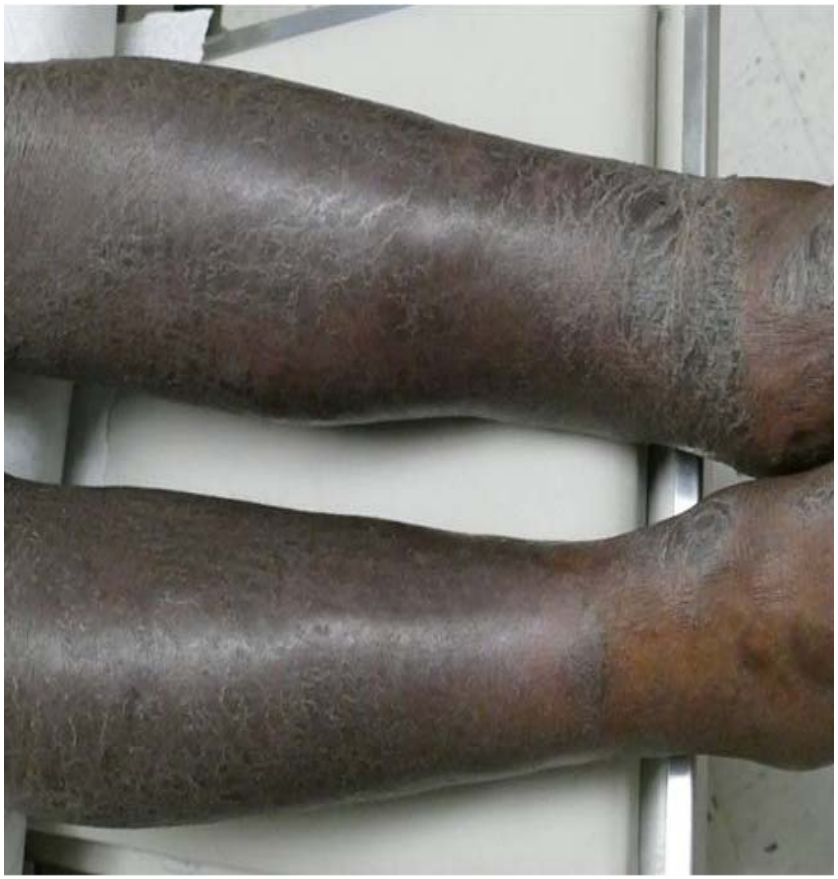
Heterogeneity in the Management of CTCL

- Presentation
- Staging
- Skin-directed therapy
- Systemic therapy
- Combination therapy

