

高雄榮民總醫院

淋巴瘤診療原則

2020年04月21日第一版

血液暨淋巴瘤醫療團隊擬訂

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
1. NON-HODGKIN' S LYMPHOMA 惡性程度分類(P6)	→NON-HODGKIN' S LYMPHOMA 惡性程度分類:：新增分類次項目並刪減已無的分類 (P6)
2. Low grade lymphoma 流程圖(P8)	→Low grade lymphoma流程圖(P8)： early stage新增治療方式(watch & wait、Surgical)、advanced stage新增R及R+B，刪除2-3nd-line C/T
3. Intermediate lymphoma 流程圖(P9)	→刪除(P9)
4. High grade lymphoma 流程圖(P10)	→刪除(P10)
5. HL流程圖(P12)	→Hodgkin' s disease修改為Hodgkin 's lymphoma 新增AVD + BV Regimen for advanced stage (P12)
6. Reference	→新增 NCCN guidelines V.1 2020 (P15)
7. 無	→新增international prognostic index及IPI risk、risk of CNS disease 表格
8. DLBCL流程圖(P21-23)	→重新整理為一張流程圖(P24)
9. DLBCL Refractory 流程圖(P25)	→重新整理為一張流程圖(P26)
10. DLBCL一線用藥Regimen EOPCH(P28)	→新增DLBCL一線用藥Regimen DA-EOPCH-R(P28)
11. 預防CNS invol. 狀況(P32)	→新增CNS IPI ≥ 4 ，修正字眼 (of disease、non-Burkitt)(P32)
12. HL一線用藥(P47)	→新增AVD+BV for advance stage(P47)
13. HL二線用藥(P49)	→刪除mini-BEAM，新增 Brentuximab、Pembrolizumab(P49)

PROTOCOLS FOR TREATMENT OF MALIGNANT LYMPHOMA

Version 1. 2020

MALIGNANT LYMPHOMA

Kaohsiung Veterans General Hospital
Clinical Practice Guideline **Version 1.2020**

General Guide

Diagnosis	Staging Work-up
<ol style="list-style-type: none">1. Adequate sampling and proper handling of the tissue2. Effective communication between the clinician and the pathologist3. Surgical biopsy of the largest lymph nodes or mass lesion*4. Needle biopsy in certain conditions5. Flow cytometry or cytogenetic studies: optional * Lymph node	<ol style="list-style-type: none">1. Complete history and physical examination including Waldeyer's rings, B symptoms, risk of HIV infection, infection, autoimmune diseases, immunosuppressive therapies2. 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, sugar4. EKG, CXR-PA, whole body CT, HBsAg, and anti-HCV5. Other evaluation: beta2-microglobulin, Urinalysis and stool analysis, cytologic study of third space fluids6. Bone marrow aspiration and biopsy7. Lumbar puncture with cytology in selected patients<ol style="list-style-type: none">a. All patients with Burkitt lymphomab. Patients with NHL in certain sites e.g. CNS, epidural space, testes, ethmoid sinus, and large cell lymphoma with bone marrow involvementc. HIV positive patients8. Gastrointestinal studies<ol style="list-style-type: none">a. Esophagogastroduodenoscopy, upper gastrointestinal plus small bowel and lower gastrointestinal series for patients with gastrointestinal tract lymphoma; Endoscopic ultrasonography for gastric MALT lymphomab. Considered in patients with positive stool occult blood9. Selected radiologic images as clinically needed, e.g. positron emission tomograph, magnetic resonance imaging, and bone scan10. Cytogenetic and molecular tests in selected patients (optional); cardiac ejection fraction for age > 60 if anthracycline will be used. Anthracycline 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)

<u>Stage</u>	<u>Involvement</u>	<u>Extranodal (E) status</u>
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

MALIGNANT LYMPHOMA

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NON-HODGKINS'S LYMPHOMA

Low grade Lymphoma	Intermediate grade lymphoma	High grade lymphoma
<p>Small lymphocytic lymphoma</p> <p>Follicular lymphoma, grade 1</p> <p>Follicular lymphoma, grade 2</p> <p>Marginal zone lymphoma</p>	<p>Follicular lymphoma, grade 3</p> <p>Mantle cell lymphoma</p>	<p>Diffuse large B cell lymphoma (DLBCL)</p> <p>High grade B cell lymphoma</p> <p>NK/T cell lymphoma</p> <p>Peripheral T cell lymphoma</p> <p>Burkitt's lymphoma</p>

MALIGNANT LYMPHOMA

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Staging of gastric MALT LYMPHOMA : comparison of different systems

