National Comprehensive Cancer Network®

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)

Non-Hodgkin's Lymphomas

Version 2.2015

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Castleman's Disease

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DIAGNOSIS[a,b,c]

ESSENTIAL:

- **Hematopathology review of all slides with at least one paraffin block representative of the lymphoproliferative disorder. Rebiopsy if consult material is nondiagnostic.**
- **An FNA or core needle biopsy alone is not generally suitable for initial diagnosis of Castleman's disease. Excisional or incisional biopsy are preferable.**
- **Adequate immunophenotyping to establish diagnosis[d]**
  - **IHC panel: kappa/lambda, CD20, CD3, CD5, CD138, HHV-8 LANA-1**
  - **EBER-ISH**

USEFUL UNDER CERTAIN CIRCUMSTANCES:

- **Molecular analysis (PCR) to detect immunoglobulin and *TCR* gene rearragements**
- **IHC: Ki-67 index; Ig heavy chains,[e] CD10, BCL2, BCL6, cyclin D1, CD21, or CD23, CD38, MUM-1, PAX-5**
- **Cell surface marker analysis by flow cytometry: kappa/lambda, CD19, CD20, CD5, CD23, CD10**

WORKUP[f]

ESSENTIAL:

- **Physical exam: attention to node-bearing areas, including Waldeyer's ring, and to size of liver and spleen**
- **Performance status**
- **Assess for criteria for active disease[g]**
- **CBC, differential, platelets**
- **Comprehensive metabolic panel**
- **LDH, CRP, ESR**
- **Beta-2-microglobulin, serum protein electrophoresis and urine electrophoresis with immunofixation, serum light chains, quantitative immunoglobulins**
- **HIV ELISA, HHV-8 DNA titer by PCR, Hepatitis B testing,[h] EBV DNA titer by PCR**
- **PET-CT scan (preferred) or chest/abdominal/pelvic CT with contrast of diagnostic quality**
- **Pregnancy testing in women of child-bearing age (if chemotherapy planned)**

USEFUL UNDER CERTAIN CIRCUMSTANCES

- **If HHV-8/KSHV or HIV positive, screening for concurrent Kaposi's sarcoma is strongly recommended**
- **Bone marrow biopsy + aspirate**
- **Neck CT with contrast**
- **MUGA scan/echocardiogram if anthracycline or anthracenedione-based regimen is indicated**
- **sIL-6, sIL10, VEGF, uric acid, ferritin[i]**
- **Hepatitis C testing**
- **Discussion of fertility issues and sperm banking**

Unicentric → **See CD-2**

Multicentric → **See CD-3**

[a] For AIDS-related Lymphoma associated with Castleman's disease, see AIDS-1. For DLBCL-associated with CD in non-HIV patients, see BCEL-1.

[b] There are 2 variants – hyaline vascular (virtually always unicentric, HHV8-) and plasma cell (may be multicentric, often HHV8+, +/- HIV+).

[c] Two types of DLBCL are associated with the HHV8+ PC type: plasmablastic (EBV-) and "germinotropic" (EBV+).

[d] See Use of Immunophenotyping/Genetic Testing in Differential Diagnosis of Mature B-Cell and NK/T-Cell Neoplasms (NHODG-A).

[e] In plasma cell variant HHV8+, plasmablasts are IgM lambda while normal plasma cells are IgG or A polytypic.

[f] If concurrent polyneuropathy and monoclonal plasma cell disorder, a workup for POEMS syndrome is recommended.

[g] See Criteria for Active Disease (CD-A).

[h] Hepatitis B testing is indicated because of the risk of reactivation with immunotherapy + chemotherapy. Tests include hepatitis B surface antigen and core antibody for a patient with no risk factors. For patients with risk factors or previous history of hepatitis B, add e-antigen. If positive, check viral load and consult with gastroenterologist.

[i] Measurement of acute phase reactants maybe helpful in monitoring therapy.

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.