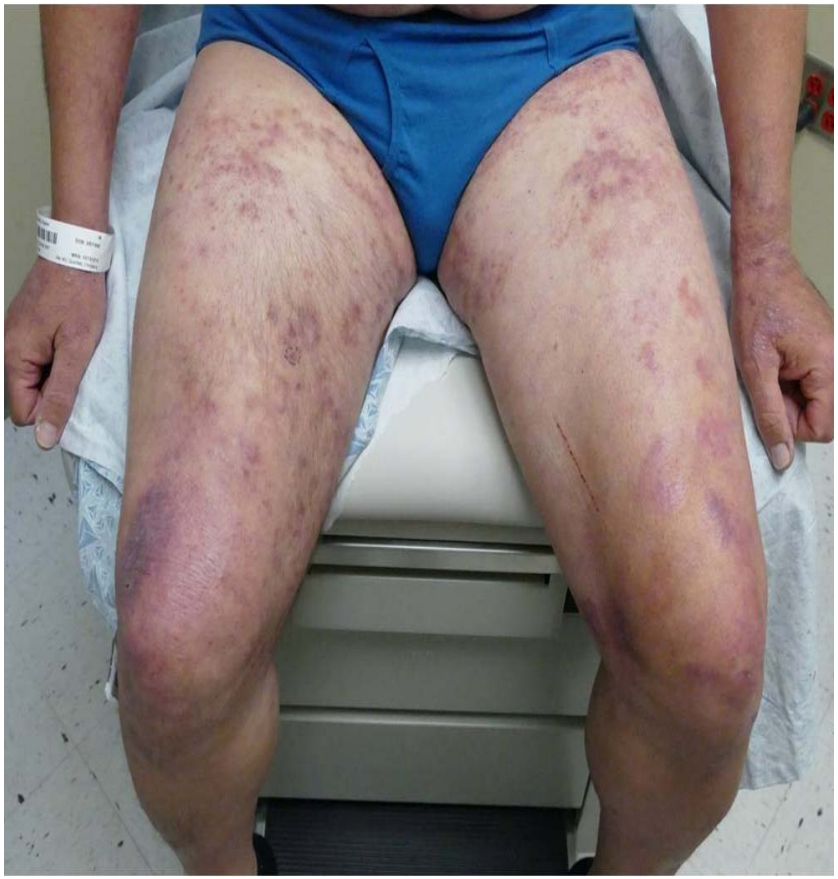
Clinical Presentation: Erythroderma



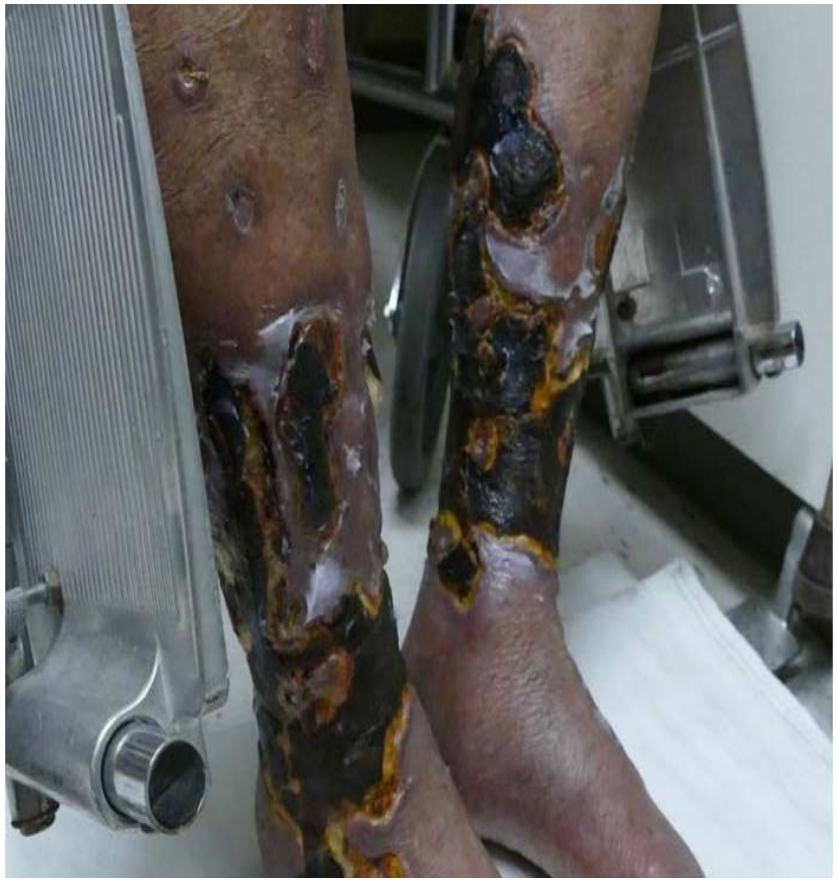
Clinical Presentation: Ichthyotic Changes



