高 雄 榮 民 總 醫 院
淋巴癌診療原則

2019年02月26日 第一版

淋巴癌醫療團隊擬訂

注意事項：這個診療原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，直接引用這個診療原則並不恰當，只有你的醫師才能決定給你最恰當的治療。

會議討論

上次會議：2018/05/22

本共識與上一版的差異

上一版	新版
無	審視最新版NCCN guidelines與本院目前制定之指引無差異故此版審視後無修改

PROTOCOLS FOR TREATMENT OF MALIGNANT LYMPHOMA

Version 1. 2019

MALIGNANT LYMPHOMA

Kaohsiung Veterans General Hospital
Clinical Practice Guideline Version 1.2019

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

Lugano Modification of Ann Arbor Staging System*
(for primary nodal lymphomas)

Stage	Involvement	Extranodal (E) status
Limited		
Stage I	One node or a group of adjacent nodes	Single extranodal lesions without nodal involvement
Stage II	Two or more nodal groups on the same side of the diaphragm	Stage I or II by nodal extent with limited contiguous extranodal involvement
Stage II bulky**	II as above with "bulky" disease	Not applicable
Advanced		
Stage III	Nodes on both sides of the diaphragm	Not applicable
	Nodes above the diaphragm with spleen involvement	
Stage IV	Additional non-contiguous extralymphatic involvement	Not applicable

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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	

MALIGNANT LYMPHOMA

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Staging of gastric MALT LYMPHOMA：comparison of different systems

Lugano Staging System for Gastrointestinal Lymphomas		Lugano Modification of Ann Arbor Staging System	TNM Staging System Adapted for Gastric Lymphoma	Tumor Extension
Stage I	Confined to GI tract[a]			
	I_1 = mucosa, submucosa	I_E	T1 N0 M0	Mucosa, submucosa
	I_2 = muscularis propria, serosa	I_E	T2 N0 M0	Muscularis propria
		I_E	T3 N0 M0	Serosa
Stage II	Extending into abdomen			
	II_1 = local nodal involvement	II_E	T1-3 N1 M0	Perigastric lymph nodes
	II_2 = distant nodal involvement	II_E	T1-3 N2 M0	More distant regional lymph nodes
Stage IIE	Penetration of serosa to involve adjacent organs or tissues	II_E	T4 N0 M0	Invasion of adjacent structures
Stage IV[b]	Disseminated extranodal involvement or concomitant supradiaphragmatic nodal involvement		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 (Stage I –II) → **Radiation therapy**

2)Advanced Stage (Stage 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

1)Early Stage
(Stage I –II)

→ **4 Courses of chemotherapy (CHOP) + ISRT**
OR
6-8 Courses of chemotherapy (CHOP)
R-CEOP For Follicular lymphoma & DLBCL

2)Advanced Stage
(Stage III–IV)

→ **a) 6-8 courses of chemotherapy (CHOP)**
R-CHOP For DLBCL
+
local radiation for bulky mass

→ **b) autologous PBSCT**

→ **i) fails to achieve 1st complete remission with initial therapy**
ii) relapse post 1st line chemotherapy
iii) consolidation for patient at high risk of relapse
high serum LDH level, bulky disease, extranodal disease, advanced stage
iv) primary refractory (overt chemotherapy resistance)

3) Relapsed intermediate grade lymphoma

→ **a) slavage chemotherapy to confirm chemo-sensitivity**

→ **b) autologous PBSCT**

MALIGNANT LYMPHOMA

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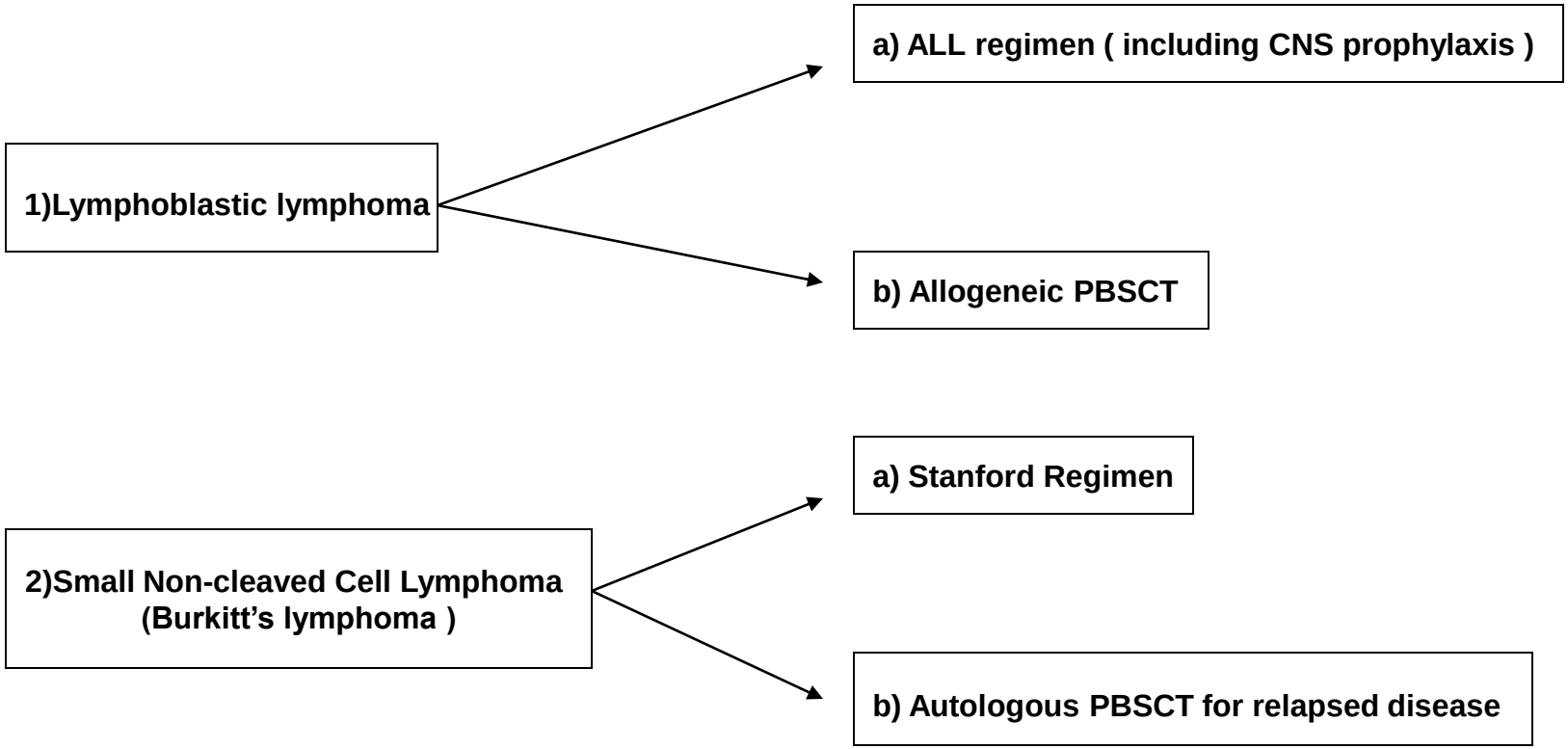
NON-HODGKINS'S LYMPHOMA