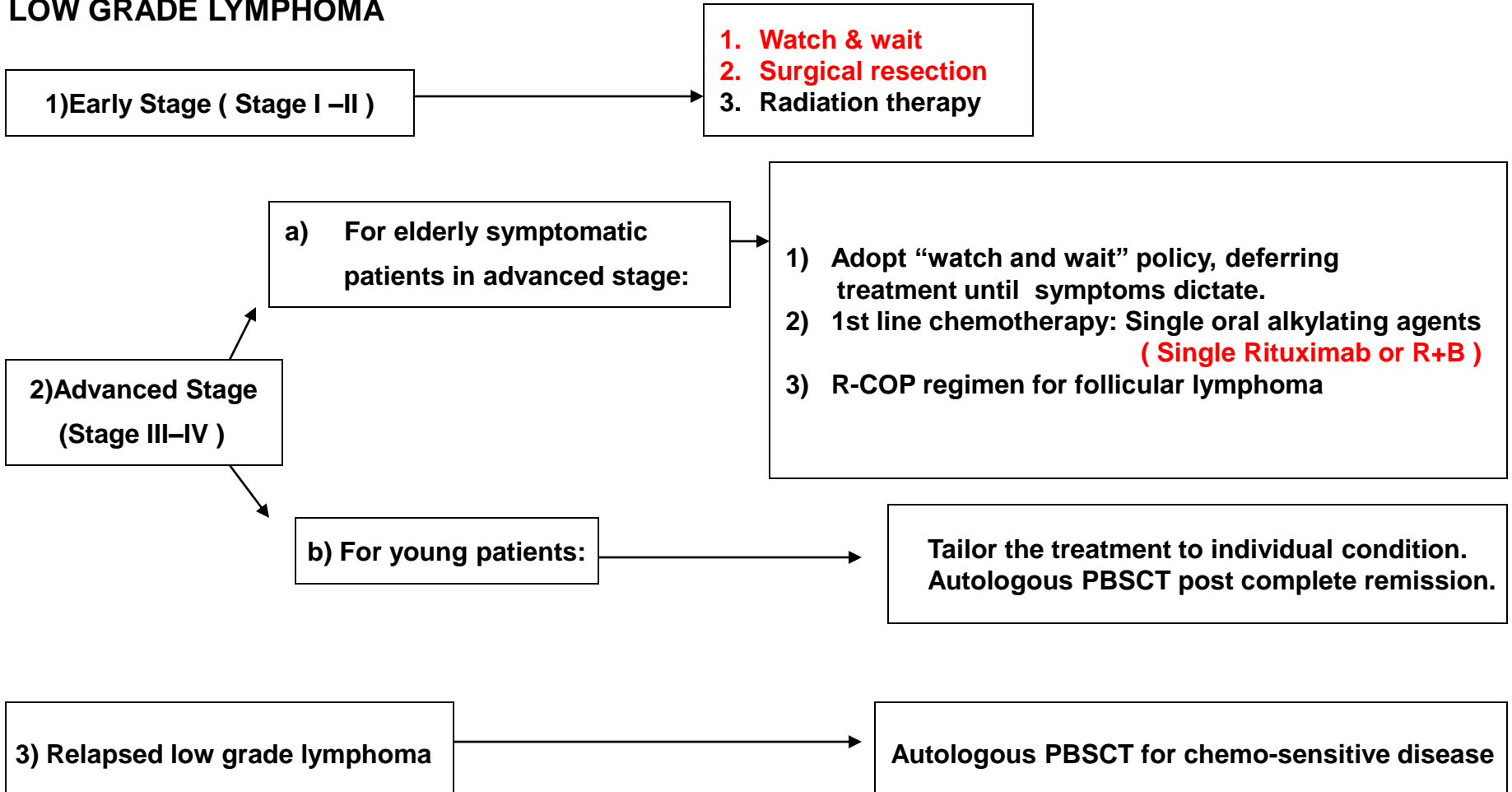
Lugano Staging System for Gastrointestinal Lymphomas		Lugano Modification of Ann Arbor Staging System	TNM Staging System Adapted for Gastric Lymphoma	Tumor Extension
Stage I	Confined to GI tract ^a			
	I ₁ = mucosa, submucosa	I _E	T1 N0 M0	Mucosa, submucosa
	I ₂ = muscularis propria, serosa	I _E	T2 N0 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	

MALIGNANT LYMPHOMA

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NON-HODGKINS'S LYMPHOMA

LOW GRADE 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 **Lymphoma**

- 1) Chemotherapy with ABVD regimen + radiation for bulky mass
- 2) Chemotherapy with AVD + BV regimen for advanced stage III-IV