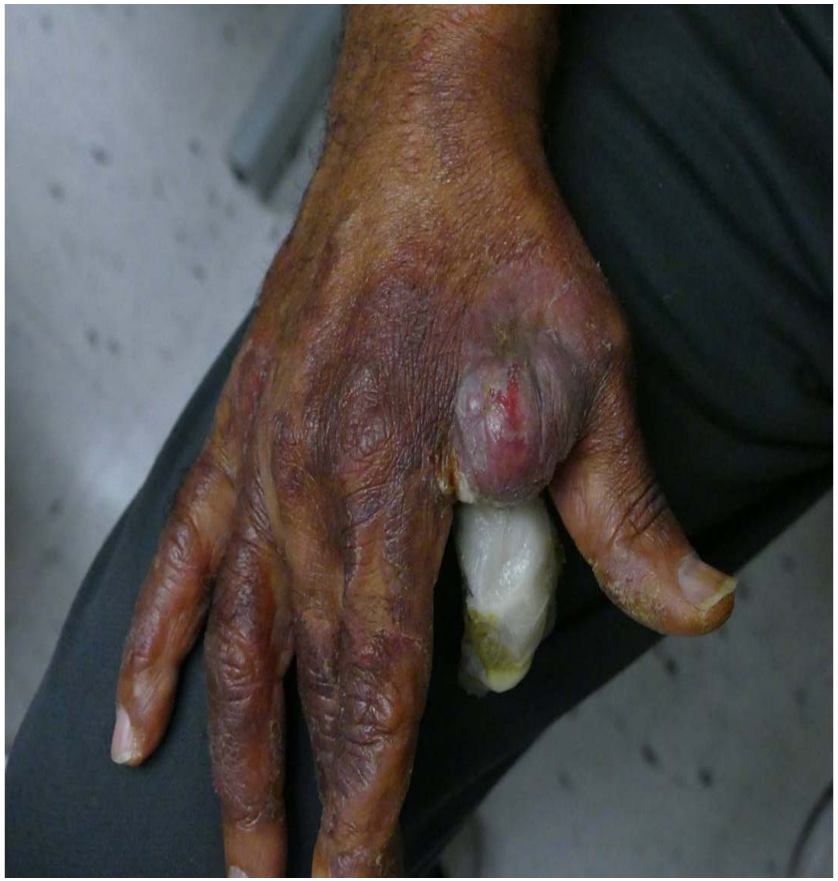
Clinical Presentation: Folliculotropic



Clinical Presentation: Necrotic lesions predebridement



Clinical Presentation: Tumor



Staging

- Based on skin, node, visceral and blood involvement
- BSA covered involved in disease
- Patches, plaques, tumors
- Sezary cell involvement- evaluate for CD4+, CD7+, and CD 26+
- Stage 1A- IVB

National Comprehensive Cancer Network®

NCCN Guidelines Version 3.2016
Mycosis Fungoides/Sezary Syndrome

SUPPORTIVE CARE FOR MF/SS

Pruritus

- **Assessment**
  - Pruritus should be assessed at each visit using consistent measurements
  - Generalized pruritus and localized pruritus should be distinguished
  - Correlation between sites of disease and localization of pruritus should be noted
  - Other potential causes for pruritus should be ruled out
- **Treatment**
  - Moisturizers and emollients
  - Topical steroid (appropriate strength for body region) ± occlusion
  - Optimize skin-directed and systemic therapy
  - Topical preparations - camphor/menthol formulations, pramoxine formulations
  - Systemic agents
    - First-line
      - Antihistamines
      - Doxepin
      - Gabapentin
    - Second-line
      - Aprepitant
      - Mirtazapine
      - Selective serotonin reuptake inhibitors
    - Third-line
      - Naltrexone

MFSS-B

National Comprehensive Cancer Network®

NCCN Guidelines Version 3.2016
Mycosis Fungoides/Sezary Syndrome

SUGGESTED TREATMENT REGIMENS

COMBINATION THERAPIES

Skin-directed* + *Systemic

- Phototherapy + retinoid
- Phototherapy + IFN
- Phototherapy + photopheresis
- Total skin electron beam + photopheresis

Systemic* + *Systemic

- Retinoid + IFN
- Photopheresis + retinoid
- Photopheresis + IFN
- Photopheresis + retinoid + IFN

MFSS-A

National Comprehensive Cancer Network®

NCCN Guidelines Version 3.2016
Mycosis Fungoides/Sezary Syndrome

SUPPORTIVE CARE FOR MF/SS
Infections

- Active or Suspected Infections
  - Cutaneous viral infections
    - High risk for skin dissemination of localized viral infections (HSV/VZV)
  - Erythroderma:
    - Skin swab and nares cultures for Staphylococcus aureus (S. aureus) infection or colonization
    - Intranasal mupirocin
    - Oral dicloxacillin or cephalexin
    - Sulfamethoxazole/trimethoprim, doxycycline if suspect MRSA
    - Vancomycin if no improvement or bacteremia
    - Bleach baths or soaks (if limited area)
  - Ulcerated and necrotic tumors:
    - Gram-negative rods (GNR) common in necrotic tumors may lead to bacteremia and sepsis
    - If high suspicion for infection, obtain blood cultures, start antibiotics even if fever absent
    - Role of wound cultures not clear due to colonization
    - Empirical therapy for both GNR and gram-positive coccal infections is necessary initially
- Prophylaxis
  - Optimize skin barrier protection
  - Mupirocin for S. aureus colonization
  - Bleach baths or soaks (if limited area)
  - Avoid central lines (especially in erythrodermic patients)
  - For patients receiving alemtuzumab, see NHODG-B.

