高 雄 榮 民 總 醫 院
淋巴癌診療原則

淋巴癌醫療團隊

2015年03月10日審視

注意事項：

這個診療準則主要作為醫師和其他保健專家診療癌症病人參考之用。

假如你是一個癌症病人，直接引用這個診療準則並不恰當，只有你的醫師才能決定給你最恰當的治療。

PROTOCOLS FOR TREATMENT OF MALIGNANT LYMPHOMA

Version 1.0 2015

MALIGNANT LYMPHOMA

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General Guide

Diagnosis	Staging Work-up
1.Adequate sampling and proper handling of the tissue 2. Effective communication between the clinician and the pathologist 3. Surgical biopsy of the largest lymph nodes or mass lesion* 4. Needle biopsy in certain conditions 5. Flow cytometry or cytogenetic studies: optional * Lymph node	1. Complete history and physical examination including Waldeyer's rings, B symptoms, risk of HIV infection, infection, autoimmune diseases, immunosuppressive therapies 2. Complete blood cell count with a differential, erythrocyte sedimentation rate (ESR) 3. Chemistry profiles: LDH, AST, ALT, Alk-p, bilirubin, uric acid, Cr, Ca, albumin, total protein, sugar 4. EKG, CXR-PA, whole body CT, HBsAg, and anti-HCV 5. Other evaluation: beta2-microglobulin, Urinalysis and stool analysis, cytologic study of third space fluids 6. Bone marrow aspiration and biopsy 7. Lumbar puncture with cytology in selected patients a. All patients with Burkitt lymphoma b. Patients with NHL in certain sites e.g. CNS, epidural space, testes, ethmoid sinus, and large cell lymphoma with bone marrow involvement c. HIV positive patients 8. Gastrointestinal studies a. Esophagogastroduodenoscopy, upper gastrointestinal plus small bowel and lower gastrointestinal series for patients with gastrointestinal tract lymphoma; Endoscopic ultrasonography for gastric MALT lymphoma b. Considered in patients with positive stool occult blood 9. Selected radiologic images as clinically needed, e.g. positron emission tomograph, magnetic resonance imaging, and bone scan 10. Cytogenetic and molecular tests in selected patients (optional); cardiac ejection fraction for age > 60 if anthracycline will be used. Anthracyline is contraindicated if ejection fraction is less than 50%.

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Staging Classification Provided by Ann Arbor

Stage I: involvement of a single lymph node region or a single extra-lymphatic organ or site
Stage II: involvement of 2 or more lymph node regions on the same side of the diaphragm
Stage III: involvement of lymph node regions on both sides of the diaphragm
Stage IV: involvement of liver or bone marrow or an extra-lymphatic organ

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NON-HODGKINS'S LYMPHOMA

Low grade Lymphoma	Intermediate grade lymphoma	High grade lymphoma
Small lymphocytic lymphoma	Follicular lymphoma, grade 3	Immunoblastic; diffuse
Follicular lymphoma, grade 1	Diffuse small cleaved cell lymphoma	Lymphoblastic lymphoma
Follicular lymphoma, grade 2	Diffuse mixed small and large cell lymphoma	Small, non-cleaved cell
	Diffuse large cell lymphoma	

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Staging of gastric MALT LYMPHOMA：comparison of different systems

Lugano Staging System for gastrointestinal lymphomas		Ann Arbor Stage	TNM Staging System adapted for gastric lymphoma	Tumor extension
Stage I_E	Confined to GI tract[a]			
	I_{E1} = mucosa, submucosa	I_E	T1 N0 M0	Mucosa, submucosa
	I_{E2} = muscularis propria, serosa	I_E	T2 N0 M0	Muscularis propria
		I_E	T3 N0 M0	Serosa
Stage II_E	Extending into abdomen			
	II_{E1} = local nodal involvement	II_E	T1-3 N1 M0	Perigastric lymph nodes
	II_{E2} = distant nodal involvement	II_E	T1-3 N2 M0	More distant regional lymph nodes
Stage II_E	Penetration of serosa to involve adjacent organs or tissues	II_E	T4 N0 M0	Invasion of adjacent structures
Stage III-IV[b]	Disseminated extranodal involvement or concomitant supradiaphragmatic nodal involvement	III_E	T1-4 N3 M0	Lymph nodes on both sides of the diaphragm/distant metastases (eg, bone marrow or additional extranodal sites)
		IV	T1-4 N0-3 M1	

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NON-HODGKINS'S LYMPHOMA

LOW GRADE LYMPHOMA

1)Early Stage (Ann Arbor I –II) → **Radiation therapy**

2)Advanced Stage (Ann Arbor III–IV)

- **a) For elderly symptomatic patients in advanced stage:** →
  - **i) Adopt "watch and wait" policy, deferring treatment until symptoms dictate.**
  - **ii) 1st line chemotherapy: Single oral alkylating agents**
  - **iii) 2nd line chemotherapy COP regimen**
  - **iv) 3rd line chemotherapy CEOP regimen**
  - **v) R-COP regimen for follicular lymphoma**
- **b) For young patients:** → **Tailor the treatment to individual condition. Autologous PBSCT post complete remission.**

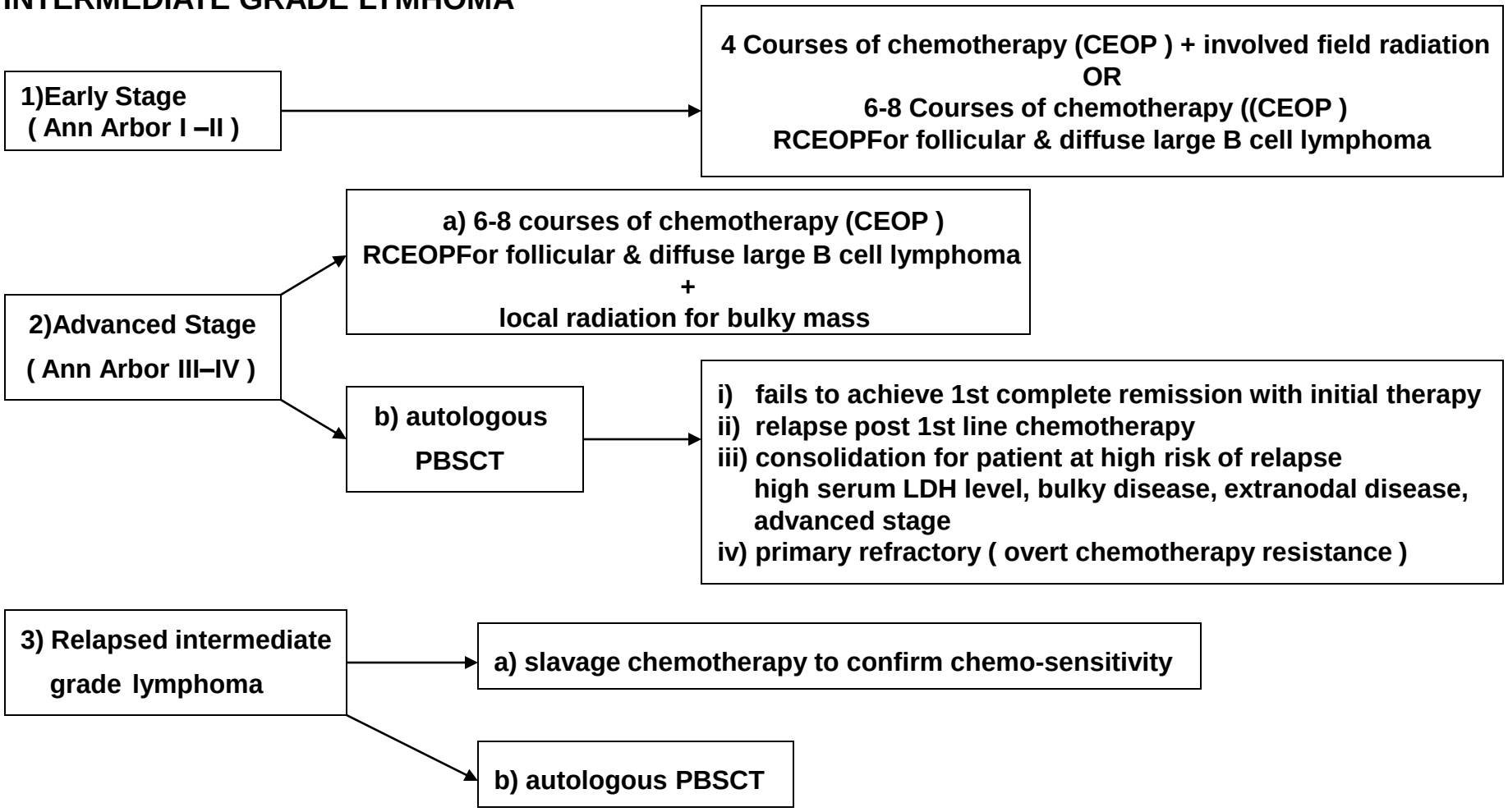
3) Relapsed low grade lymphoma → **Autologous PBSCT for chemo-sensitive disease**