HIGH GRADE LYMPHOMA



MALIGNANT LYMPHOMA

- 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

MALIGNANT 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

MALIGNANT LYMPHOMA

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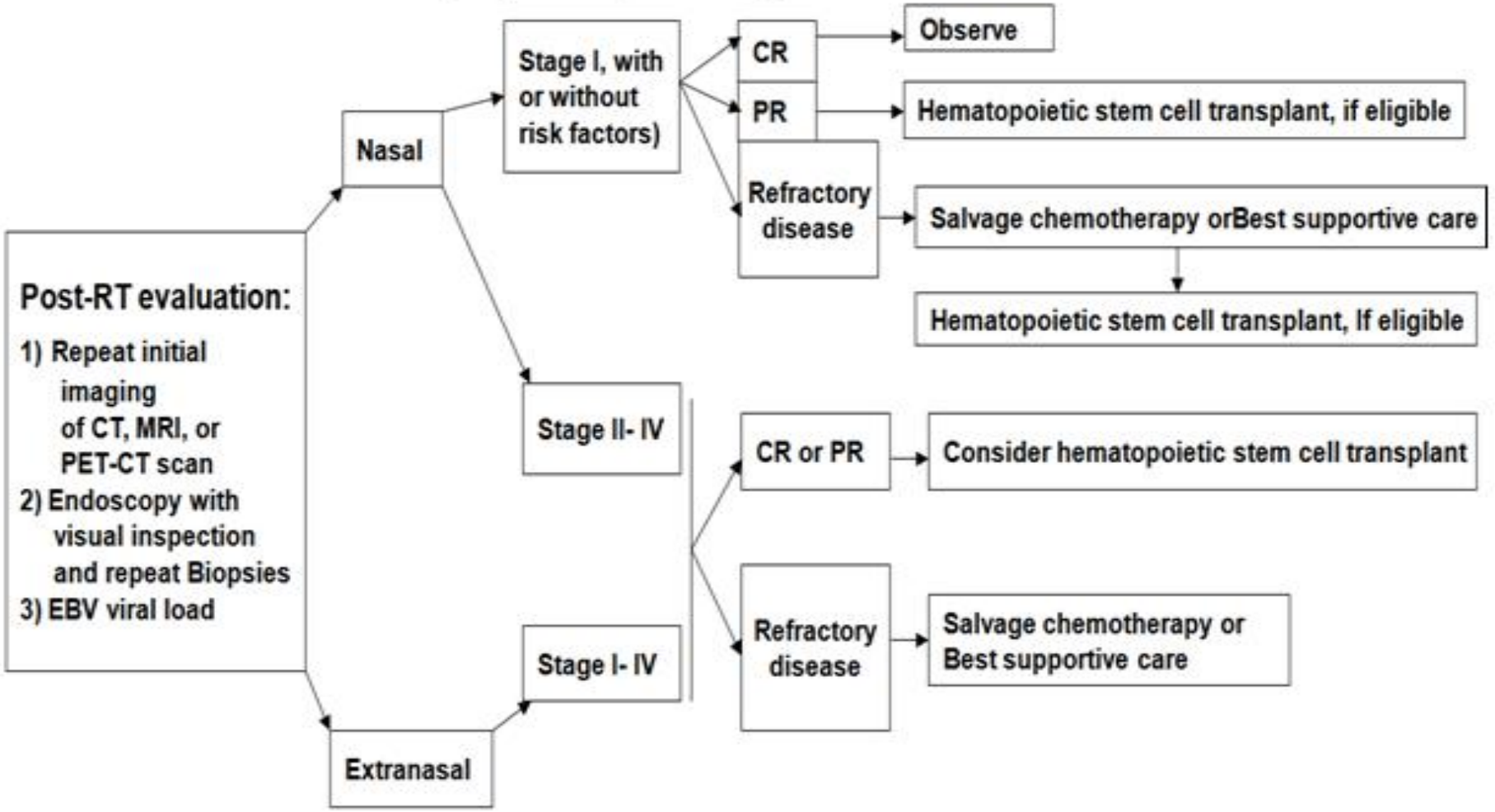
Extranodal NK/T-cell Lymphoma, nasal type



MALIGNANT LYMPHOMA

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NK/T CELL LYMPHOMA PROGNOSTIC INDEX

PROGNOSTIC INDEX OF NATURAL KILLER LYMPHOMA (PINK)[a]

RISK FACTORS	
Age >60 y	
Stage III or IV disease	
Distant lymph-node involvement	
Non-nasal type disease	
	Number of risk factors
Low	0
Intermediate	1
High	≥2

PROGNOSTIC INDEX OF NATURAL KILLER CELL LYMPHOMA WITH EPSTEIN-BARR VIRUS DNA (PINK-E)[a]

RISK FACTORS	
Age >60 y	
Stage III or IV disease	
Distant lymph-node involvement	
Non-nasal type disease	
Epstein-Barr virus DNA	
	Number of risk factors
Low	0–1
Intermediate	2
High	≥3

References:

1.NCCN guidelines of Hodgkin's disease/lymphoma, V.3 2018

2.NCCN guidelines of Non-Hodgkin' s lymphomas, V.4 2018

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。

2018/02/26 審視

Diffuse large B cell lymphoma

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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 ※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 ＊ Beta2- microglobulin

Diffuse large B cell lymphoma

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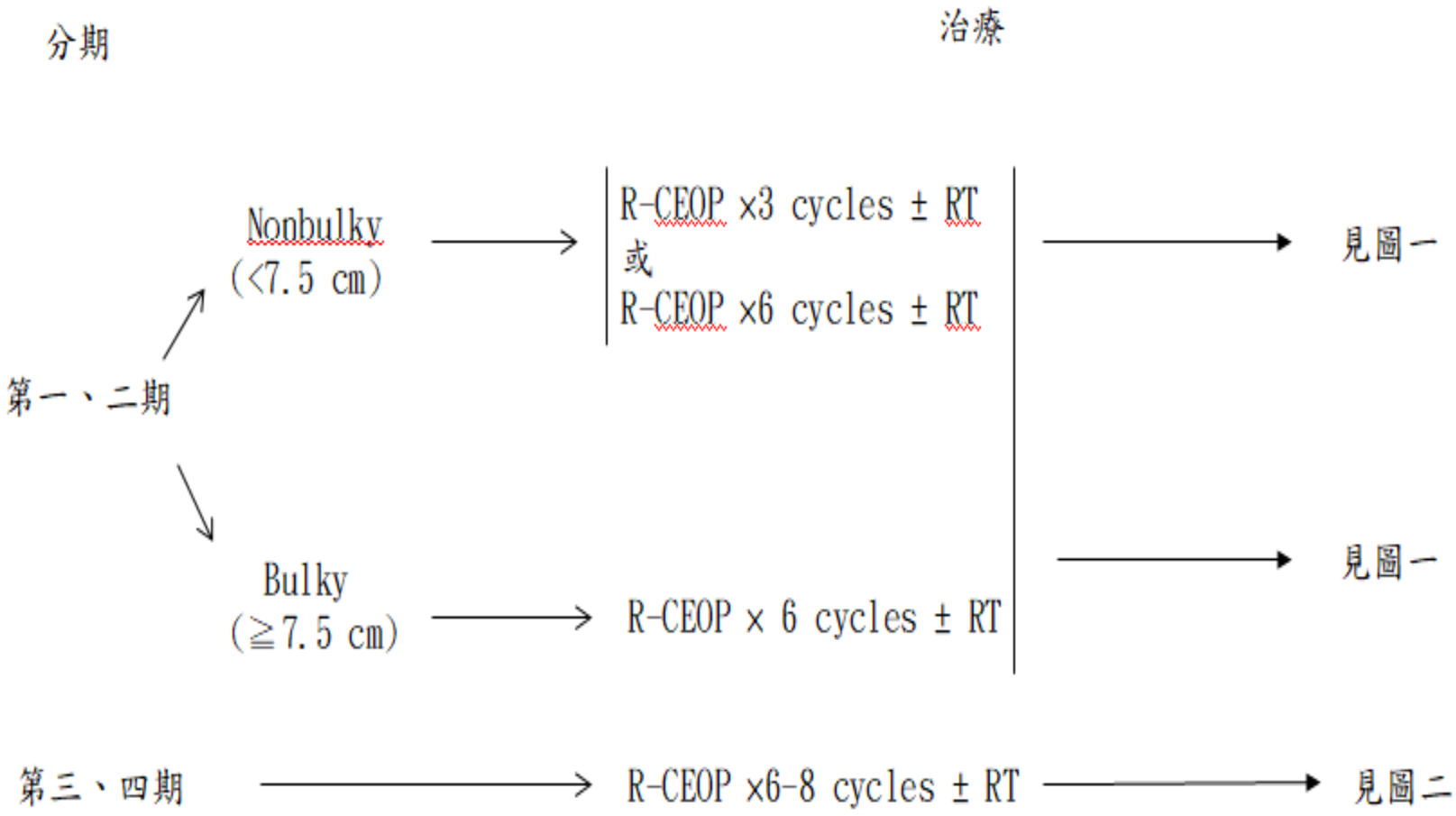