MFSS-B

Skin-directed Therapies

- Topical corticosteroids
- Topical chemotherapy
  - Topical nitrogen mustard
- Topical retinoids/rexinoids
  - Bexarotene
  - Tazarotene
- Phototherapy
  - NB-UVB
  - PUVA
- Radiation therapy
  - Total skin electron beam therapy (TSEBT)
  - Local radiation site specific

Topical Corticosteroids

- Skin irritation, allergy
- Skin thinning, stretch marks
- Systemic absorption when high potency steroid utilized on multiple areas
- Utilize lowest potency with maximum efficacy
- Assess for systemic effects

Topical Nitrogen Mustard

- Topical chemotherapy
- Requires care when applying. Utilization of gloves important
- Darkening of skin; often occurs as lesions are resolving. Patients may think disease is progressing
- Skin irritation

  SIGNIFICANT redness, burning
- Appropriate patient education
- Apply thin layer only to affected areas
- Apply corticosteroid to areas of nitrogen mustard therapy application in the AM and/or PM
- Refrigerate topical steroid prior to application

Chase et al. *Clin J Oncol Nurs* 2015;19:E131-139.

Topical Retinoids

- Vitamin A derivatives
- Applied once daily
- Redness, itching, warmth, swelling, burning, scaling or other irritation
- Increases sensitivity to light
- Apply once every other day for first week; titrate as tolerated

See Package Insert for Bexarotene Gel for full prescribing information. Available at http://www.accessdata.fda.gov/

Phototherapy: PUVA or Narrowband-UVB

- Stops the abnormal proliferation of malignant T-cells in the skin by preventing the cells from duplicating their DNA
- Long-term responses
- Skin burn
- Itch-may worsen or mitigate pre-existing
- Nausea with psoralen use
- Increased risk for skin cancers with UV exposure
- Follow established protocol based on skin typing to minimize skin burn
- Itch- Moisturizers, camphor based formulation, antihistamine, SSRI, SNRI, tricyclic antidepressant, gabapentin, aprepitant, mirtazapine, naltrexone
- Nausea – appropriate antiemetic therapy
- Vigilance with skin surveillance

Systemic Therapy

- Retinoids
- Interferon
- Cytotoxic Agents
- Monoclonal Antibodies
- HDAC Inhibitors

Retinoids: Bexarotene

- Systemic retinoid
- Metabolized by P450 3A4
- Can cause primary hypothyroidism
- Can lead major lipid abnormalities
- Monitor TSH, and Free T4, triglyceride every 8 weeks
- Leukopenia and neutropenia
- Take with food

See Package Insert for Bexarotene capsules for full prescribing information. Available at http://www.accessdata.fda.gov/

Interferon

- Multiple adverse reactions
- Injection site issues
- Psychological changes
- Influenza like symptoms

Cytotoxic Agents/Antimetabolites

- Pralatrexate/Methotrexate
- Myelosuppression
- Significant risk for infection
- Neuropathy

Monoclonal Antibodies

- Reactivation of previous viral infection
- Hepatic issues
- Tumor lysis syndrome (TLS)
- Infusion reaction
- Progressive Multifocal Leukoencephalopathy (PML)

HDAC Inhibitors

- Vorinostat, Romidepsin, Belinostat
- QT Interval prolongation
- Specific parameters for potassium and magnesium levels prior to administration
- Underestimated emetogenic potential
- Nutritional deficiency
- Myelosuppression

See Package Insert for Vorinostat for full prescribing information. Available at http://www.accessdata.fda.gov/.
See Package Insert for Romidepsin for full prescribing information. Available at http://www.accessdata.fda.gov/.

Treatment on the Horizon

- MicroRNA (miRNA) Inhibitors
- Immunotherapy
- PI3 kinase inhibitors
- SGX301 (PDT using synthetic hypericin)
- Anti-CCR4 antibody

Clinical Pearls

- Disease and treatment burden high
- Assess symptoms and side effects often and thoroughly
- Provide multiple options for supportive care management
- Supportive care complements curative care and is critical to maintaining quality of life
- Patient knows best

Case Study
R.F.