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NON-HODGKINS'S LYMPHOMA

INTERMEDIATE GRADE LYMHOMA

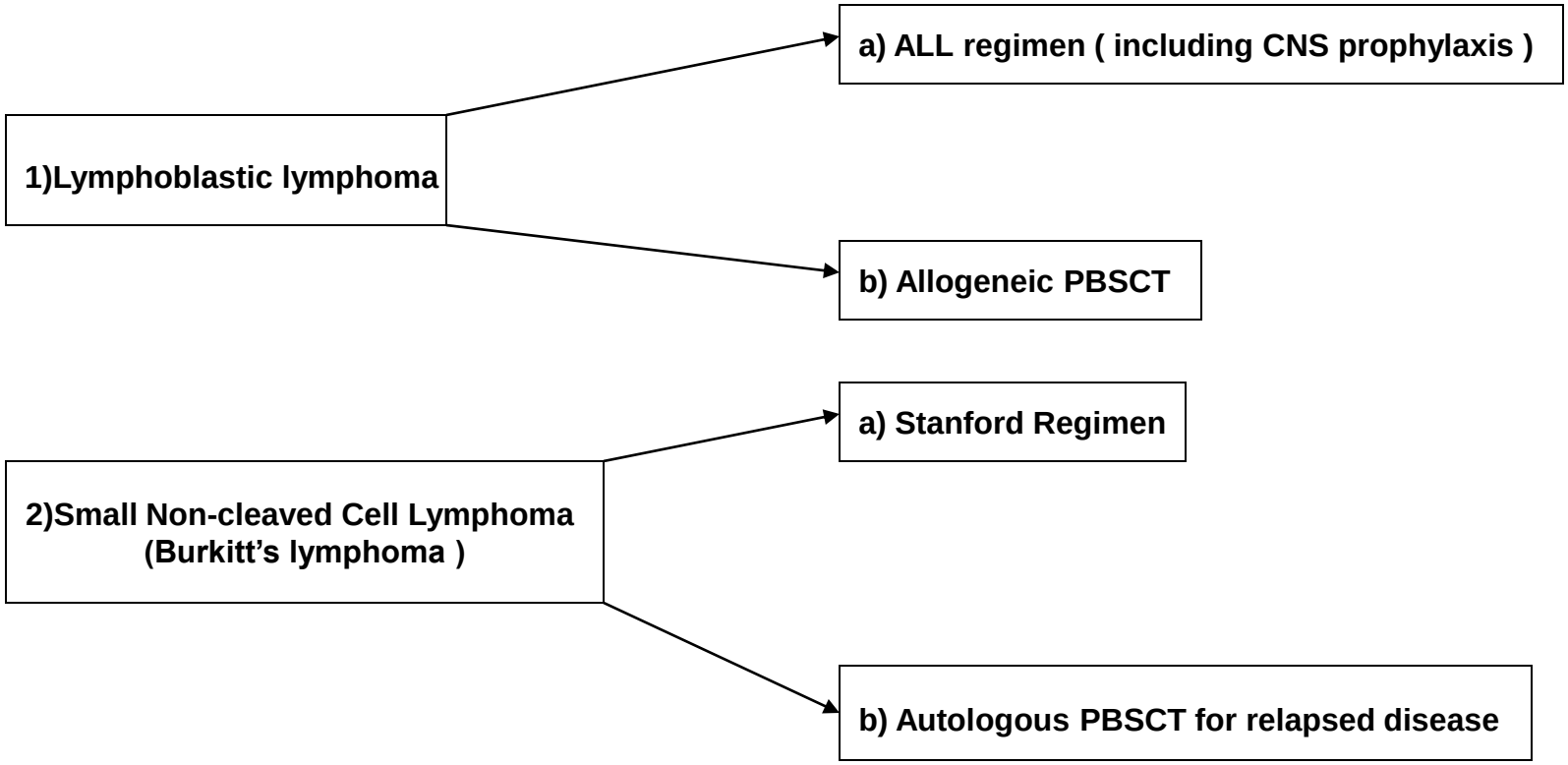


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NON-HODGKINS'S LYMPHOMA

HIGH GRADE LYMPHOMA



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- Lumbar puncture for cerebrospinal fluid (CSF)examination should be performed in patients with the following conditions:
  Diffuse aggressive NHL with
  - bone marrow
  - epidural
  - testicular
  - paranasal sinus
  - nasopharyngeal involvement
  - or patient with two or more extranodal sites of disease.
  - High-grade lymphoblastic lymphoma
  - High-grade small noncleaved cell lymphomas (eg, Burkitt and non-Burkitt types)
  - HIV-related lymphoma
  - Primary CNS lymphoma
  - Patients with neurologic signs and symptoms
  - breast lymphoma

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HODGKIN'S DISEASE

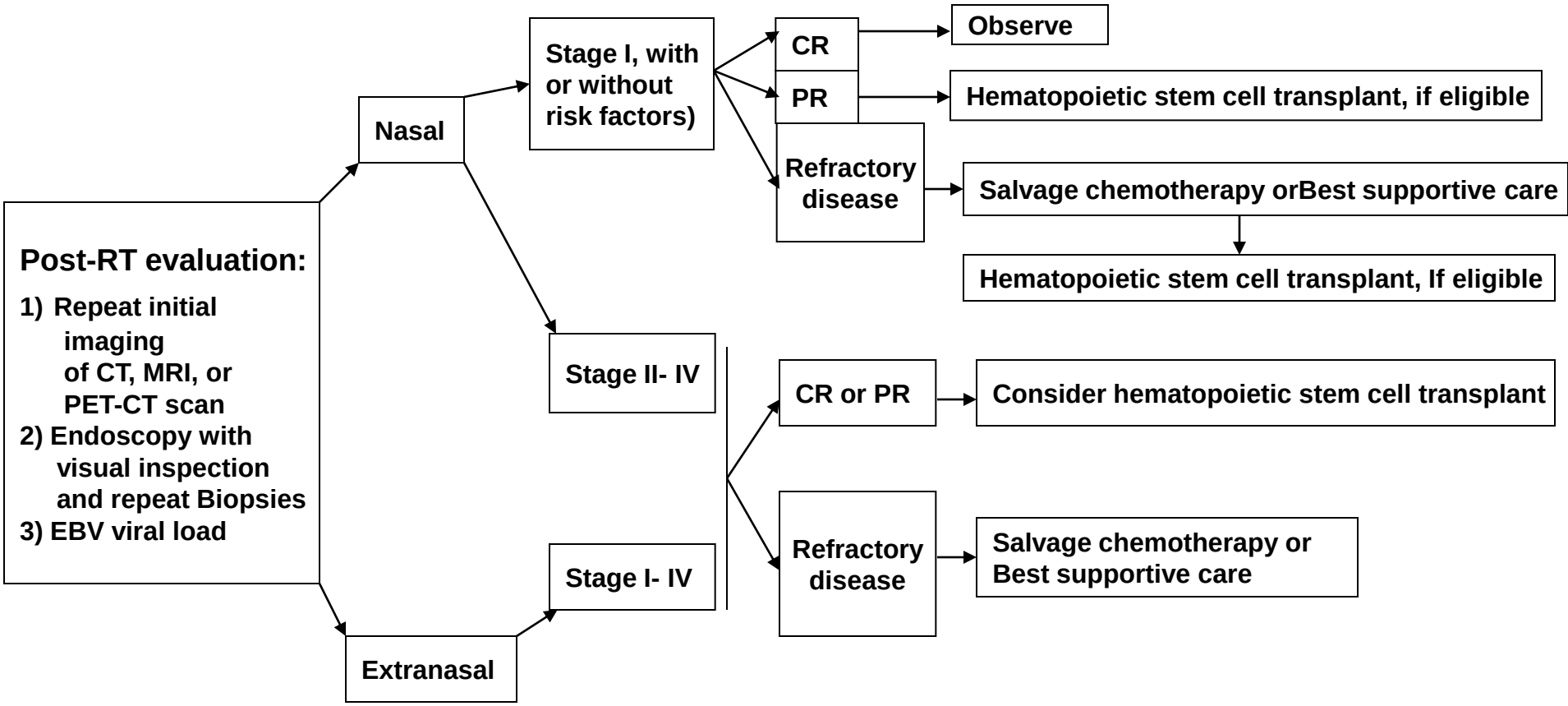
1)Chemotherapy with ABVD regimen
+
radiation for bulky mass

2)Autologous PBSCT → **a)Stage IVb disease post complete remission**
b)Failure to achieve 1st complete remission
c) Relapsed disease

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Extranodal NK/T-cell Lymphoma, nasal type



MALIGNANT LYMPHOMA

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NK/T CELL LYMPHOMA PROGNOSTIC INDEX

ALL PATIENTS

Serum LDH > 1 x normal
B symptoms
Lymph nodes, N1 to N3, not M1
Ann Arbor Stage III

	Number of risk factors
Low	**0**
Low intermediate	**1**
High intermediate	**2**
High	**3 or 4**

MALIGNANT LYMPHOMA

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References:

1. **NCCN guidelines of Hodgkin's disease/lymphoma, V.2. 2009**
2. **NCCN guidelines of Non-Hodgkin' s lymphomas, V.4. 2009**
3. **http://www.uptodateonline.com/online/content/search.do**
4. **http://chemoregimen.com/Lymphoma-c-44-55.html**
5. **http://chemoregimen.com/Dosage-for-Renal-Dysfunction-c-59-68.html**
6. **Baxter Oncology - Selected Schedules of Therapy for Malignant Tumors, 11th edition.**
7. **A cooperative study on ProMACE-CytaBOM in aggressive non-Hodgkin's lymphomas. Leuk Lymphoma 1994; 13:111-8.**

附註

- 依據本院2009年淋巴瘤年報，罹患瀰漫性大B型淋巴瘤及濾泡型淋巴瘤病患，使用標靶治療rituximab併用化療CEOP較單用化療處方CEOP顯著增加整體存活率（p值為0.0001）。此統計結論與西方國家的研究報告相同，因此2010年7月本院淋巴瘤治療指引修正為：瀰漫性大B型淋巴瘤及濾泡型淋巴瘤使用rituximab併用化療CEOP處方，台灣病患治療成績證實與西方國家同樣優秀，因而在療效更好的處方問世前，淋巴瘤團隊建議持續使用rituximab併用化療處方CEOP。