Diffuse large B cell lymphoma

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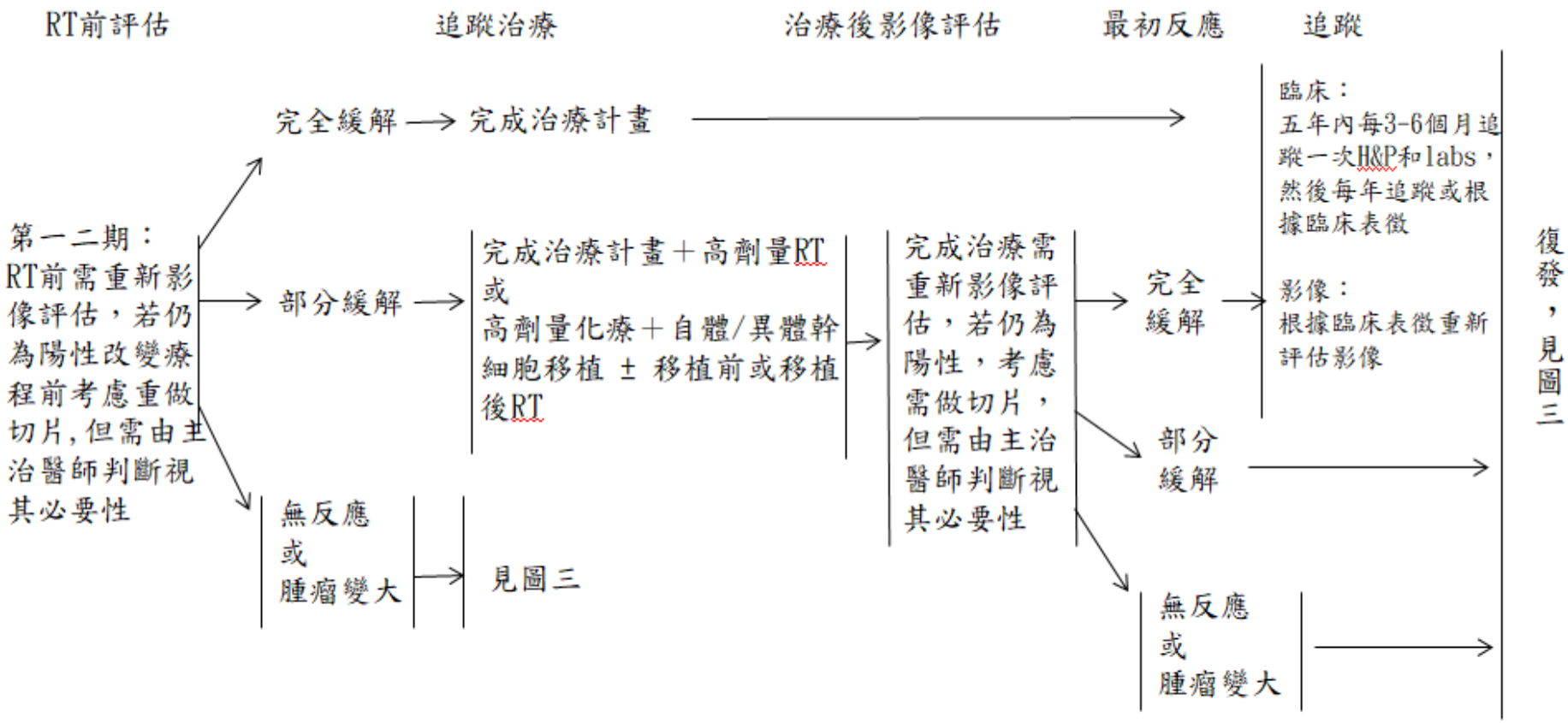

圖一

Diffuse large B cell lymphoma

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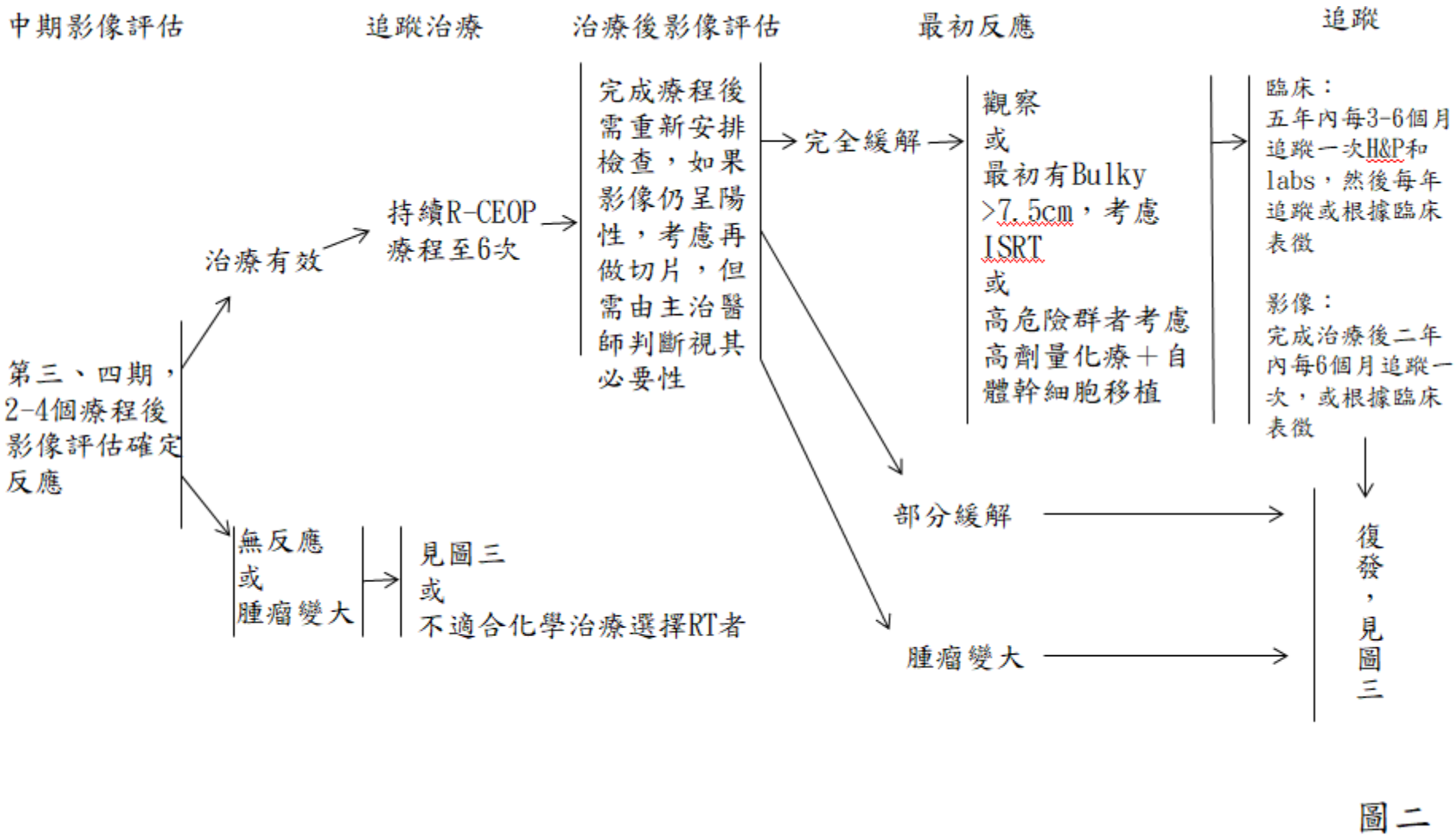

圖二

Diffuse large B cell lymphoma

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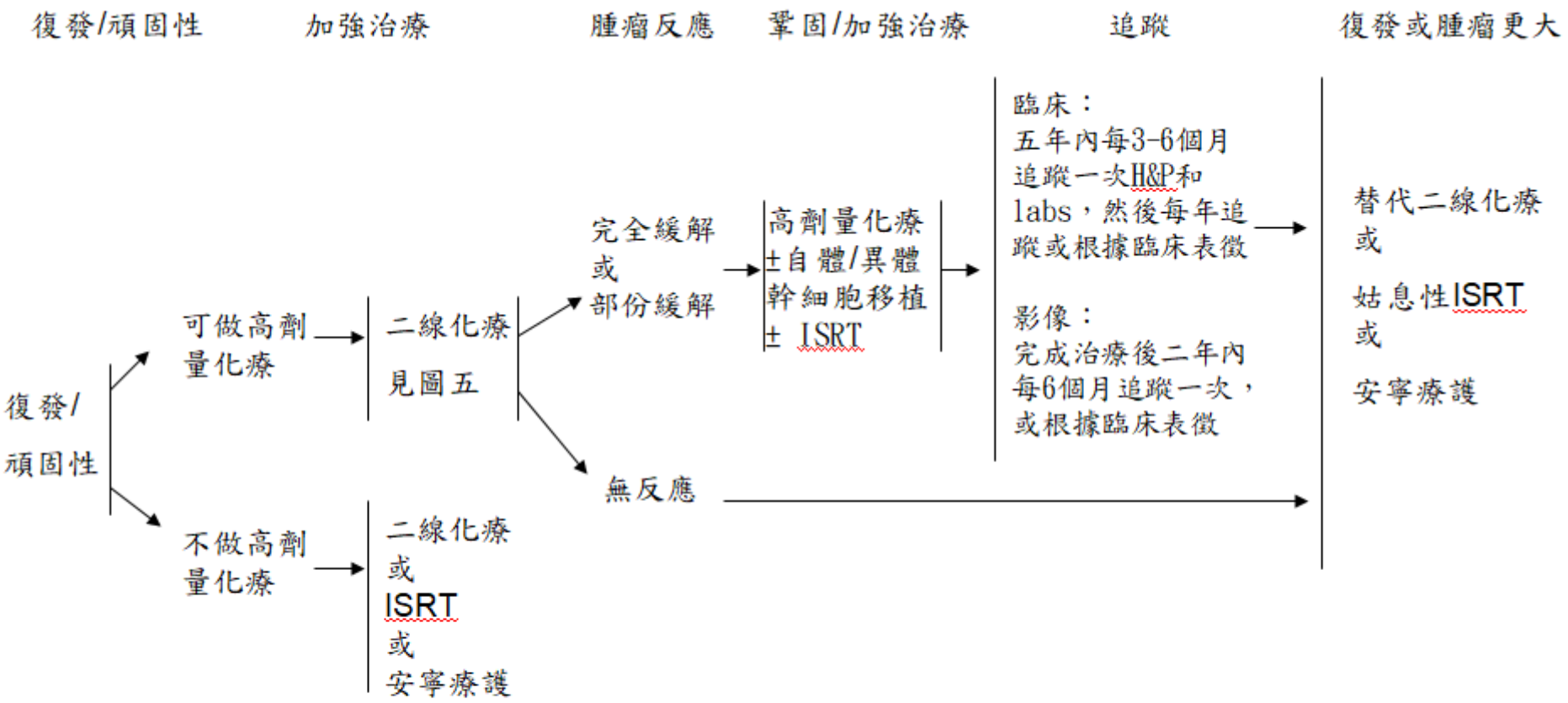