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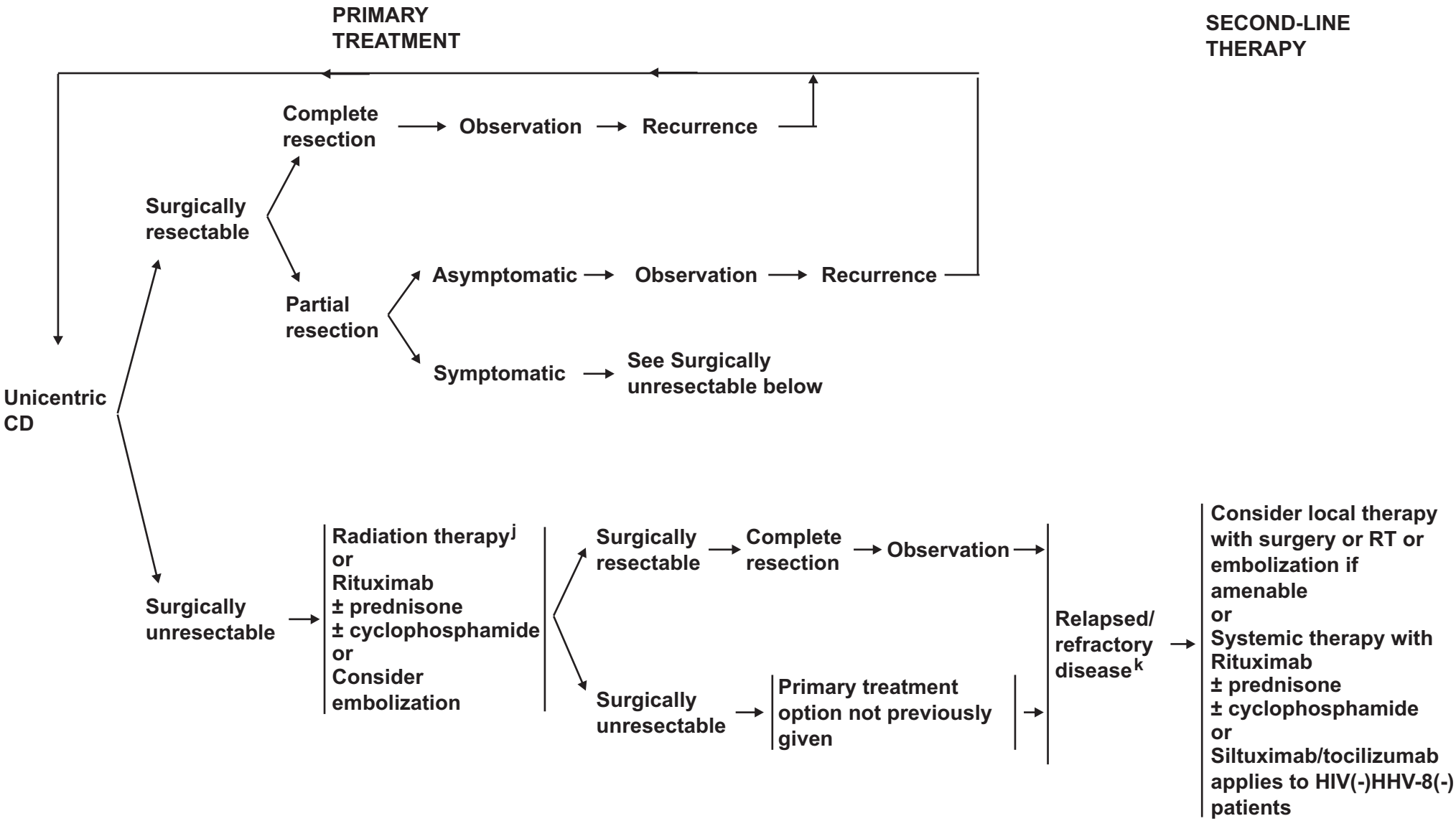

[j]Patients with non-bulky disease may be observed after RT.
[k]Encourage biopsy to rule out transformation to DLBCL or concomitant development of other malignancies or opportunistic infections.