Diffuse large B cell lymphoma

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注意事項：

此治療準則主要作為本院醫療團隊診療病人參考之用途，
並非適合所有病人，需由主治醫師視個別性選擇治療方式

2013/09/10修訂

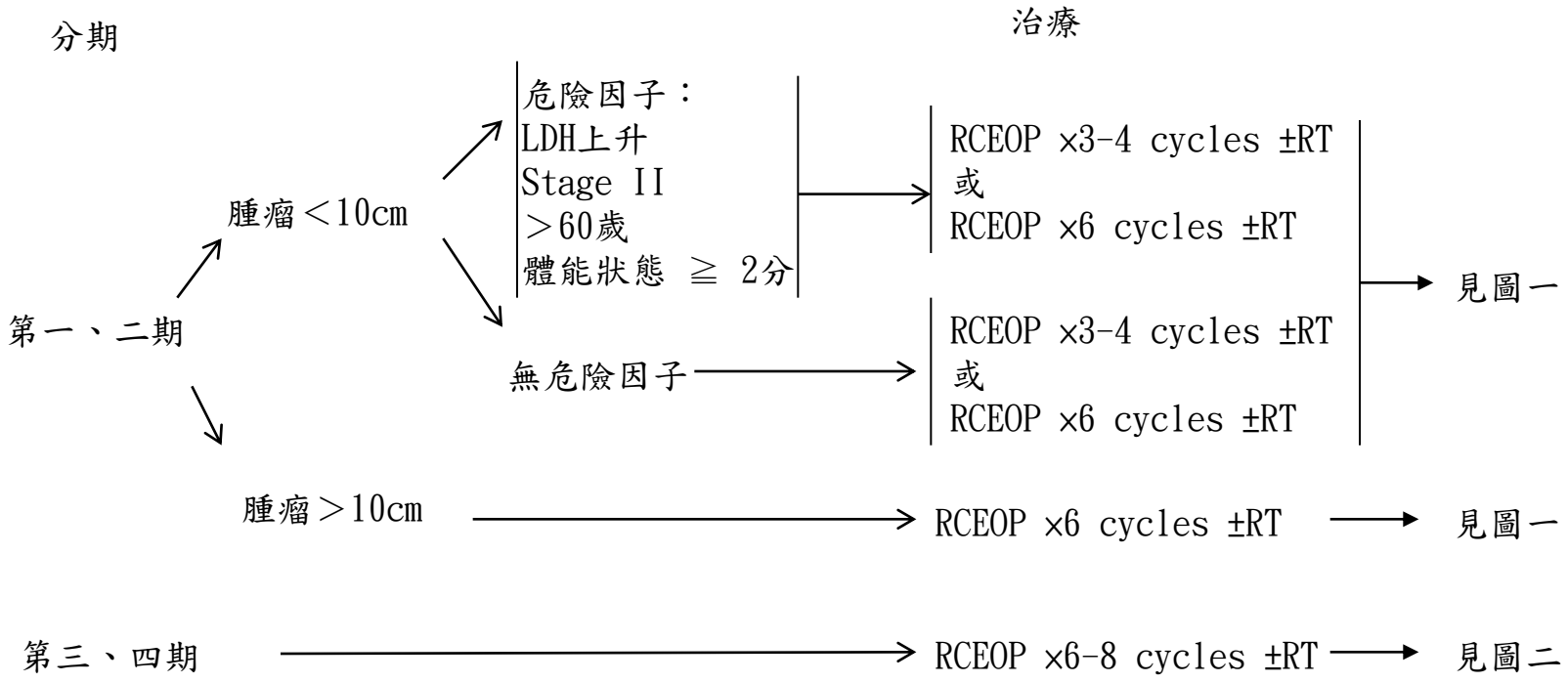
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Diagnosis	**Staging Work-up**
requirement： ＊Hematopathology review of all slides with at least one paraffin block representative of tumor.Rebiopsy if consult material is nondiagnostic. ＊An FNA or core needle biopsy alone is not generally suitable for the initial diagnosis of lymphoma. In certain circumstances, when a lymph nodes is not easily accessible for excisional or incisional biopsy, a combination of core biopsy of FNA biopsies in conjunction with appropriate ancillary techniques for the differential diagnosis may be sufficient for diagnosis. ※IHC panel：CD20, CD3 (as description of the pathologist) Useful under certain circumstances： ※IHC panel：CD30,CD5,CD10,CD45,BCL2,BCL6,Ki-67, IRF4/MUM1或 ※Cell surface marker analysis by flow cytomerty：kapp/lambda, CD45,CD3,CD5,CD19,CD10,CD20 ＊Additional immunohistochemical studies to establish lymphoma subtype ※IHC panel：Cyclin D1, kapp/lambda,CD30,CD138,EBER-ISH ,ALK,HHV8 ＊Molecular analysis to detect：antigen receptor gene rearrangements；CCND1；BCL2；BCL6；MYC Rearrangements by either FISH or IHC ＊Cytogenetics or FISH：t（14；18）,t（3；v）,t（8；14）	requirement： ＊Physical exam：attention to node-bearing areas,including Waldeyer's rings, B- symptoms and to size of liver and spleen ＊Performance status ＊CBC,differential,platelets,LDH,Uric acid＊ Comprehensive metabolic panel ＊CT：face/chest/abdominal/pelvic or PET ＊bone marrow biopsy±aspirate ＊ IPI SCORE ＊Hepatitis B、C testing ＊echocardiogram or ejection fraction 選擇性： ＊HIV ＊Discussion of fertility issues and sperm banking ＊Lumbar puncture（見第十頁） ＊ Beta2- microglobulin

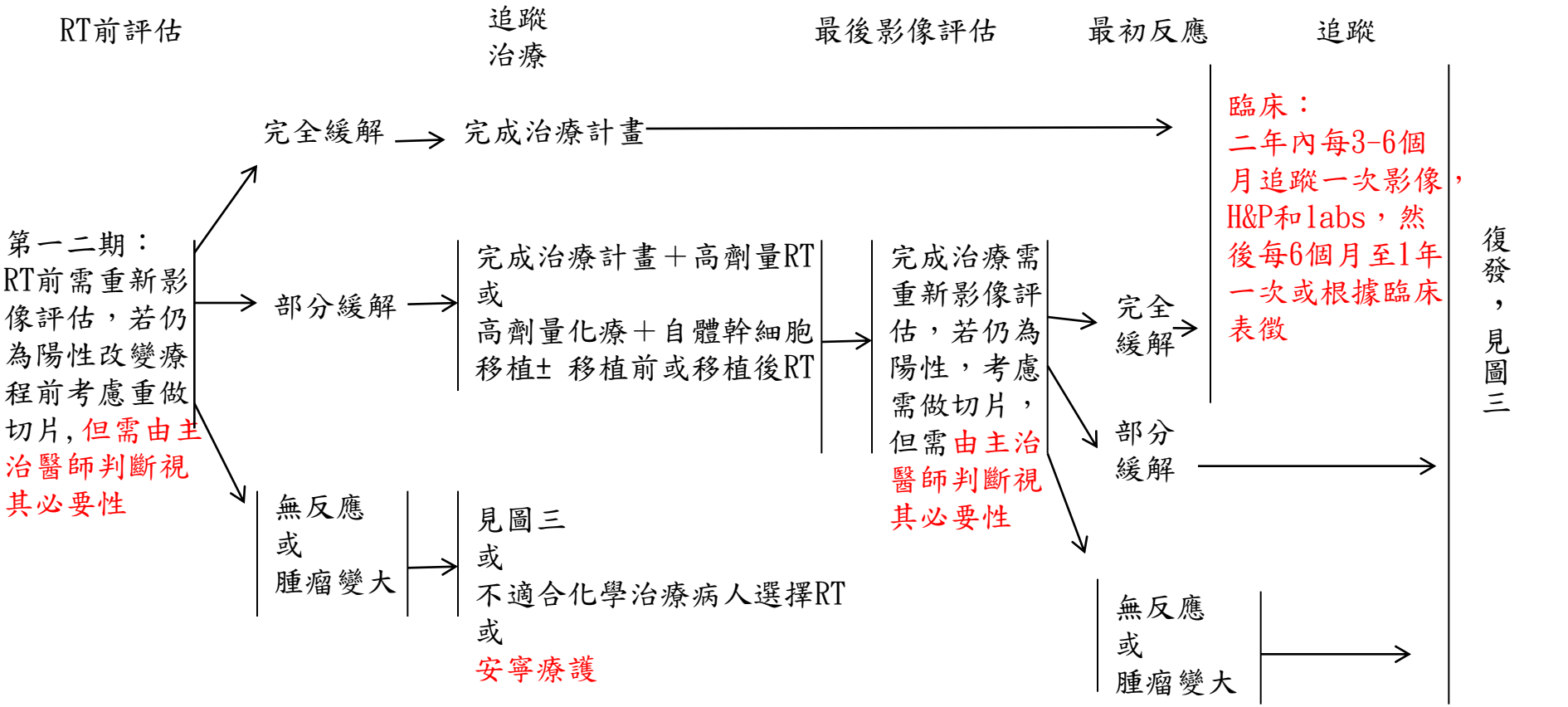
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Diffuse large B cell lymphoma

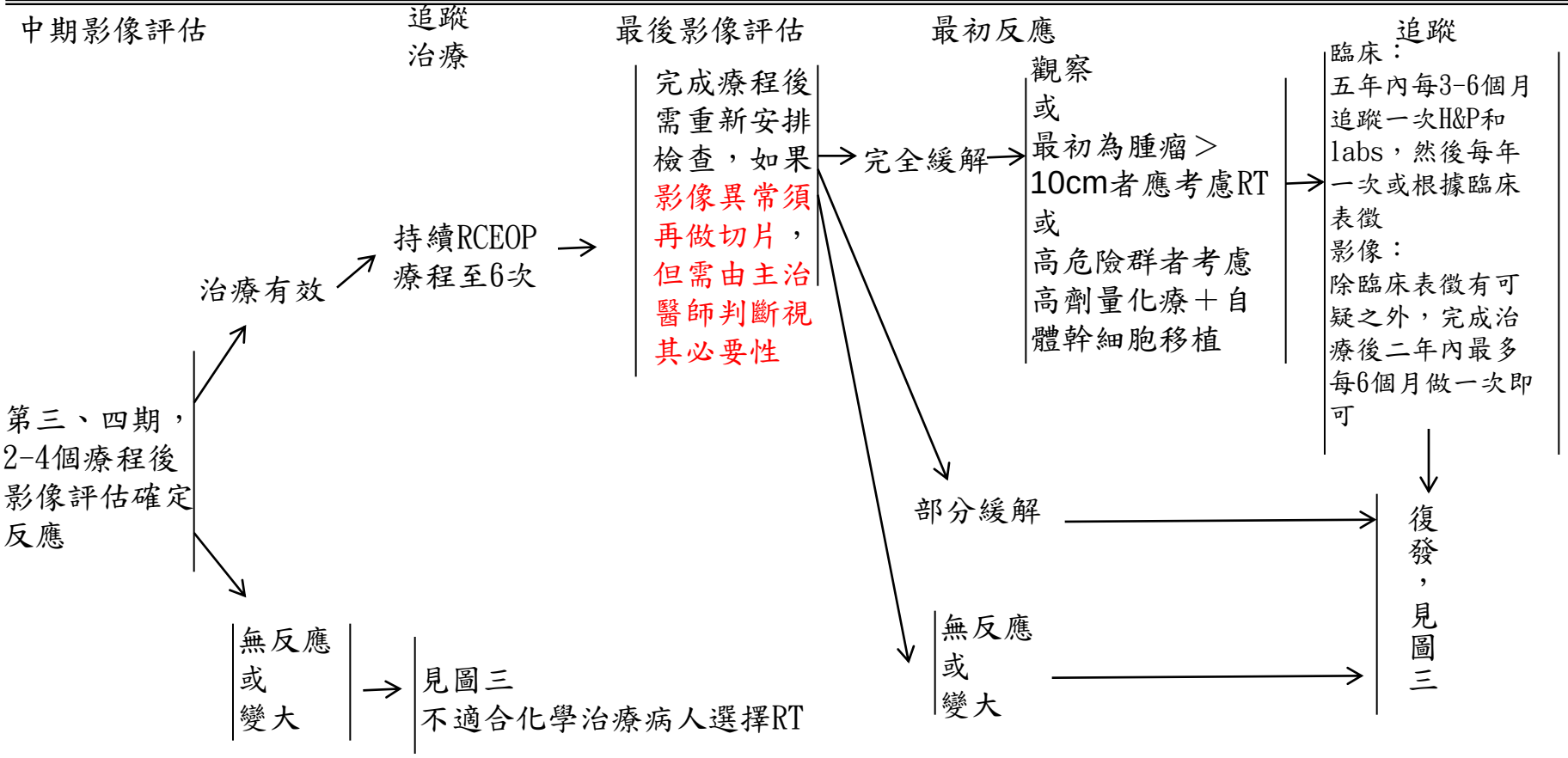
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圖一