圖三

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 or SC 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
R-CHOP	± Rituximab 375MG/M2 IVA or SC on D1
	Cyclophosphamide 750MG/M2 IVA on D1 or D2
	Doxor 50MG/M2 IVA on D1 or D2
	Vincristine 2MG IVA on D1 or D2
	Prednisone 5MG 10TAB BID po for 5days
	References:NO 2

Diffuse large B cell lymphoma

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一線化療	
DA-EPOCH-R	Etoposide 50MG/M2 IVA D1-4
	Prednisone 10TAB PO BID for 5days
	Vincristine 0.4MG/M2 IVA D1-4
	Epicin 15MG/M2 IVA D1-4
	Cyclophosphamide 750MG/M2 IVA D5
	± Rituximab 375MG/M2 IVA or SC D1 References: NO 3

Diffuse large B cell lymphoma

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一線化療(適用於年紀大或心臟功能不好病人)	
R-CNOP	± Rituximab 375MG/M2 IVA or SC 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 4
R-COP	± Rituximab 375MG/M2 IVA or SC on D1
	Cyclophosphamide 800MG/M2 IVA on D1 or D2
	Vincristine 2MG IVA on D1 or D2
	Prednisone 5MG 10TAB BID po for 5days
	References : NO 4

Diffuse large B cell lymphoma

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建議治療療程

二線化療（適用於執行高劑量化療+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 : NO5
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 : NO6

Diffuse large B cell lymphoma

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建議治療療程

二線化療（適用於執行高劑量化療+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 : NO7
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

二線化療（適用於無法執行高劑量化療者）	
Bendamustine 50~150MG/M2 IVA ± Rituximab	References : NO8、9
Gemox 1000~1250MG/M2 IVA ± Rituximab	References : NO10

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

References:

1.NCCN guidelines of Non-Hodgkin' s lymphomas, V.4 2018

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.Purroy N, Bergua J, Gallur L, et al. Long-term follow-up of dose-adjusted EPOCH plus rituximab(DA-EPOCH-R), in untreated patients with poor prognosis large B cell lymphoma. A phase II study conducted by the Spanish PETHEMA Group. Br J Haematol 2015;169:188-198.

4.Zaja F, Tomadini V, Zaccaria A,et al.CHOP-rituximab with pegylated liposomal doxorubicin for the treament of elderly patients with diffuse large B-cell lymphoma. Leuk Lymphoma 2006;47:2174-2180.

5.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.

6.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.

7.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.

8. Weidmann E, Kim SZ, Rost A,et al.Bendamustine is effective in relapsed or refractory aggressive non-Hodgkin's lymphoma.Ann Oncol 2002;13:1285-1289.

9.Vacirca JL, Acs PI, Tabbara IA, et al. Bendamustine combined with rituximab for patients with relapsed or refractory diffuse large B cell lymphoma. Ann Hematol 2014;93:403-409.

10.Lopez A, Gutierrez A, Palacios A, et al. GEMOX-R regimen is a highly effective salvage regimen in patients with refractory/relapsing diffuse large-cell lymphoma:a phase II study. Eur J Haematol 2008;80:127-132.

Hodgkin 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

2019/2/26審視

Hodgkin Lymphoma

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Table 1

Definitions of Stages in Hodgkin's Disease

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 (eg, 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 with permission from the American Association for Cancer Research: 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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Unfavorable Risk Factors for Stage I-II Classic Hodgkin Lymphoma

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

GHSG = German Hodgkin Study Group
EORTC = European Organization for the Research and Treatment of Cancer
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

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/mm³)**
- **Lymphocytopenia (lymphocyte count less than 8% of white blood cell count, and/or lymphocyte count less than 600/mm³)**

†From: Hasenclever D, Diehl V. A prognostic score for advanced Hodgkin's disease: International Prognostic Factors Project on Advanced Hodgkin's Disease. N Engl J Med 1998;339:1506-1514. Copyright © 1998 Massachusetts Medical Society. Adapted with permission.

Hodgkin Lymphoma

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DIAGNOSIS/WORKUP

- Excisional biopsy (recommended)
- Core needle biopsy may be adequate if diagnostic[a]
- Immunohisto-chemistry evaluation[b]

Essential:

- H&P including: B symptoms (unexplained fever >38°C; drenching night sweats; or weight loss >10% of body weight within 6 mo of diagnosis), alcohol intolerance, pruritus, fatigue, performance status, examination of lymphoid regions, spleen, liver
- CBC, differential, platelets
- Erythrocyte sedimentation rate (ESR)
- Comprehensive metabolic panel, lactate dehydrogenase (LDH), and liver function test (LFT)
- Pregnancy test for women of childbearing age
- Diagnostic CT[c] (contrast-enhanced)
- PET/CT scan[d] (skull base to mid-thigh)
- Counseling: Fertility, smoking cessation, psychosocial (See NCCN Guidelines for Supportive Care)

Useful in selected cases:

- Fertility preservation[e]
- Diagnostic neck CT with contrast, if neck is PET/CT+ or if neck RT contemplated
- Pulmonary function tests (PFTs incl. diffusing capacity [DLCO])[f] if ABVD or escalated BEACOPP are being used
- Pneumococcal, H-flu, meningococcal vaccines, if splenic RT contemplated
- HIV and hepatitis B/C testing (encouraged)
- Chest x-ray (encouraged, especially if large mediastinal mass)
- Adequate bone marrow biopsy if there are cytopenias and negative PET[g]
- Evaluation of ejection fraction if doxorubicin-based chemotherapy is indicated
- MRI or PET/MRI (skull base to mid-thigh) with contrast unless contraindicated

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

Hodgkin Lymphoma

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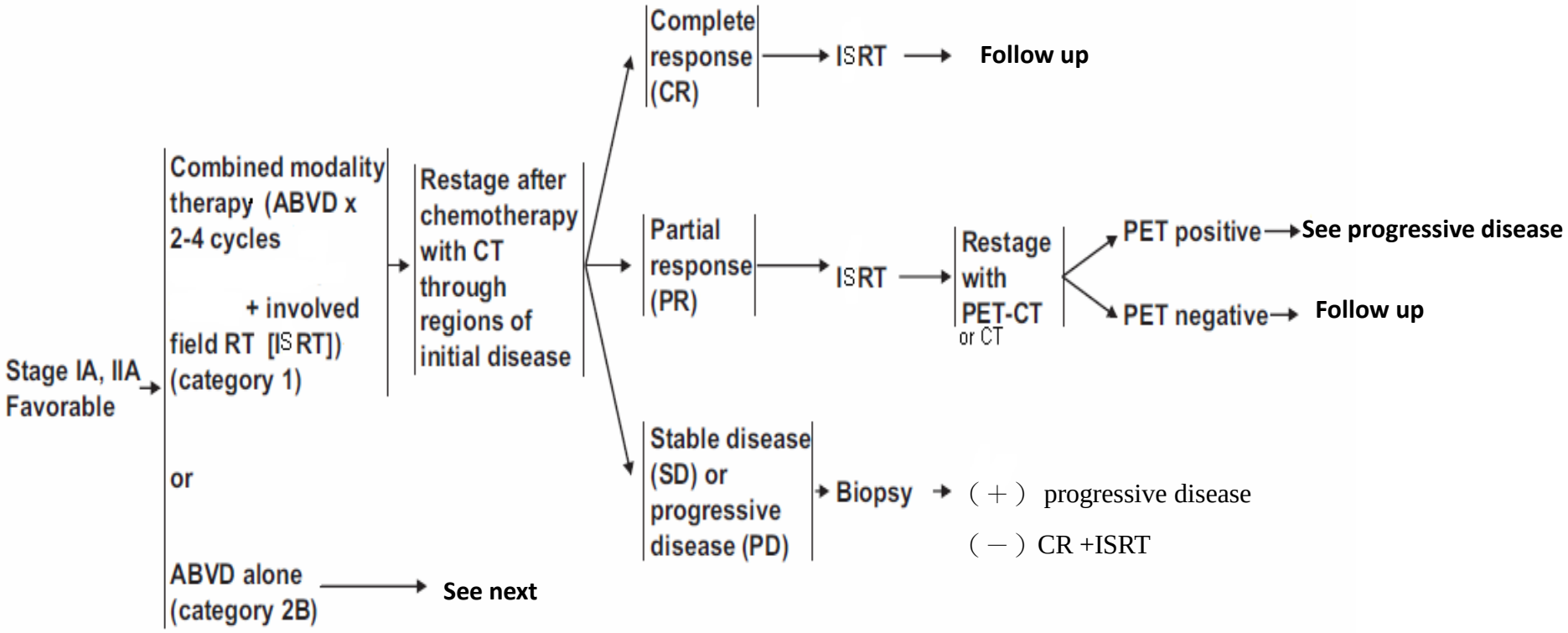
Classical Hodgkin Lymphoma Stage IA-IIA Favorable