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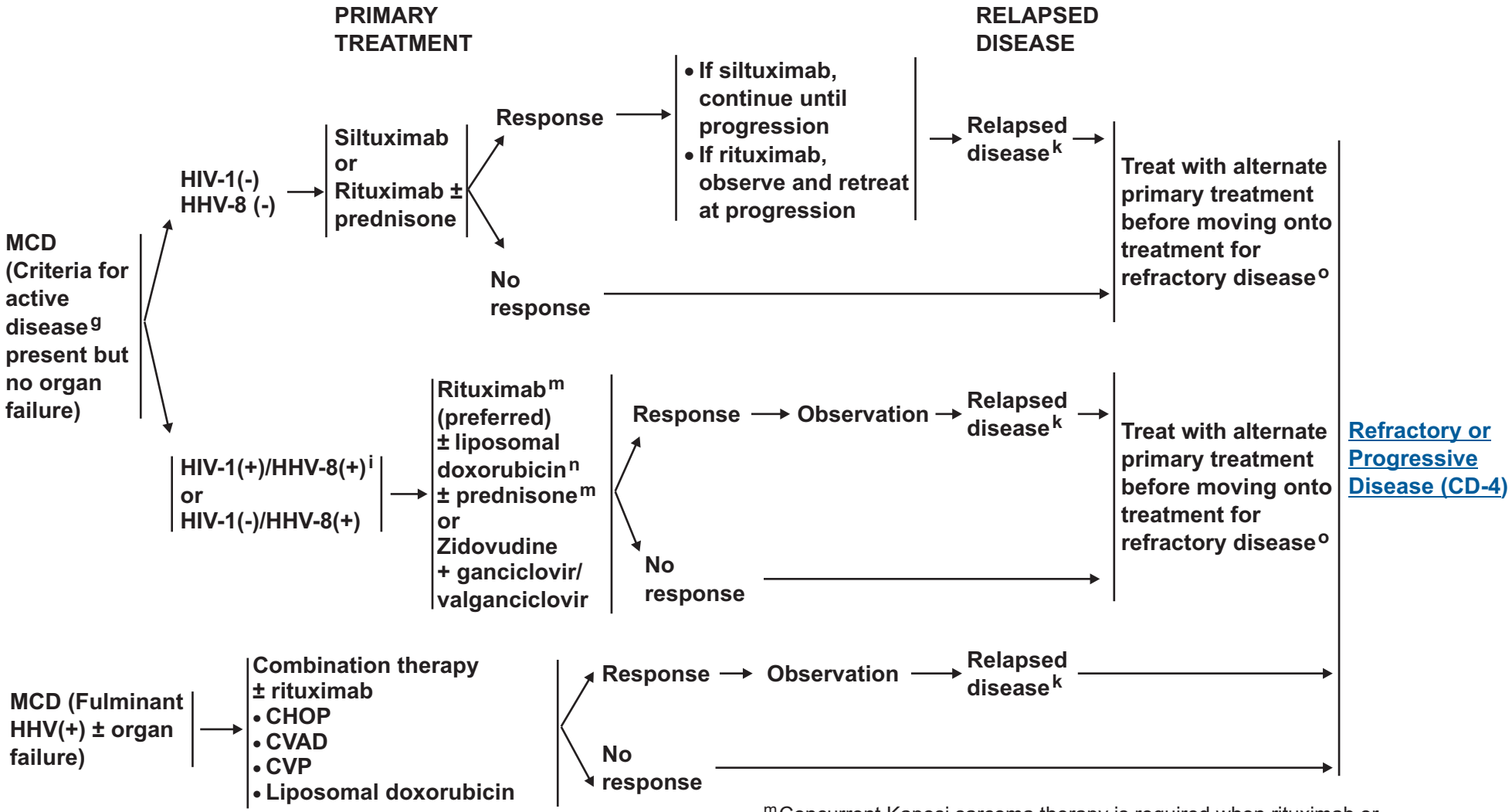

[g] See Criteria for Active Disease (CD-A).

[k] Encourage biopsy to rule out transformation to DLBCL or concomitant development of other malignancies or opportunistic infections.

[l] All HIV+ patients should be on combination antiretroviral therapy (cART).

[m] Concurrent Kaposi sarcoma therapy is required when rituximab or prednisone is given for primary treatment.

[n] Combination of rituximab and liposomal doxorubicin is strongly recommended for patients with Kaposi sarcoma to avoid flare-up.

[o] Rituximab ± prednisone may repeat without limit if progression ≥6 months of completion of rituximab.