Diffuse large B cell lymphoma

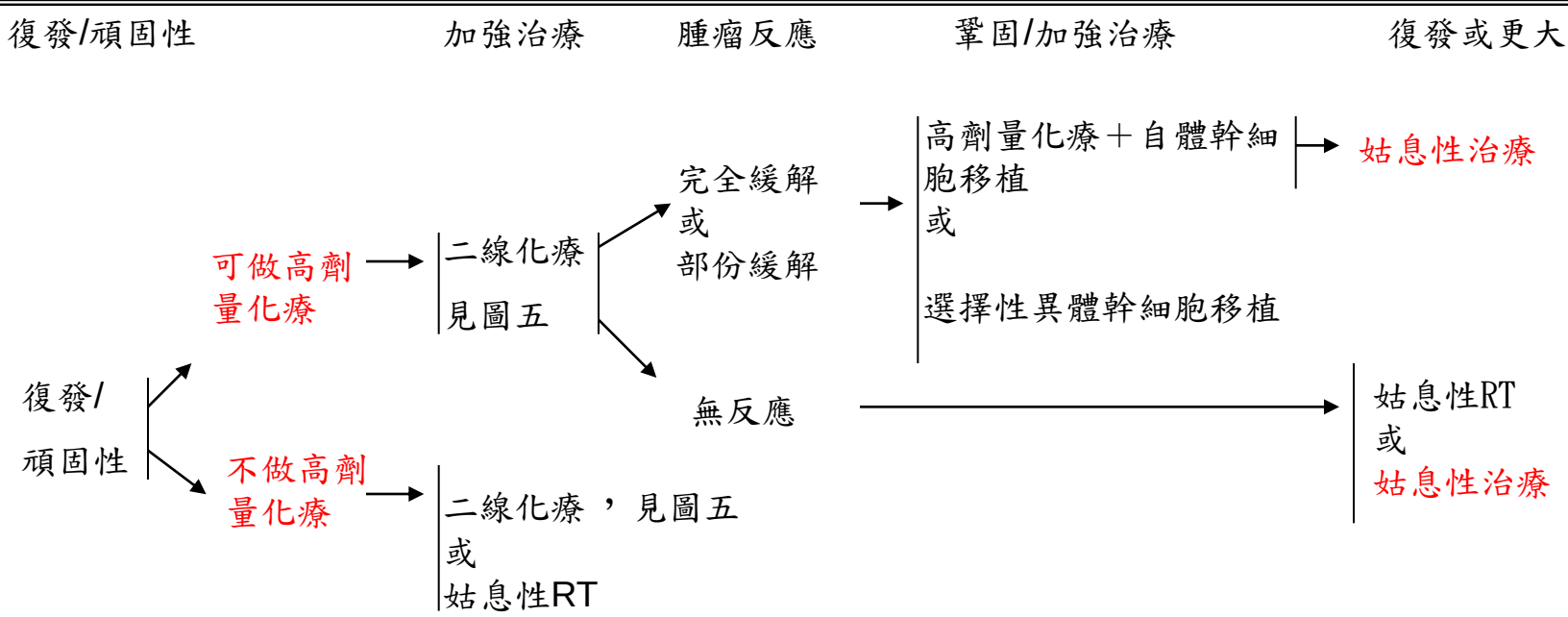
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圖二

Diffuse large B cell lymphoma

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圖三

Diffuse large B cell lymphoma

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建議治療療程

一線化療	
R-CEOP	Rituximab 375MG/M2 IVA on D1
	Cyclophosphamide 750MG/M2 IVA on D1 or D2
	Epirubicin 75MG/M2 IVA on D1 or D2
	Vincristine 2MG IVA on D1 or D2
	Prednisone 5MG 10TAB BID po for 5days
	References:NO 2

一線化療適用於心臟功能不好病人	
R-CNOP	Rituximab 375MG/M2 IVA on D1
	Cyclophosphamide 750MG/M2 IVA on D1 or D2
	Mitoxantrone 10MG/M2 IVA on D1 or D2
	Vincristine 2MG IVA on D1 or D2
	Prednisone 5MG 10TAB BID po for 5days
	References:NO 3

圖四

Diffuse large B cell lymphoma

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建議治療療程

二線化療（針對有意執行高劑量化療+自體幹細胞移植者）	
DHAP	Dexamethasone 40MG for 4 days
	Cisplatin 100MG/M2/ Carboplatin AUCx1.25MG IVA on D1
	Cytarabine 2000MG/M2 IVA Q12H on D2
	註：CCr ＜60 使用Carboplatin References:NO4
ESHAP	Solu-Medrol 500MG IVA for 5days on D1-5
	Etoposide 40MG/M2 IVA for 4days on D1-4
	Cisplatin 25MG/M2 / Carboplatin AUCx1.25MG IVA for 4days on D1-4
	Cytarabine 2000MG/M2 IVA on D5
	註：CCr ＜60 使用Carboplatin References:NO5

圖五-1

Diffuse large B cell lymphoma

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建議治療療程

二線化療（針對有意執行高劑量化療+自體幹細胞移植者）	
DICE	Ifosfamide 1GM/M2 IVA for 4day on D1-4
	Cisplatin 25MG/M2 / Carboplatin AUCx1.25MG IVA for 4day on D1-4
	Etoposide 100MG/M2 IVD for 4day on D1-4
	Dexamethasone 40MG IVA for 4day on D1-4
	註：CCr ＜60 使用Carboplatin References:NO6
MINE	Mesna 1.33GM/M2 IVA for 3days on D1-3
	Ifosfamide 1.33GM/M2 IVA for 3days on D1-3
	Mitoxantrone 8MG/M2 IVA on D1
	Etoposide 65MG/M2 IVA for 3days on D1-3 References:NO7

Diffuse large B cell lymphoma

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Lumbar puncture for cerebrospinal fluid (CSF)examination should be performed in patients with the following conditions:

Diffuse aggressive NHL with

- bone marrow
- epidural
- testicular
- paranasal sinus
- nasopharyngeal involvement or patient with two or more extranodal sites of disease.
- High-grade lymphoblastic lymphoma
- High-grade small noncleaved cell lymphomas (eg, Burkitt and non-Burkitt types)
- HIV-related lymphoma
- Primary CNS lymphoma
- Patients with neurologic signs and symptoms
- breast lymphoma

Diffuse large B cell lymphoma

References:

1.NCCN guidelines of Non-Hodgkin’ s lymphomas, V.1. 2013

2.FEUGIER p,Van Hoof A, Sebban C,et al. Long-term results of the R-CHOP study in the treatment of elderly patients with diffuse large B-cell lymphoma:a study by the Groupe d′Etude des lymphomes de I′Adulte. J Clin Oncol 2005;23:4117-4126.

3.Bessell EM,Burton A, Haynes AP,et al. A randomised multicentre trial of modified CHOP versus MCOP in patients aged 65 years and over with aggressive non-Hodgkin′s lymphoma. Ann Oncol 2003;14:258-267.

4.Velasquez WS. Cabanillas F, Salvador P, et al. Effective salvage therpy for lymphoma with cisplatin in combination with high-dose Ara-C and dexamethasone(DHAP). Blood 1988;71:177-122.

5.Velasquez WS, McLaughin P,Tucker S, ET AL. ESHAP-an effective chemotherpy regimen in refractory and relapsing lymphoma:a 4-year follow-up study.J Clin Oncol 1994;12:1169-1176.

Diffuse large B cell lymphoma

References:

6.Gisselbrecht C, Glass B, Mounier N, et al. Salvage regimens with autologous transplantation for relapsed large B-cell lymphoma in the rituximab era. J Clin Oncol 2010;28:4184-4190.

7.Ifosfamide and etoposide-based chemotherapy as salvage and mobilizing regimen for poor prognosis lymphoma.Bone Marrow Transplantation,(1999)23,413-419.

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注意事項：

此治療準則主要作為本院醫療團隊診療病人參考之用途，
並非適合所有病人，需由主治醫師視個別性選擇治療方式

2013/11/19修訂

Hodgkin Lymphoma

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Table 1

Definitions of Stages in Hodgkin's Disease[1]

Stage I Involvement of a single lymph node region (I) or localized involvement of a single extralymphatic organ or site (I_E).

Stage II Involvement of two or more lymph node regions on the same side of the diaphragm (II) or localized involvement of a single associated extralymphatic organ or site and its regional lymph node(s), with or without involvement of other lymph node regions on the same side of the diaphragm (II_E).

Note: The number of lymph node regions involved may be indicated by a subscript (e.g. II_3).

Stage III Involvement of lymph node regions on both sides of the diaphragm (III), which may also be accompanied by localized involvement of an associated extralymphatic organ or site (IIIE), by involvement of the spleen (III_S), or by both (III_{E+S}).

Stage IV Disseminated (multifocal) involvement of one or more extralymphatic organs, with or without associated lymph node involvement, or isolated extralymphatic organ involvement with distant (nonregional) nodal involvement.

A No systemic symptoms present
B Unexplained fevers >38 C; drenching night sweats; or weight loss >10% of body weight (within 6 months prior to diagnosis)

Adapted from **Carbone PP, Kaplan HS, Musshoff K et al. Report of the Committee on Hodgkin's Disease Staging Classification. Cancer Res 1971;31(11):1860-1.**

Hodgkin Lymphoma

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Examples of Unfavorable Risk Factors for Stage I-II Hodgkin Disease

Risk Factor	GHSG	EORTC	NCIC	NCCN
Age		≥ 50	≥ 40	
Histology			MC or LD	
ESR and B symptoms	> 50 if A; > 30 if B	> 50 if A; > 30 if B	> 50 or any B sx	> 50 or any B sx
Mediastinal mass	MMR > .33	MTR > .35	MMR > .33 or > 10 cm	MMR > .33
# Nodal sites	> 2*	> 3	> 3	> 3
E lesion	any			
Bulky				> 10 cm

GHSG = German Hodgkin Study Group
EORTC = European Organization for the Research and Treatment of Cancer
NCIC = National Cancer Institute, Canada
MC = Mixed cellularity
LD = Lymphocyte depleted
MMR = Mediastinal mass ratio, maximum width of mass/maximum intrathoracic diameter
MTR = Mediastinal thoracic ratio, maximum width of mediastinal mass/intrathoracic diameter at T5-6
*The GHSG definition of nodal sites differs from the Ann Arbor system in that the infraclavicular region is included with the ipsilateral cervical/supraclavicular, the bilateral hila are included with the mediastinum, and the abdomen is divided into 2 regions, upper (spleen hilum, liver hilum, celiac) and lower.