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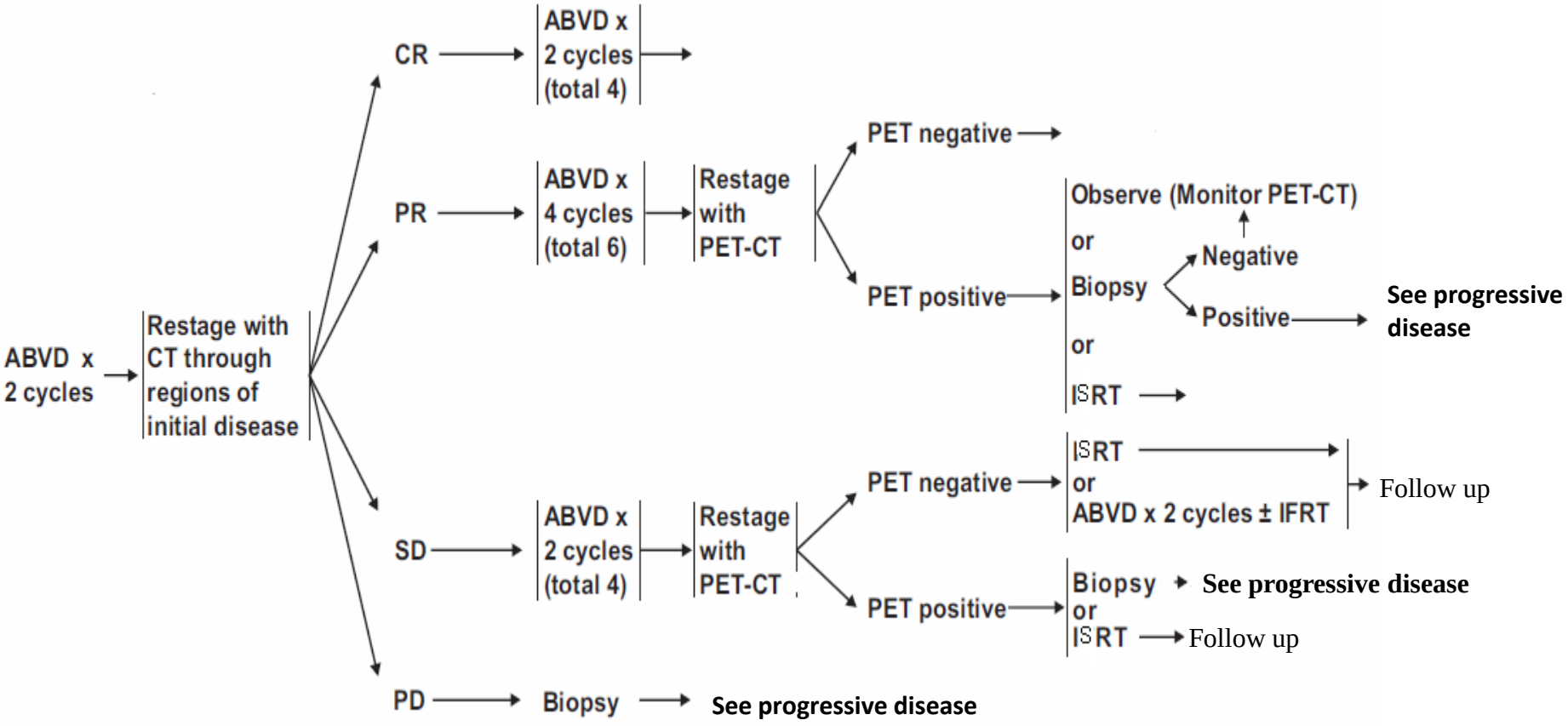
Classical Hodgkin Lymphoma Stage IA-IIA Favorable (C/T alone first)



Hodgkin Lymphoma

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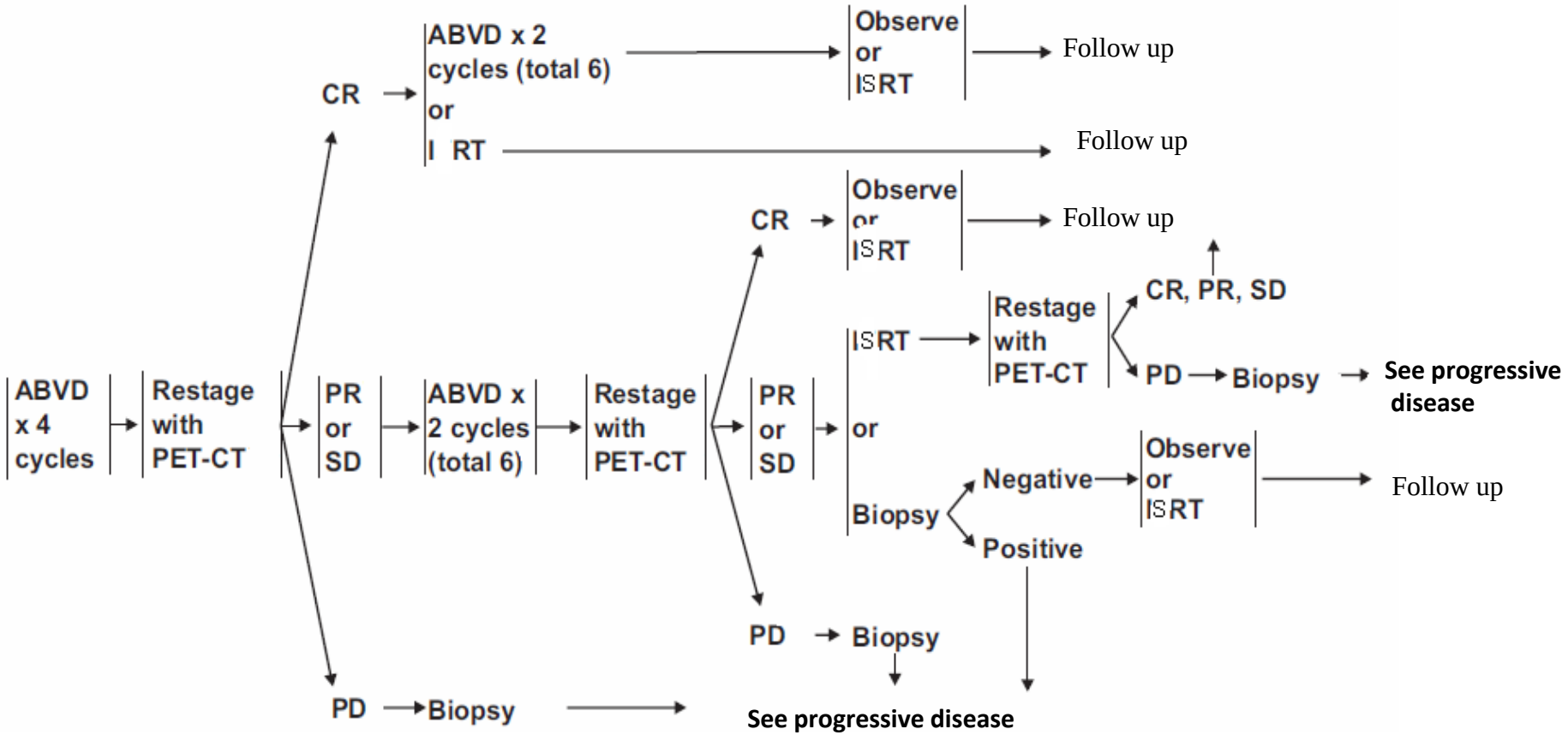
Classical Hodgkin Lymphoma Stage I-II Unfavorable (Non-bulky, C/T alone first)