- 44-year-old female diagnosed with Mycosis fungoides
- Transformed with multiple skin nodules and severe pruritus
- Failed multiple lines of therapy including brentuximab vedotin and chemotoxic agents
- Started on lenalidomide and romidepsin
- Admitted to hospital for hypotension and fever with AKI
- Ultimate diagnosis???

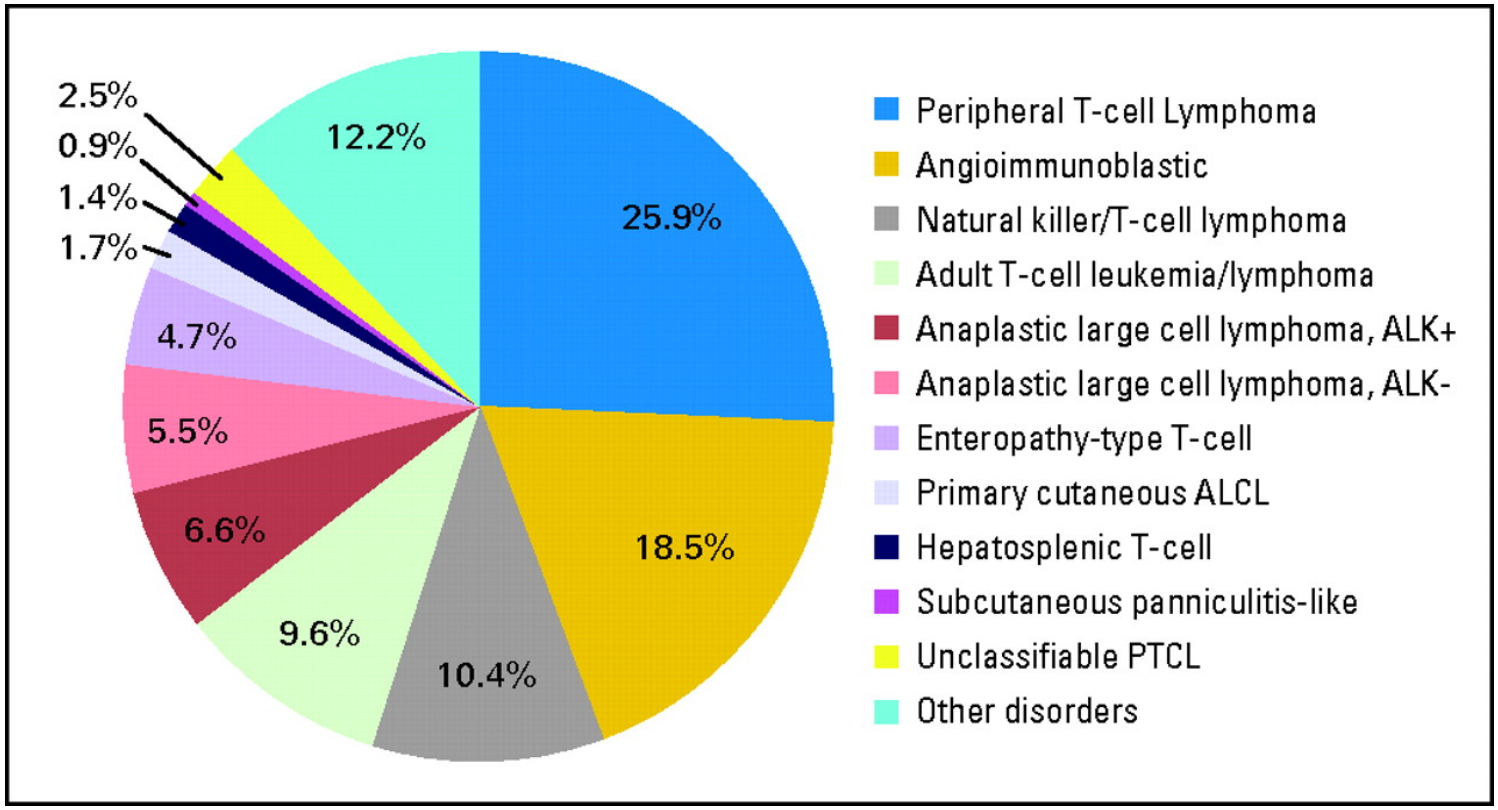
Peripheral T-Cell lymphoma

- Rare among the Non-Hodgkin lymphomas
- Diverse presentation and disease course
- Many times extra nodal
- Diagnosis and treatment difficult
- Upfront treatment not curative
- Combination therapy often indicated
- Under recognized risk for Tumor Lysis Syndrome