International Prognostic Score (IPS) 1 point per factor (advanced disease)

- Albumin < 4 g/dL
- Hemoglobin < 10.5 g/dL
- Male
- Age ≥ 45 years
- Stage IV disease
- Leukocytosis (white blood cell count at least 15,000/mm)
- Lymphocytopenia (lymphocyte count less than 8% of white blood cell count, and/or lymphocyte count less than 600/mm)

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DIAGNOSIS	WORKUP	
• Excisional biopsy (recommended) • Core needle biopsy may be adequate if diagnostic • Immunohisto-chemistry highly recommended for Hodgkin lymphoma →	<u>Essential</u>: • H&P including: B symptoms, alcohol intolerance, pruritus, fatigue, performance status, exam lymphoid regions, spleen, liver • CBC, differential, platelets • Erythrocyte sedimentation rate (ESR) • LDH, LFT, albumin • BUN, creatinine • Pregnancy test: women of childbearing age • Chest x-ray • Diagnostic Face and neck/abdomimal CT • Adequate bone marrow biopsy in stage IB, IIB and stage III-IV • Evaluation of ejection fraction for doxorubicin-containing regimens	<u>Useful in selected cases</u>: • Semen cryopreservation, if chemotherapy or pelvic RT contemplated • IVF or ovarian tissue or oocyte cryopreservation • Oophoropexy in pre-menopausal women if pelvic RT is contemplated • Neck CT • Pulmonary functions tests (PFTs incl. DLCO) if ABVD • Pneumococcal, H-flu, meningococcal vaccines, if splenic RT contemplated • PET-CT scan • HIV test

Hodgkin Lymphoma

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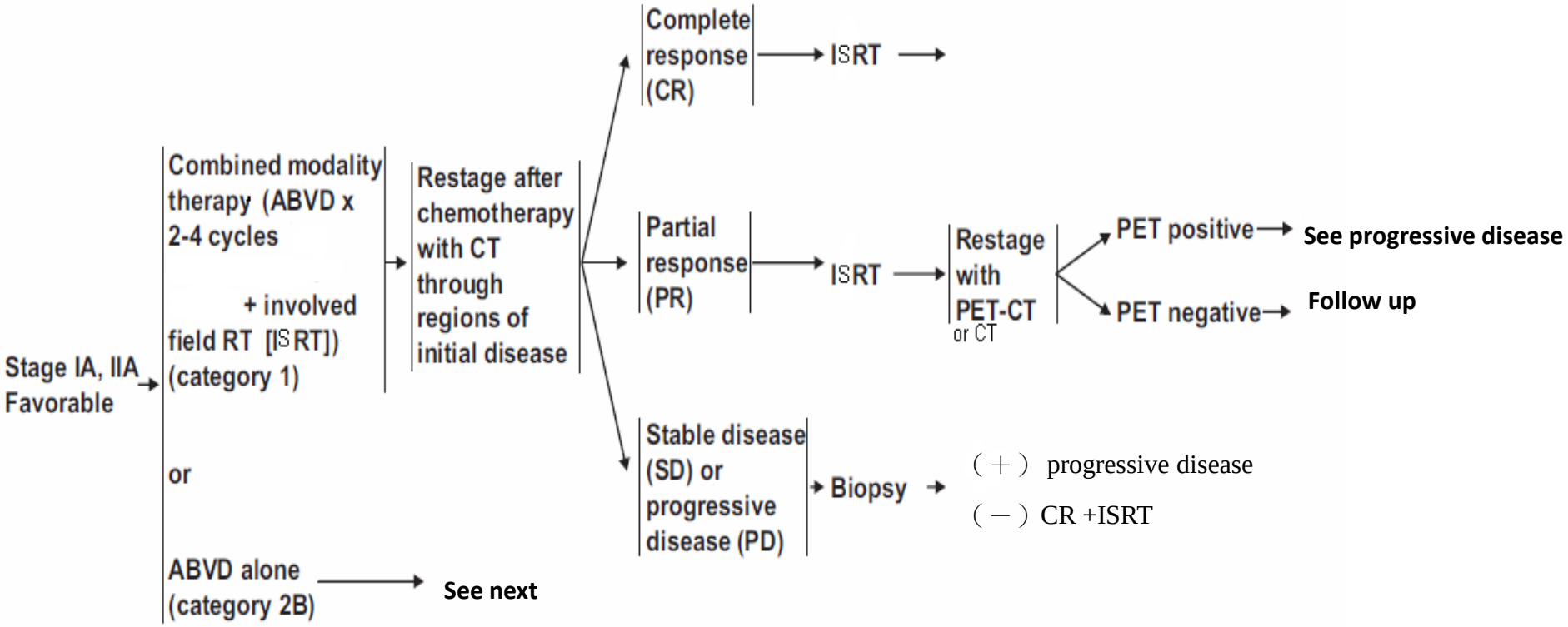
Summary

- Stage IA/IIA (favorable)
  Standard: combined modality with ABVD x 2-4 cycles + ISRT
  ABVD x 6 cycles (or 4 cycles) in selected case
- Stage I/II (unfavorable, non-bulky)
  ABVD x 6 cycles +/- ISRT
- Stage I/II (unfavorable, bulky)
  ABVD x 6 cycles + ISRT
- Stage III/IV
  ABVD x 6 cycles +/- ISRT

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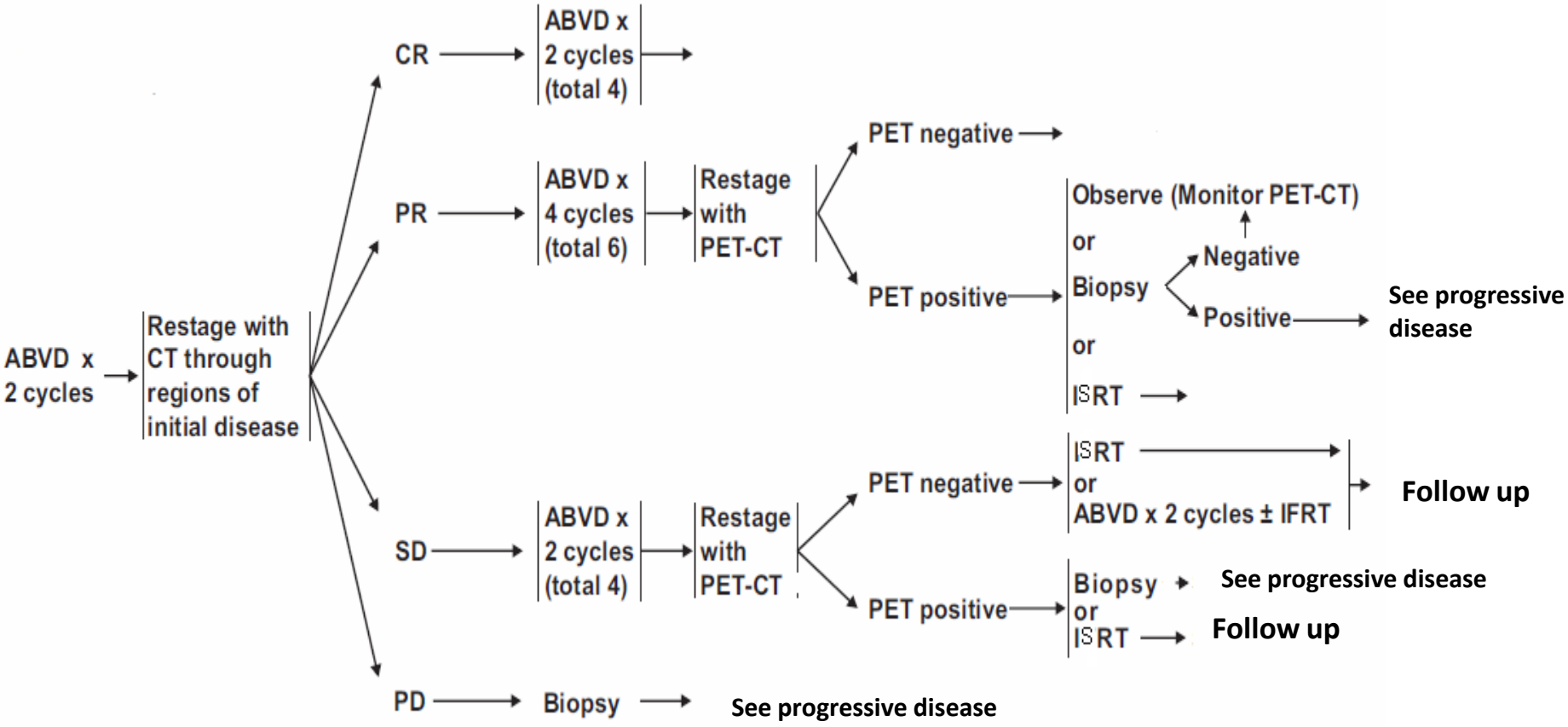
Classical Hodgkin Lymphoma Stage IA-IIA Favorable



Hodgkin Lymphoma

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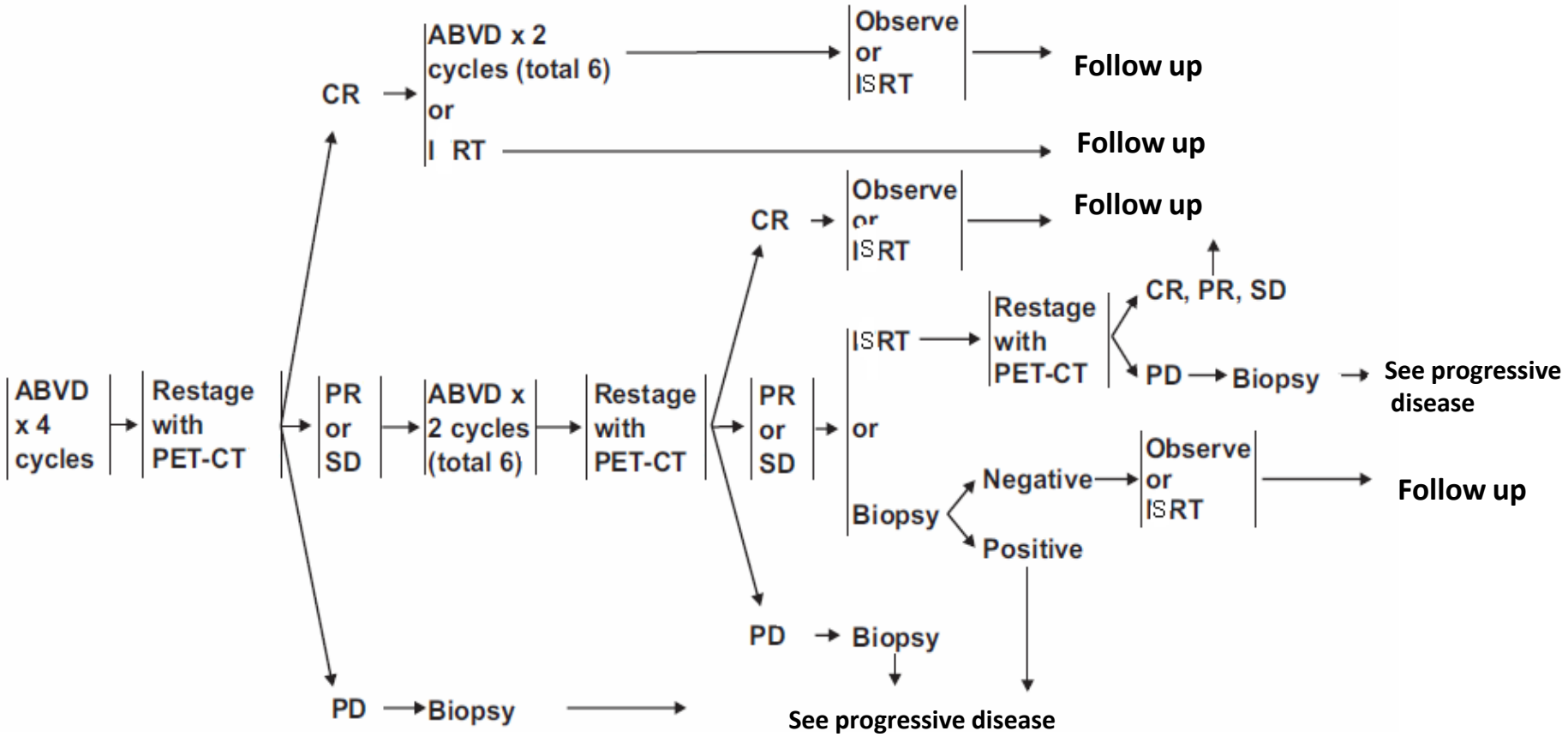
Classical Hodgkin Lymphoma Stage IA-IIA Favorable (C/T alone first)