Hodgkin Lymphoma

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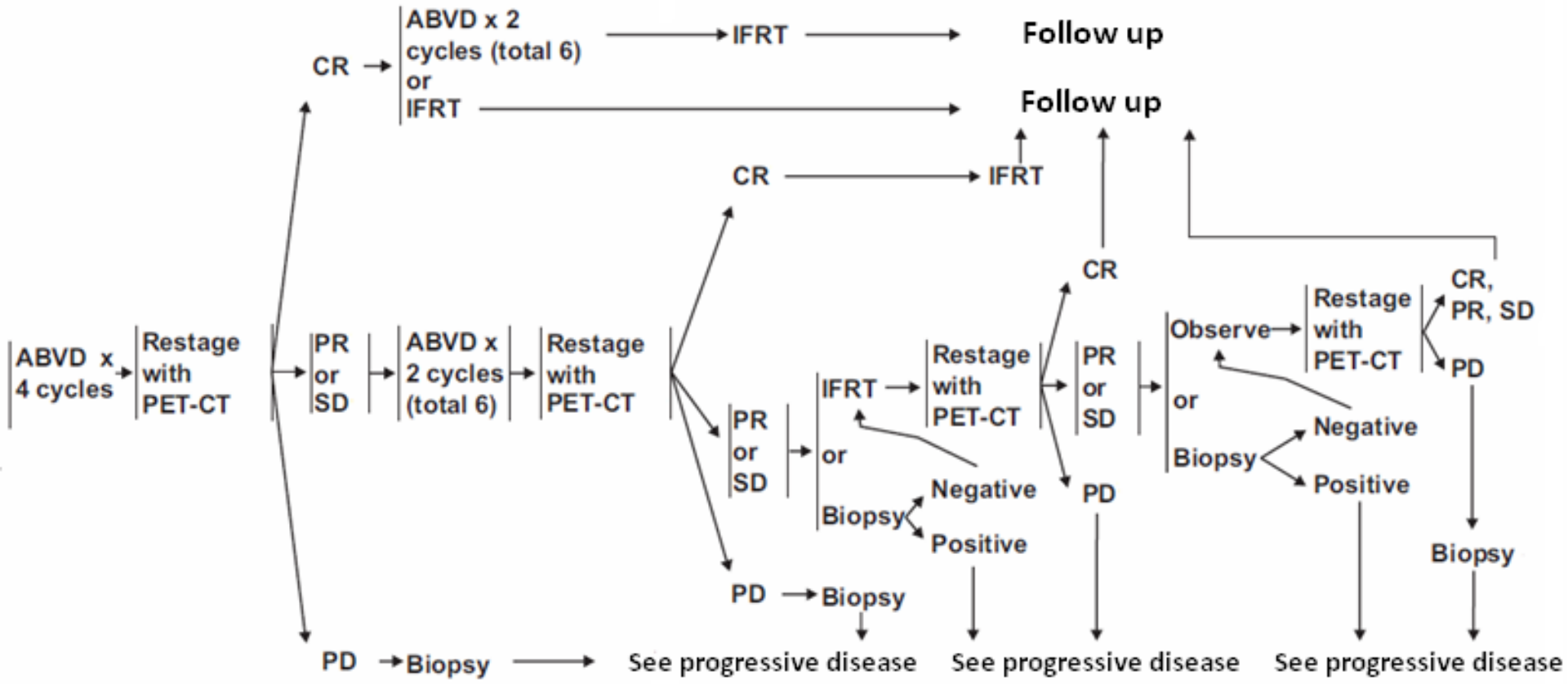
Classical Hodgkin Lymphoma Stage I-II Unfavorable (Bulky, C/T alone first)



Hodgkin Lymphoma

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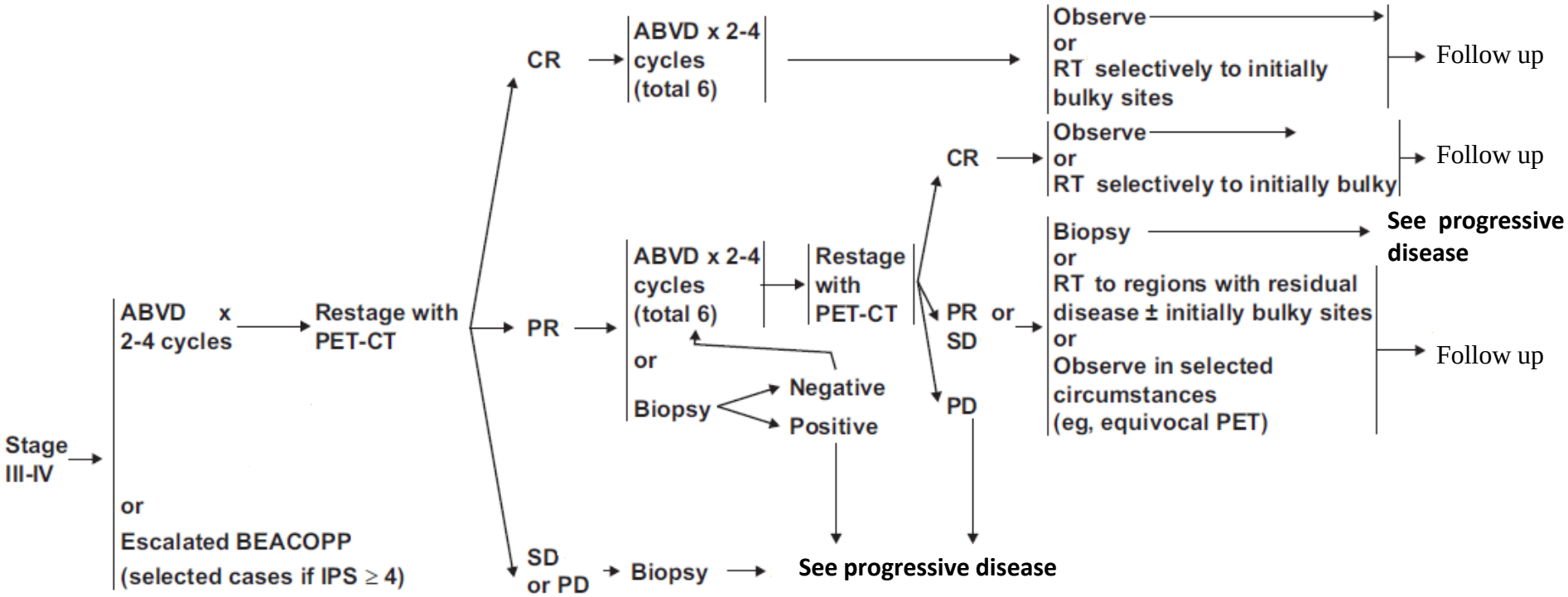
Classical Hodgkin Lymphoma Stage III-IV



Hodgkin Lymphoma

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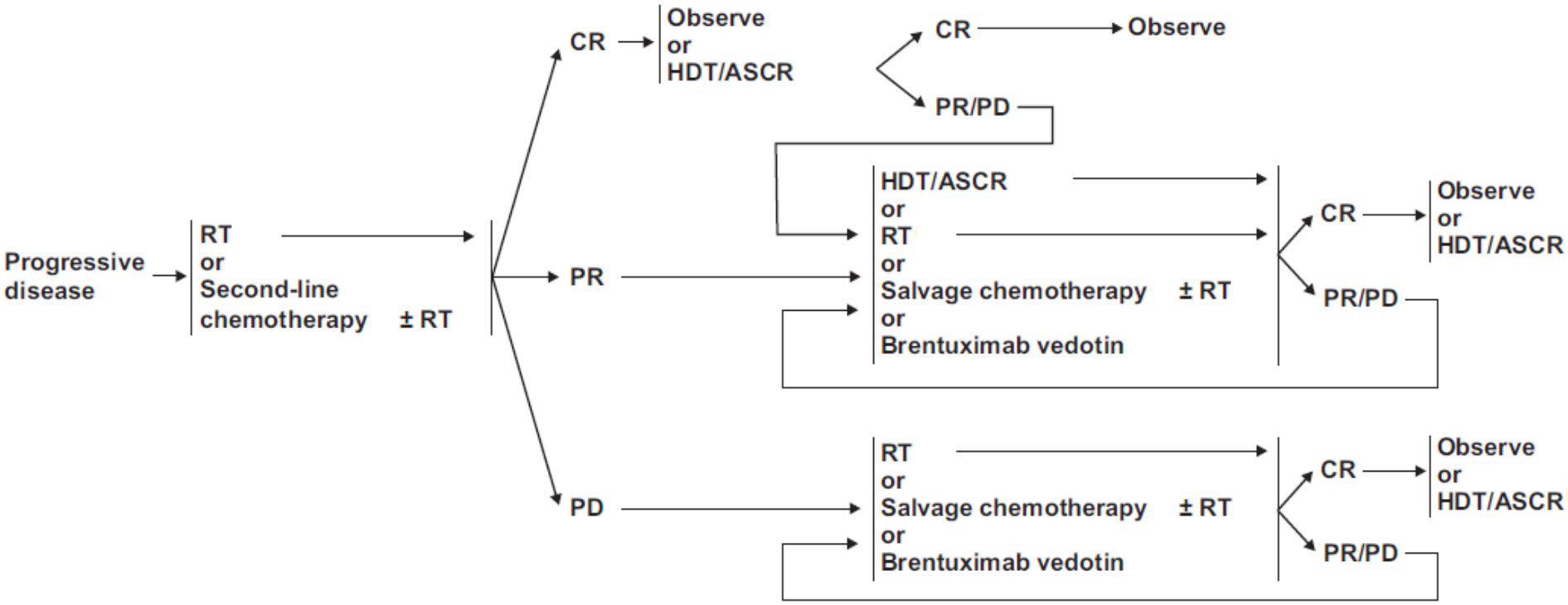
Classical Hodgkin Lymphoma (progressive disease or relapse)