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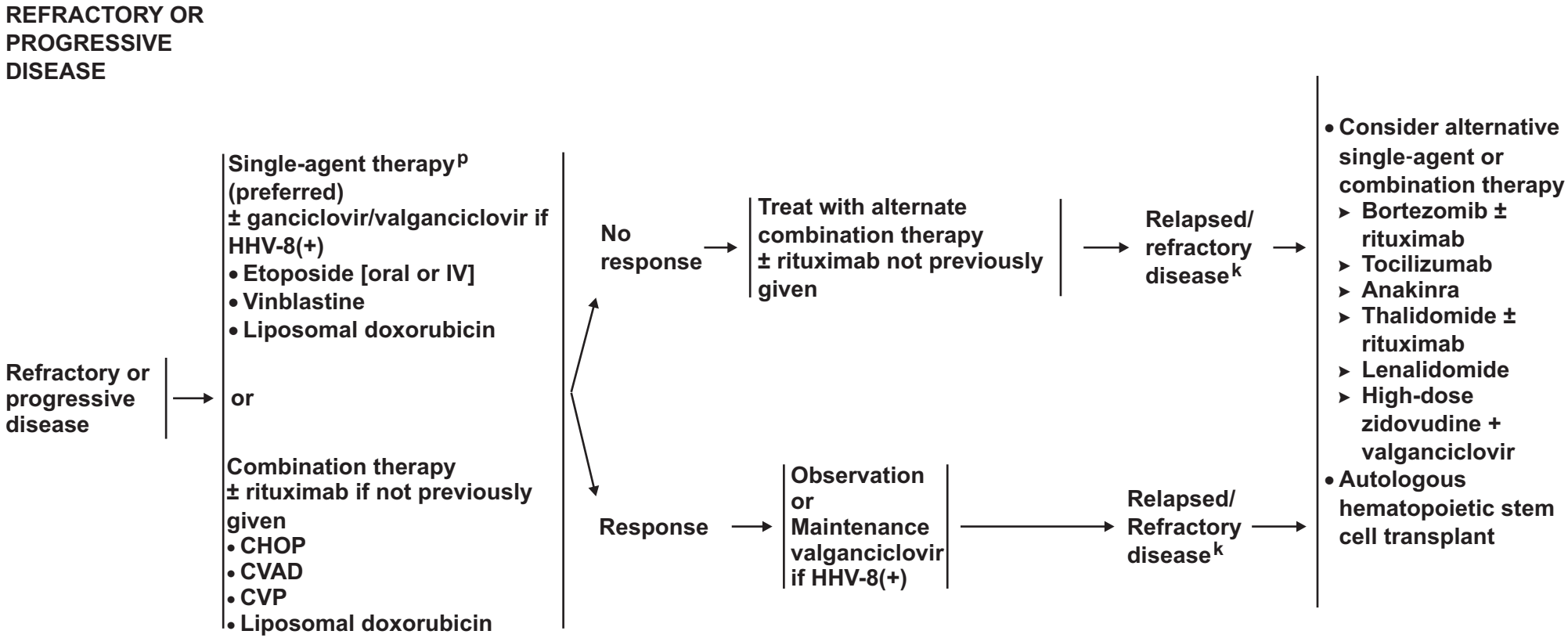

[p] Single agent therapy is preferred for asymptomatic patients with no organ failure; combination therapy is preferred for patients with fulminant disease and organ failure.

[g] See Criteria for Active Disease (CD-A).

[k] Encourage biopsy to rule out transformation to DLBCL or concomitant development of other malignancies or opportunistic infections.

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CRITERIA FOR ACTIVE DISEASE[a]

- **Fever**
- **Increased serum C-reactive protein level >20 mg/L in the absence of any other etiology**
- **At least three of the following other MCD-related symptoms**
  - **Peripheral lymphadenopathy**
  - **Enlarged spleen**
  - **Edema**
  - **Pleural effusion**
  - **Ascitis**
  - **Cough**
  - **Nasal obstruction**
  - **Xerostomia**
  - **Rash**
  - **Central neurologic symptoms**
  - **Jaundice**
  - **Autoimmune hemolytic anemia**

[a] Gérard L, Bérezné A, Galicier L, et al. Prospective study of rituximab in chemotherapy-dependent human immunodeficiency virus associated multicentric Castleman's disease: ANRS 117 CastlemaB Trial. J Clin Oncol 2007;25:3350-3356.

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