Hodgkin Lymphoma

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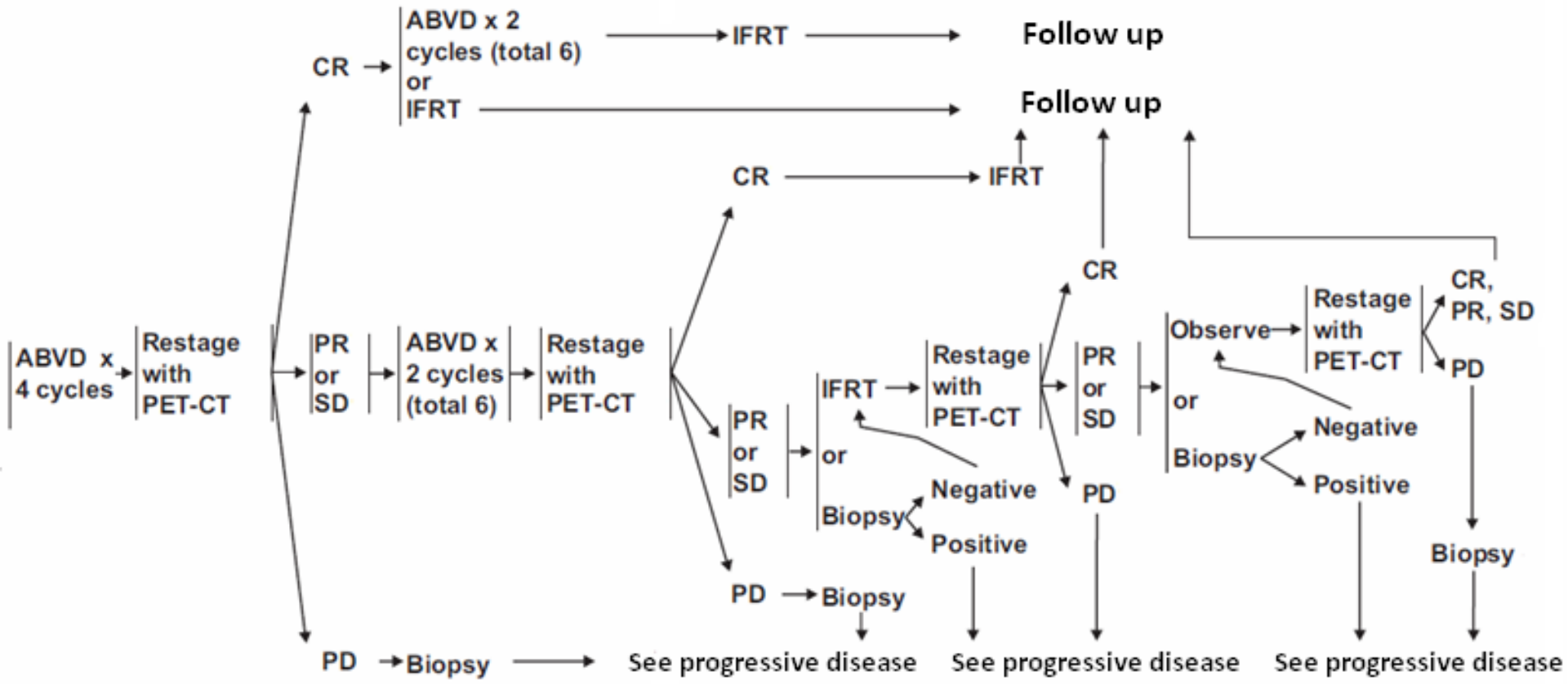
Classical Hodgkin Lymphoma Stage I-II Unfavorable (Non-bulky, C/T alone first)



Hodgkin Lymphoma

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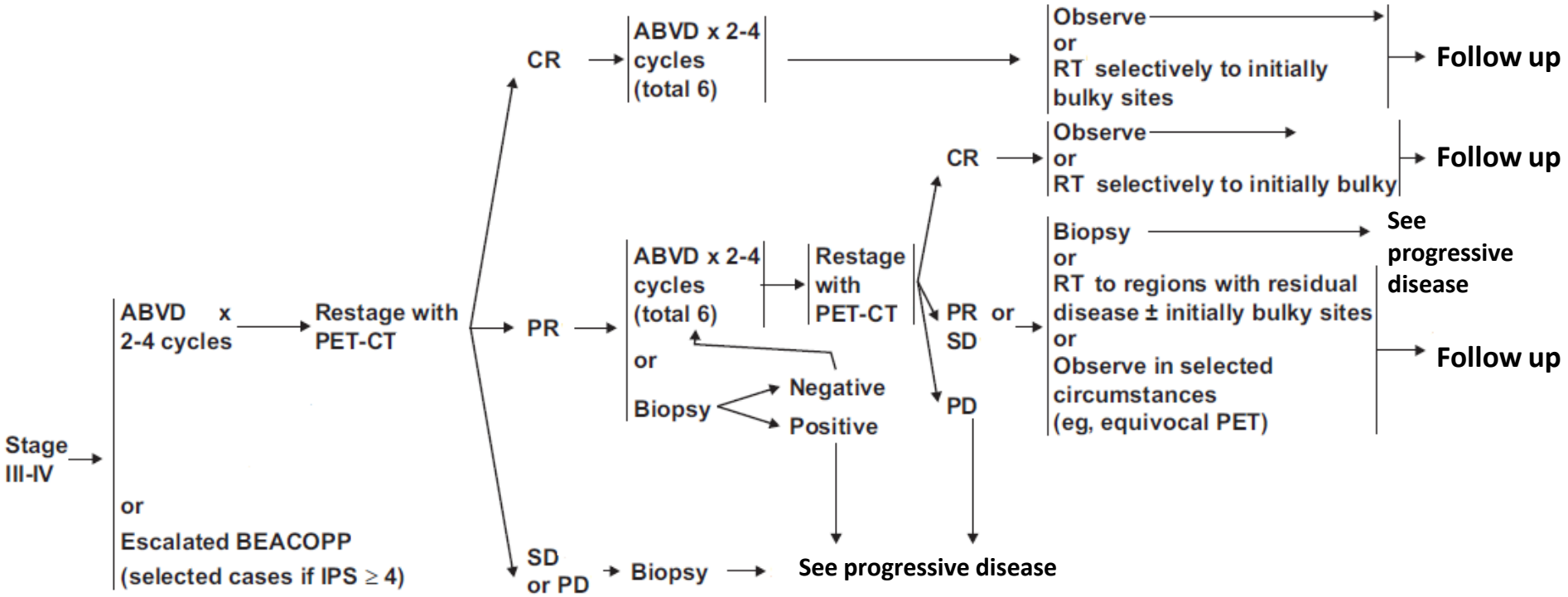
Classical Hodgkin Lymphoma Stage I-II Unfavorable (Bulky, C/T alone first)



Hodgkin Lymphoma

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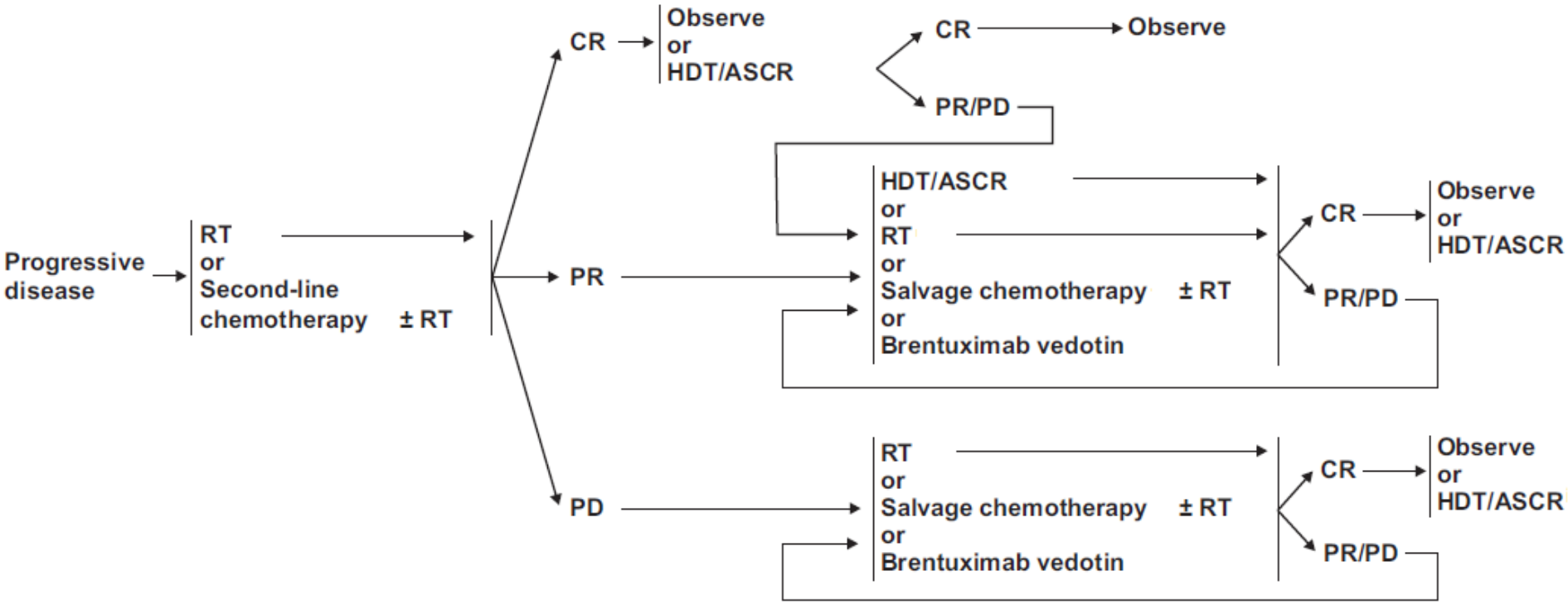
Classical Hodgkin Lymphoma Stage III-IV