Hodgkin Lymphoma

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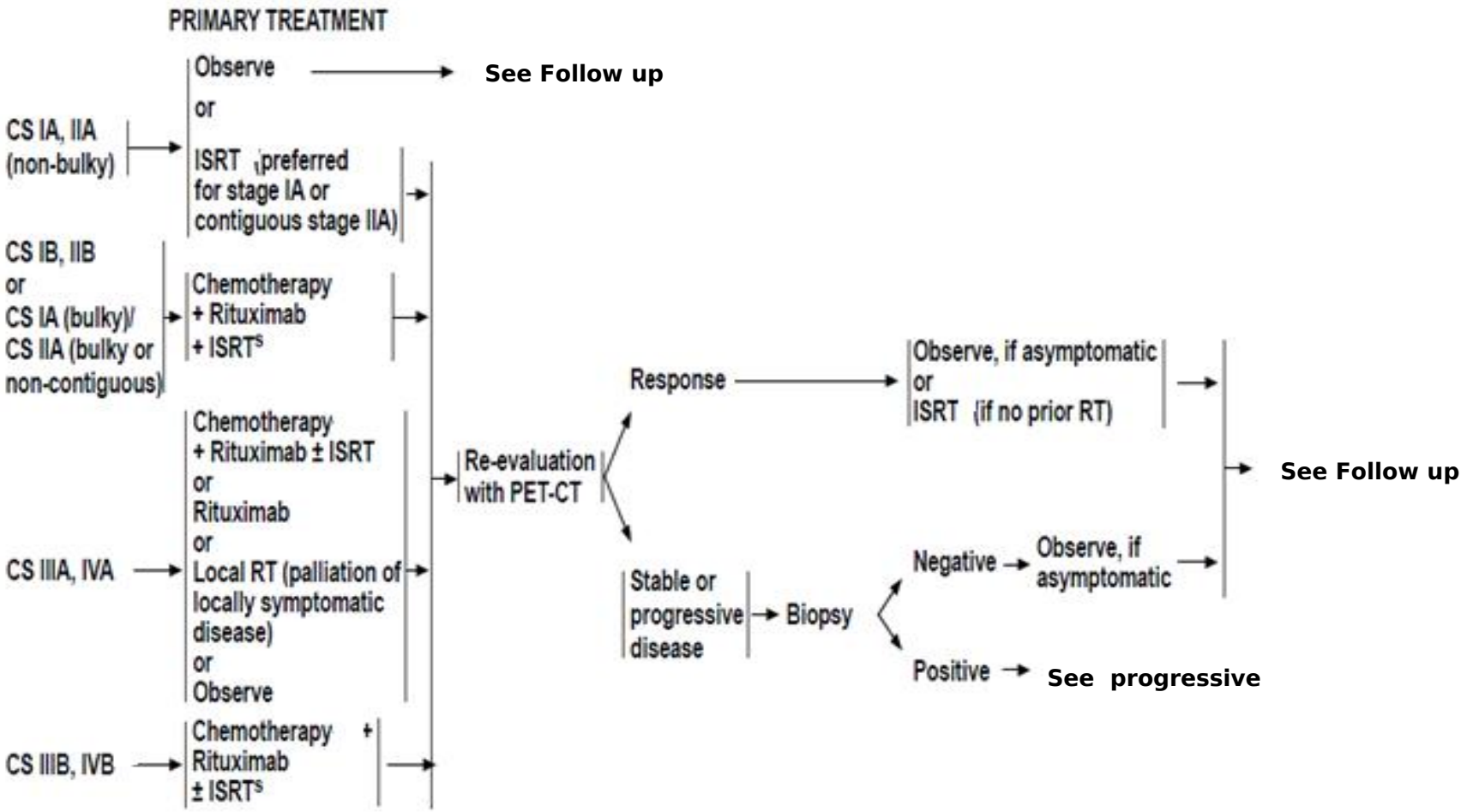
Lymphocyte-predominant Hodgkin Lymphoma



Hodgkin Lymphoma

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Hodgkin lymphoma-Commonly used chemotherapy regimen

ABVD (Q4W)	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
	References : NO3、4

Hodgkin Lymphoma

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Second –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 : NO5
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 : NO6、7

Hodgkin Lymphoma

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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 : NO8
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 : NO8

Hodgkin Lymphoma

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Reference

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Follicular 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

2019/02/26審視

Follicular lymphoma

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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 Essential：

＊Physical exam：attention to node-bearing areas , including Waldeyer's rings, and to size of liver and spleen
＊Performance status
＊B- symptoms
＊CBC & differential, LDH, Uric acid
＊Comprehensive metabolic panel
◆ CT：face / chest / abdominal / pelvic or PET
◆ bone marrow biopsy ± aspirate
＊~~IPI SCORE~~
＊Hepatitis B、C testing
＊Echo cardiogram or ejection fraction

選擇性：
＊HIV
＊Discussion of fertility issues and sperm banking
＊Lumbar puncture
＊Beta2 - microglobulin

Stage I,II

Stage III,IV

See Page 2

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

Follicular lymphoma（grade 1-2）

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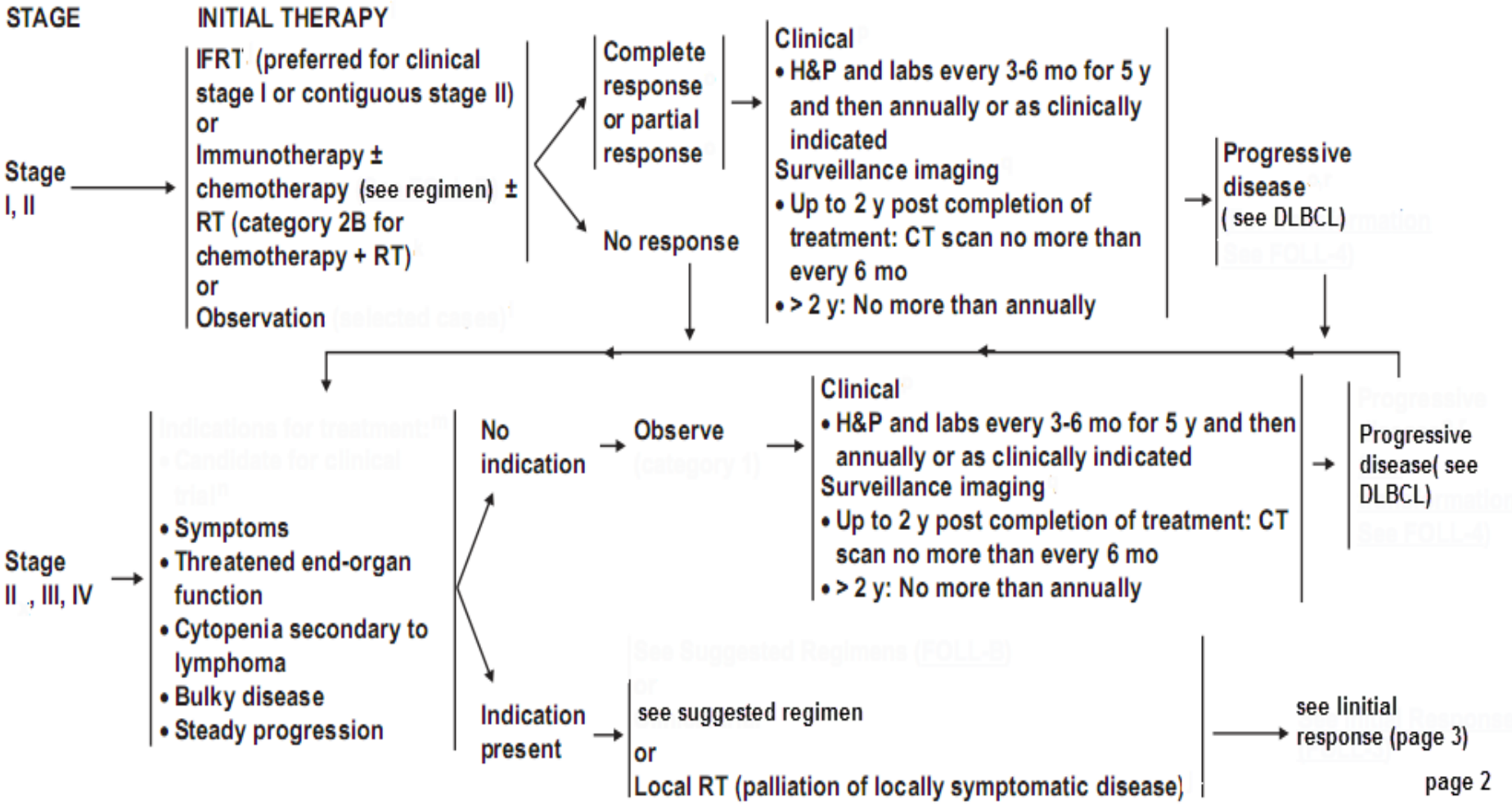