Practical Classification of PTCL/NK T-Cell Lymphoma

Nodal	Cutaneous	Extranodal	Primary Leukemic	Varied presentation
Peripheral T-cell lymphoma, not otherwise specified (PTCL-NOS) Angioimmunoblastic T-cell lymphoma (AITL) Anaplastic large cell lymphoma (ALCL), ALK+ Anaplastic large cell lymphoma (ALCL) , ALK-	Mycosis fungoides Sezary syndrome Primary cutaneous CD30-positive T-cell lymphoproliferative disorders - Lymphomatoid papulosis - Primary cutaneous anaplastic large cell lymphoma Primary cutaneous γδ T-cell lymphoma Primary cutaneous CD8-positive aggressive epidermotropic cytotoxic T-cell lymphoma Primary cutaneous CD4-positive small medium T-cell lymphoma	Extranodal NK/T-cell lymphoma, nasal type Enteropathy associated T- cell lymphoma Hepatosplenic T-cell lymphoma Subcutaneous panniculitis like T- cell lymphoma Seroma associated ALCL of breast	Aggressive NK-cell leukemia T-cell prolymphocytic leukemia T-cell large granular lymphocytic leukemia Adult T-cell leukemia lymphoma	Chronic lymphoproliferative disorder of NK cells Systemic EBV positive T-cell lymphoproliferative disease of childhood Hydroa vacciniforme-like lymphoma Systemic EBV+ T-cell lymphoproliferative disease-associated with hemophagocytic syndrome

SUBTYPE DISTRIBUTION



Vose J, Armitage J, Weisenburger D; International T Cell Lymphoma J Clin Oncol 26:4124-4130

TLS in PTCL:
Risk Factors and Presentation

Risk Factors

- Bone marrow involvement
- Pre-existing elevated uric acid (>7.5mg/dL)
- High tumor proliferation rate
- Responsiveness of malignancy to therapy
- Large tumor burden
- Preexisting renal dysfunction and/or exposure to nephrotoxic agents
- Dehydration during treatment
- Risk by disease
  - High risk- ATLL, PTCL with elevated LDH and a bulky mass
  - Intermediate risk-ATLL, PTCL with elevated LDH

- Cairo-Bishop Definition
  - Hyperkalemia
  - Hyperuricemia
  - Hyperphosphatemia
  - Hypocalcemia
  - 2 or more of the identified metabolic abnormalities presenting within 3 days before or within seven days after initiation of chemotherapy
  - Clinical TLS defined as the combination of laboratory TLS plus one or more of the following:
    - serum creatinine $\geq$ 1.5 times ULN
    - cardiac arrhythmia/sudden death
    - seizure
- Nausea/Vomiting, shortness of breath, cardiac rhythm, abnormalities, lethargy, urine changes, joint discomfort

Tumor lysis syndrome: Definition, pathogenesis, clinical manifestations, etiology, and risk factors; Uptodate.com. Retrieved 9/1/16

National Comprehensive Cancer Network®

NCCN Guidelines Version 3.2016
Non-Hodgkin's Lymphomas

SUPPORTIVE CARE FOR NHL

Tumor Lysis Syndrome (TLS)

- 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 for hyperuricemia
    - Allopurinol beginning 2–3 days prior to chemotherapy and continued for 10–14 days

      or

      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.

NHODG-B

Management of TLS

- Prevention and management of hyperuricemia: allopurinol 2-3 days prior to treatment. Adjust based on patient response/uric acid level
- Rigorous hydration-volume expansion considered most important intervention before, during, and after chemotherapy
- Aggressive monitoring and correction of electrolyte imbalance
- Rasburicase as indicated
  - Pretreatment with rasburicase if high-risk

Howard SC et al. N Engl Journal Med.2011;364(19);1844-1854

NCCN Member Institutions