Hodgkin Lymphoma

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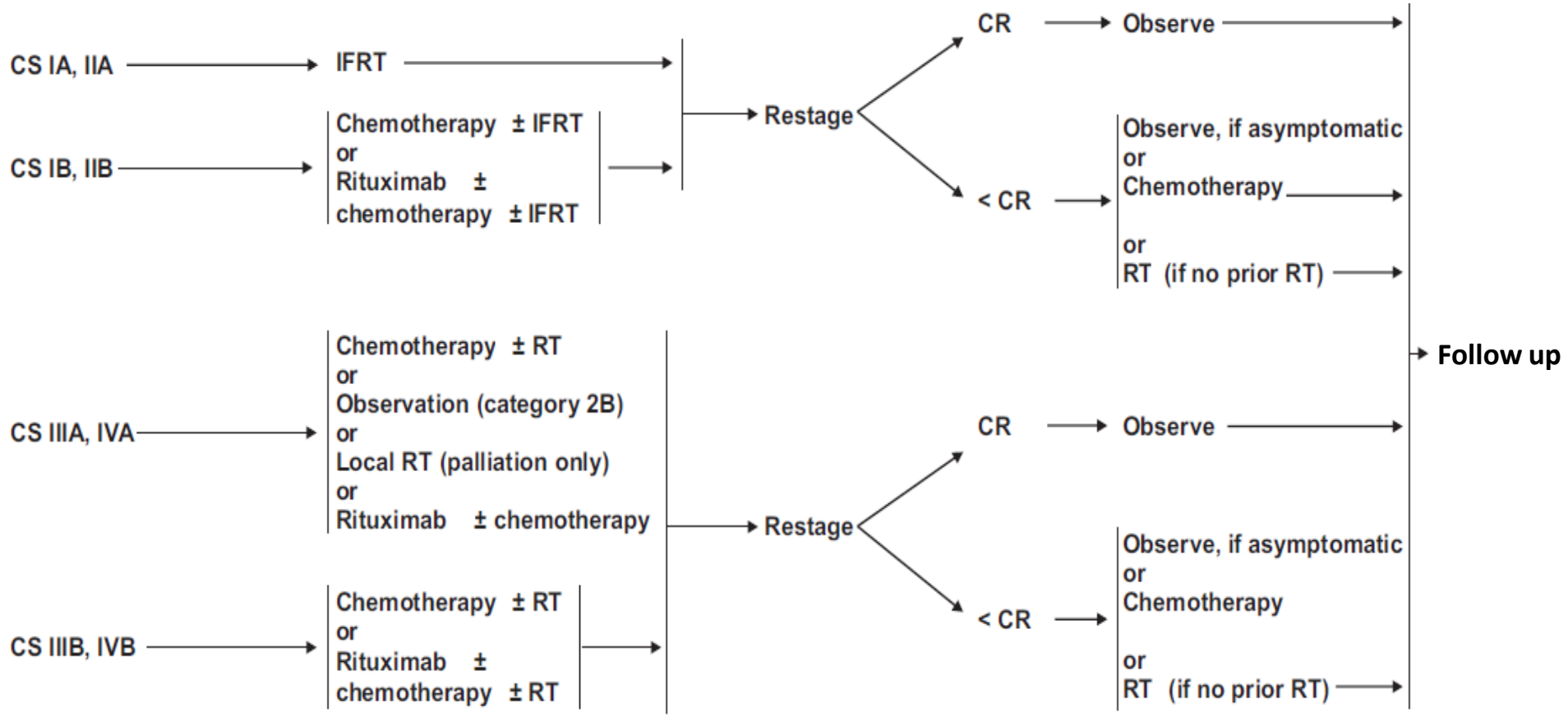
Classical Hodgkin Lymphoma (progressive disease or relapse)



Hodgkin Lymphoma

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Lymphocyte-predominant Hodgkin Lymphoma



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Hodgkin lymphoma-Commonly used chemotherapy regimen

- **ABVD** Q4w (References:NO10)

Doxorubicin (Adriamycin) 25 mg/m2 iv d1 and 15
Bleomycin 10 U/m2 iv d1 and 15
Vinblastine 6 mg/m2 iv d1 and 15
Dacarbazine (DTIC) 375 mg/m2 iv d1 and 15

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Sceond –line chemotherapy regimen

Bendamustine 50~150MG/M2 IVA for 2days	
DHAP	Dexamethasone 40MG for 4 days
	Cisplatin 100MG/M2/ Carboplatin AUCx1.25MG IVA on D1
	Cytarabine 2000MG/M2 IVA Q12H on D2
	註：CCr ＜60 使用Carboplatin References:NO4
ESHAP	Solu-Medrol 500MG IVA for 5days on D1-5
	Etoposide 40MG/M2 IVA for 4days on D1-4
	Cisplatin 25MG/M2 / Carboplatin AUCx1.25MG IVA for 4days on D1-4
	Cytarabine 2000MG/M2 IVA on D5
	註：CCr ＜60 使用Carboplatin References:NO5

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Sceond –line chemotherapy regimen

MINE	Mesna 1.33GM/M2 IVA for 3days on D1-3
	Ifosfamide 1.33GM/M2 IVA for 3days on D1-3
	Mitoxantrone 8MG/M2 IVA on D1
	Etoposide 65MG/M2 IVA for 3days on D1-3 References:NO7
Mini-BEAM	Carmustine 60MG/M2 IVA on D1
	Cytarabine 100MG/M2 Q12H IVA on D2 × 4 days
	Etoposide 40MG/M2 IVA on D2 ×4 days
	Alkeran 30MG/M2 IVA on D6 References:NO11

Hodgkin Lymphoma

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Reference

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Hodgkin Lymphoma

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Follicular Lymphoma（**grade 1-2**）

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注意事項：

此治療準則主要作為本院醫療團隊診療病人參考之用途，
並非適合所有病人，需由主治醫師視個別性選擇治療方式

2014/02/11制定

Follicular lymphoma（**grade 1-2**）

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Diagnosis

Essential：

＊Hematopathology review of all slides with at least one paraffin block representative of tumor.Rebiopsy if consult material is nondiagnostic.

＊An FNA or core needle biopsy alone is not generally suitable for the initial diagnosis of lymphoma. In certain circumstances, when a lymph nodes is not easily accessible for excisional or incisional biopsy, a combination of core biopsy of FNA biopsies in conjunction with appropriate ancillary techniques for the differential diagnosis may be sufficient for diagnosis.

※IHC panel：CD20, CD3
(as description of the pathologist)

Useful under certain circumstances：

※IHC panel：CD30,CD5,CD10,CD45,BCL2,BCL6,Ki-67, IRF4/MUM1或

※Cell surface marker analysis by flow cytomerty：kapp/lambda, CD45,CD3,CD5,CD19,CD10,CD20

＊Additional immunohistochemical studies to establish lymphoma subtype

※IHC panel：Cyclin D1, kapp/lambda,CD30,CD138,EBER-ISH ,ALK,HHV8

＊Molecular analysis to detect：antigen receptor gene rearrangements；CCND1；BCL2；BCL6；MYC Rearrangements by either FISH or IHC

＊Cytogenetics or FISH：t（14；18）,t（3；v）,t（8；14）

Work-up

Eaaential：

＊Physical exam：attention to node-bearing areas,including Waldeyer’s rings, B- symptoms and to size of liver and spleen