Follicular lymphoma（grade 1-2）

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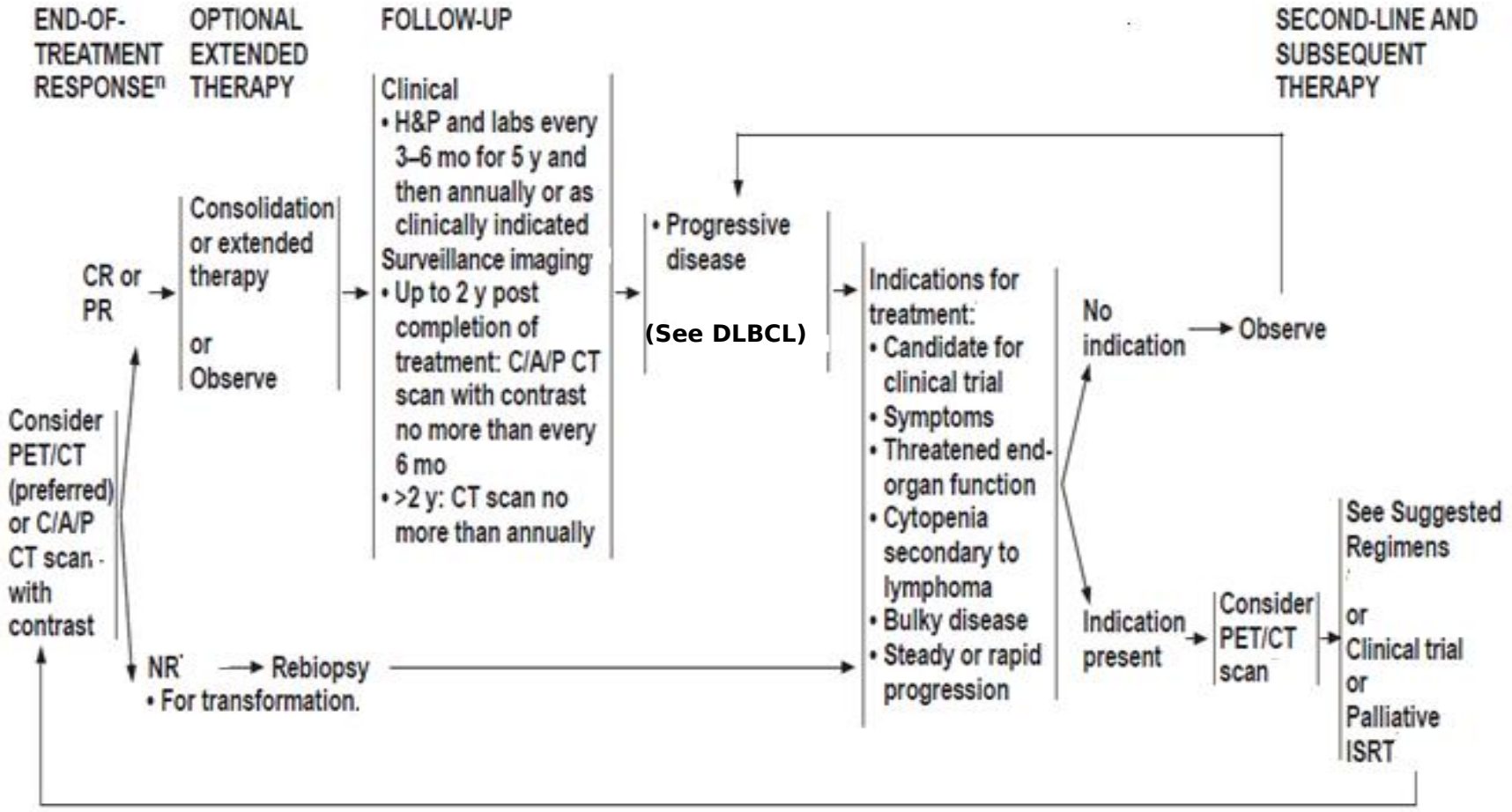

Follicular lymphoma

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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)

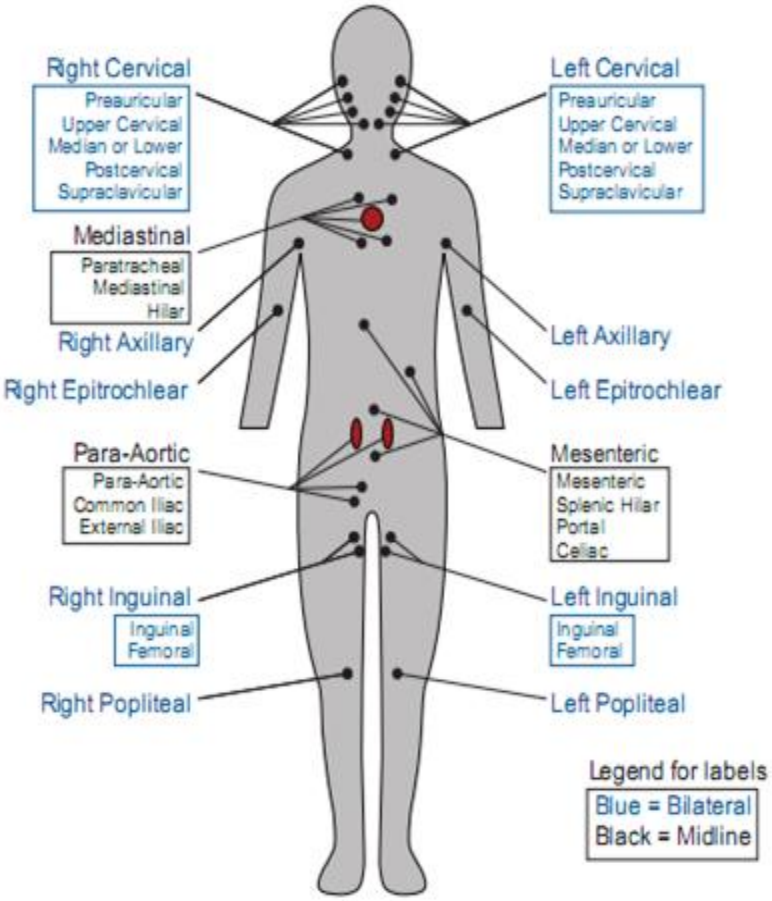
FLIPI - 1 CRITERIA

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



Follicular lymphoma（grade 1-2）

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First line regimen：

1.R-CHOP	Rituximab 375mg/m^2 IVA or SC on D1
	Cyclophosphamide 750mg/m^2 IVA on D1 or D2
	Doxor 50mg/m^2 IVA on D1 or D2
	Vincristine 2MG IVA on D1 or D2
	Prednisone 5MG 10TAB BID po for 5days Reference:NO2.3
2.R-CEOP	Rituximab 375mg/m^2 IVA or SC on D1
	Cyclophosphamide 750mg/m^2 IVA on D1 or D2
	Epirubicin 75mg/m^2 IVA on D1 or D2
	Vincristine 2MG IVA on D1 or D2
	Prednisone 5MG 10TAB BID po for 5days Reference:NO2.3

Follicular lymphoma（grade 1-2）

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First line regimen：

3.R-COP	Rituximab 375mg/m^2 IVA or SC on D1	
	Cyclophosphamide 800mg/m^2 IVA on D1 or D2	
	Vincristine 2MG IVA on D1 or D2	
	Prednisone 5MG 10TAB BID po for 5days	Reference:NO4
4.R+B	Rituximab 375mg/m^2 IVA or SC on D1	
	Bendamustine 50-150mg/m^2 IVA on D1	Reference:NO6
5. Rituximab 375mg/m^2 IVA or SC weekly for 4 doses		Reference:NO5

Follicular lymphoma（grade 1-2）

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First line regimen for elderly or infirm：

1.Rituximab 375MG/M2 IVA or SC weekly for 4 dose
2.Single-agent alkylators ± Rituximab Reference:NO7

First line consolidation or extended dosing（optional）：

1.Rituximab 375mg/m^2 one dose every 12weeks for 8dose
2.Obinutuzumab 1000mg every 8weeks for 12 dose
3.If initially treated with single-agent Rituximab,consolidation with Rituximab 375mg/m^2 one dose every 8weeks for 4 dose
Reference:NO8

Follicular lymphoma（grade 1-2）

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Second line and subsequent therapy ：

1.Bendamustine 50~150mg/m^2 + Rituximab 375mg/m^2
2.R-FCM（Rituximab 375mg/m^2,Fludarabine25mg/m^2 D1-3, Cyclophosphamide 200mg/m^2 D1-3, Mitoxantrone 8mg/m^2 D1）
3.Fludarabine ＋ Rituximab
4.Rituximab
5.RFND（Rituximab, Fludarabine, Mitoxantrone,Dexamethasone20MG/M2） Reference:NO9.10.11.12

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/m^2 one dose every 3 months up to 2years
Reference: NO11

Follicular lymphoma（grade 1-2）

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Follicular lymphoma（grade 1-2）

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