＊Performance status

＊CBC,differential,platelets,LDH,Uric acid＊Comprehensive metabolic panel

＊CT：face/chest/abdominal/pelvic or PET

＊bone marrow biopsy±aspirate

＊ IPI SCORE

＊Hepatitis B、C testing

＊echocardiogram or ejection fraction

選擇性：

＊HIV

＊Discussion of fertility issues and sperm banking

＊Lumbar puncture

＊ Beta2- microglobulin

Stage I,II

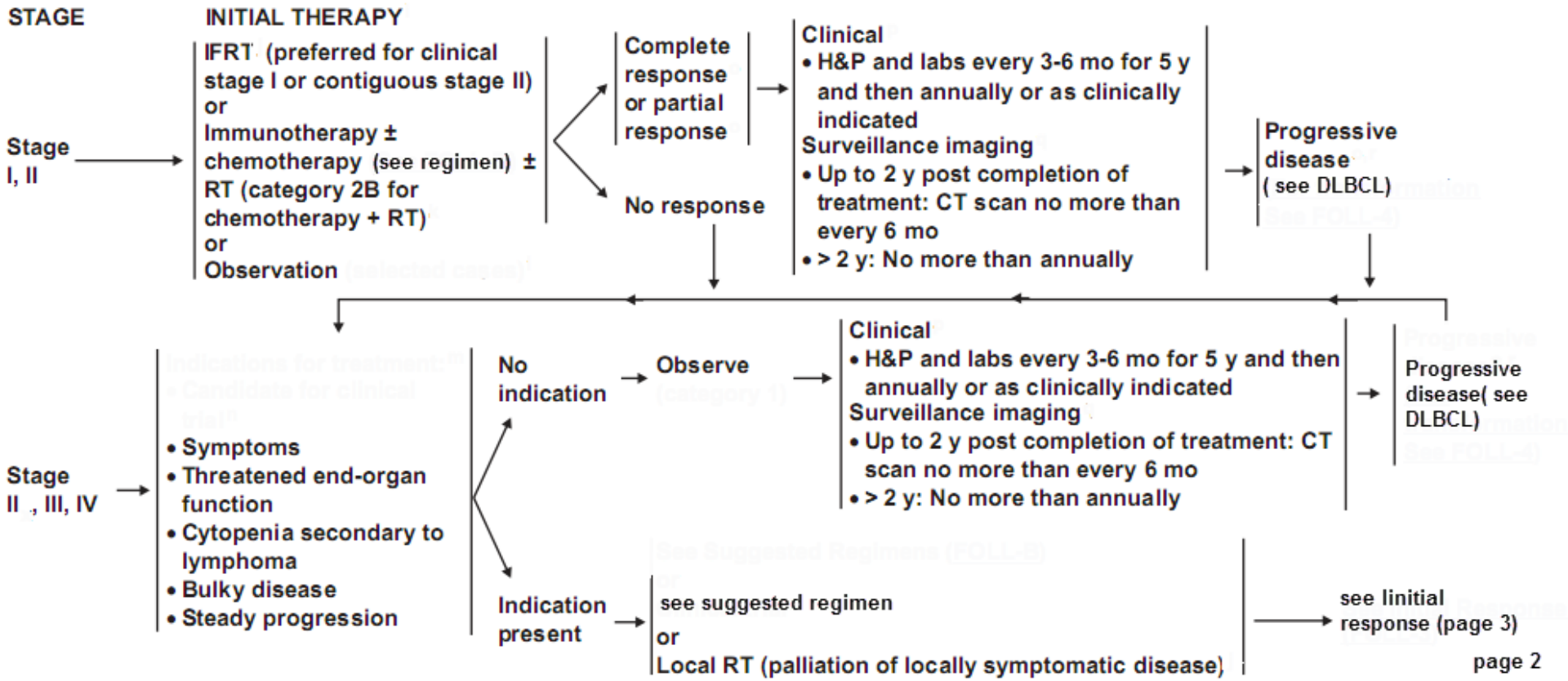
Stage II,III,IV

See Page 2

備註：1.Follicular lymphoma grade 3 is commonly treated according to the DLBCL

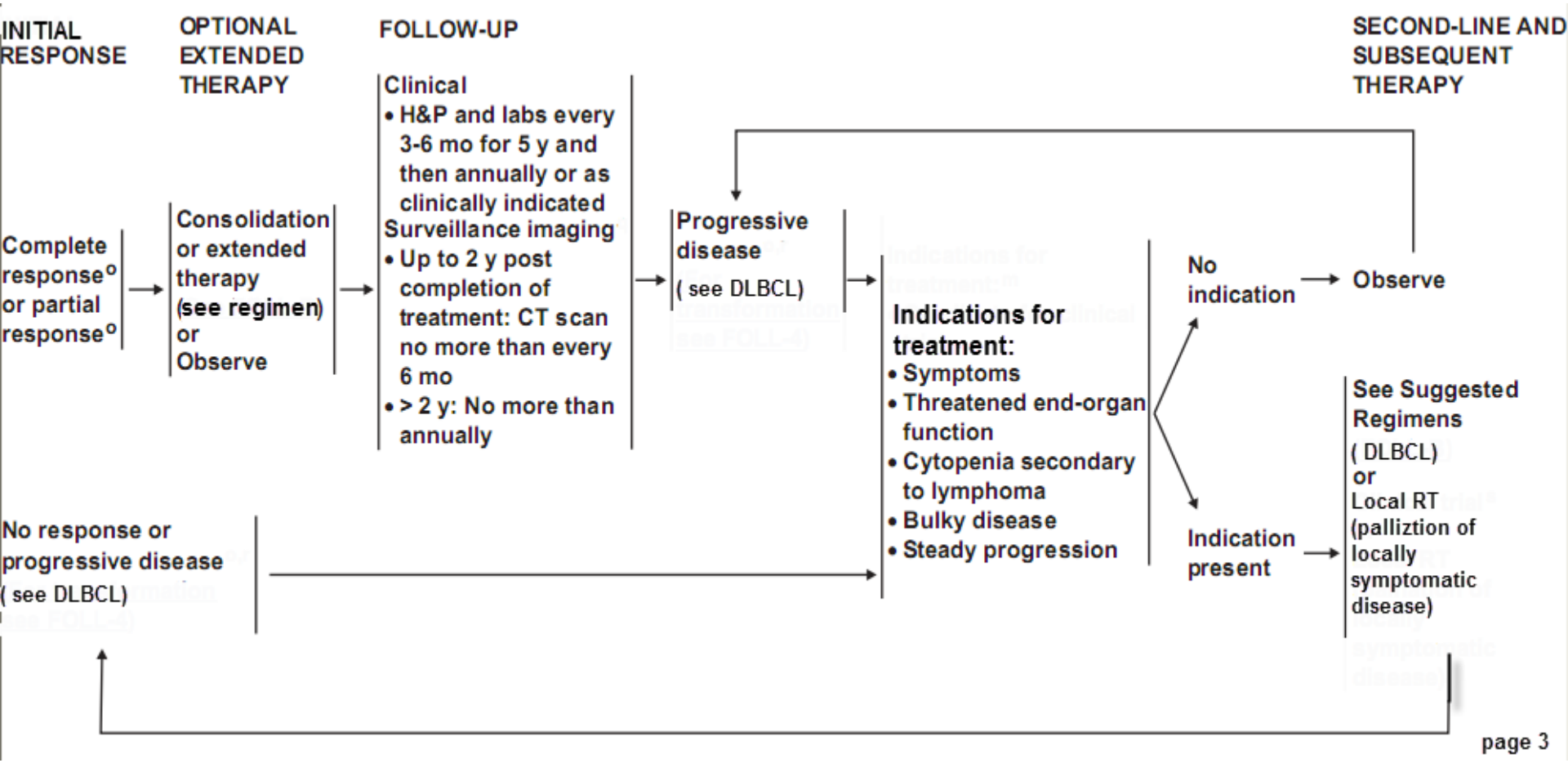
Follicular lymphoma（grade 1-2）

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Follicular lymphoma（**grade 1-2**）

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Follicular lymphoma（grade 1-2）

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GELF CRITERIA

- Involvement of ≥ 3 nodal sites, each with a diameter of ≥ 3 cm
- Any nodal or extranodal tumor mass with a diameter of ≥ 7 cm
- B symptoms
- Splenomegaly
- Pleural effusions or peritoneal ascites
- Cytopenias (leukocytes < 1.0 x 10^9/L and/or platelets < 100 x 10^9/L)
- Leukemia (> 5.0 x 10^9/L malignant cells)

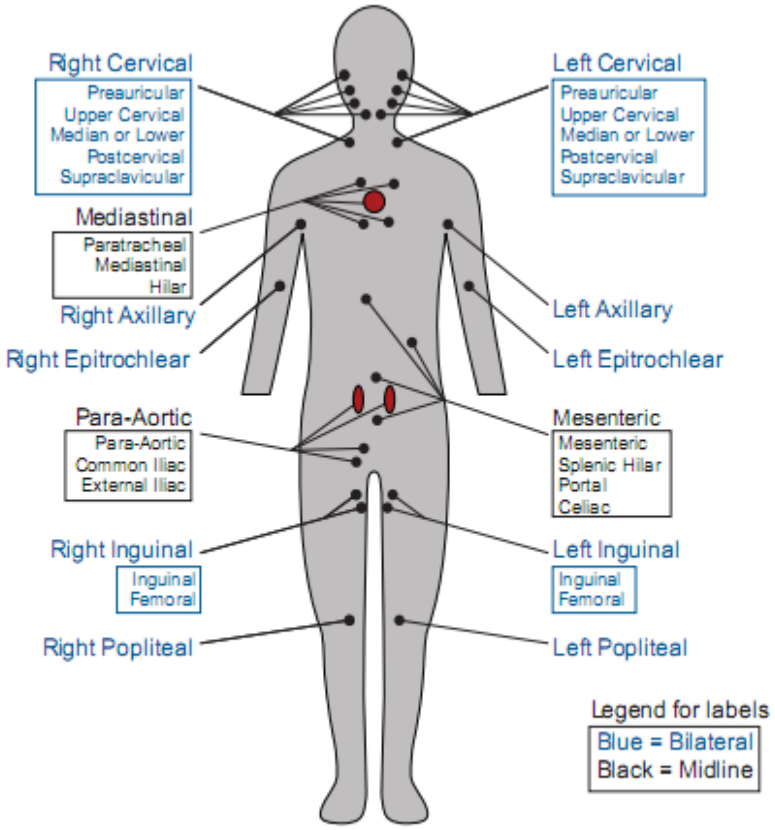
FLIPI - 1 CRITERIA

Age	≥ 60 y
Ann Arbor stage	III-IV
Hemoglobin level	< 12 g/dL
Serum LDH level	> ULN (upper limit of normal)
Number of nodal sites[d]	≥ 5

Risk group according to FLIPI chart

	Number of factors
Low	0-1
Intermediate	2
High	≥ 3

Nodal Areas



Mannequin used for counting the number of involved areas.[a]

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Follicular lymphoma（**grade 1-2**）

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First line regimen：

1.R-CEOP	Rituximab 375MG/M2 IVA on D1
	Cyclophosphamide 750MG/M2 IVA on D1 or D2
	Epirubicin 75MG/M2 IVA on D1 or D2
	Vincristine 2MG IVA on D1 or D2
	Prednisone 5MG 10TAB BID po for 5days Reference:NO2

2.R-COP	Rituximab 375MG/M2 IVA on D1
	Cyclophosphamide 800MG/M2 IVA on D1 or D2
	Vincristine 2MG IVA on D1 or D2
	Prednisone 5MG 10TAB BID po for 5days Reference:NO2

3. Rituximab 375MG/M2 IVA on D1 WEEKLY for 4 doses Reference:NO3

Follicular lymphoma（**grade 1-2**）

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First line regimen for elderly or infirm：

1.Rituximab 375MG/M2 IVA on D1
2.Single-agent alkylators±Rituximab
3.Radioimmunotherapy Reference:NO4

First line consolidation or extended dosing（optional）：

1.Rituximab maintenance 375MG/M2 one dose every 3 months up to 2y for patients initially presenting with high tumor burden
2.Chemotherapy followed by radioimmunotherapy Reference:NO5

Follicular lymphoma（**grade 1-2**）

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Second line and subsequent therapy：

1.Bendamustine 50~150MG/M2 +Rituximab 375MG/M2
2.FCMR（Fludarabine25MG/M2 D1-3, Cyclophosphamide 200MG/M2 D1-3,
Mitoxantrone 8MG/M2 D1,Rituximab 375MG/M2）
3.Fludarabine＋ Rituximab
4.Rituximab
5.RFND（Rituximab, Fludarabine, Mitoxantrone,Dexamethasone20MG/M2）
6.Radioimmunotherapy

Reference:NO6、NO7、NO8 、NO9

Second line consolidation or extended dosing：

1.High dose therapy with autologous stem cell rescue
2.Allogeneic stem cell transplant for highly selected patients
3.Rituximab maintenance 375MG/M2 one dose every 3 months up to 2years(optional)

Reference: NO10

Follicular lymphoma（grade 1-2）

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Follicular lymphoma（**grade 1-2**）

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