3) Autologous PBSCT

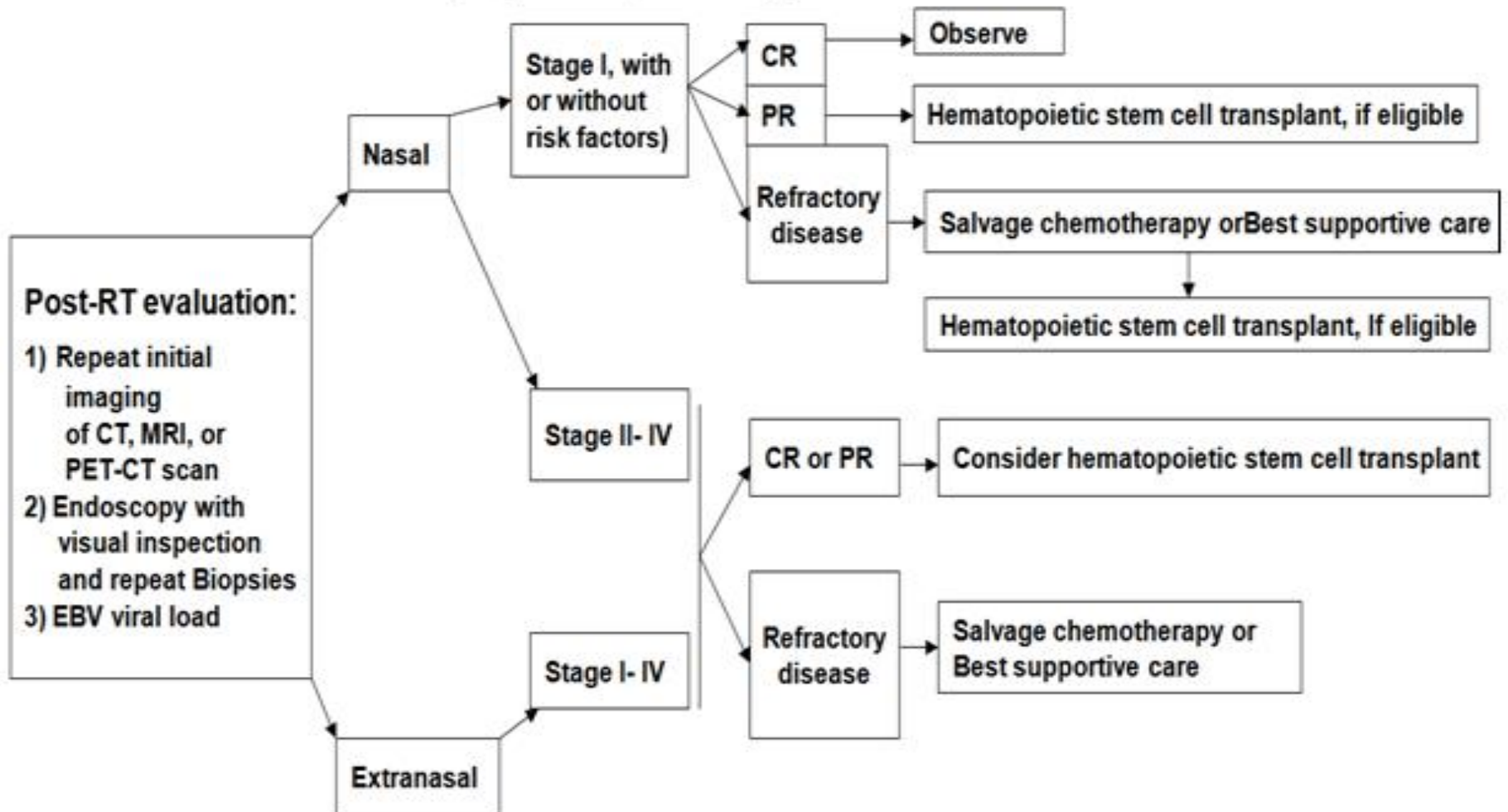


- a) Stage IVb disease post complete remission
- b) Failure to achieve 1st complete remission
- c) Relapsed disease

MALIGNANT LYMPHOMA

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Extranodal NK/T-cell Lymphoma, nasal type



MALIGNANT LYMPHOMA

Kaohsiung Veterans General Hospital
Clinical Practice Guideline **Version 1.2019**

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

MALIGNANT LYMPHOMA

Kaohsiung Veterans General Hospital
Clinical Practice Guideline **Version 1.2020**

References:

1. **NCCN guidelines of Non-Hodgkin' s lymphomas, V.1 2020**
2. NCCN guidelines of Hodgkin's disease/lymphoma, V.3 2018
3. NCCN guidelines of Non-Hodgkin' s lymphomas, V.4 2018
4. <http://www.uptodateonline.com/online/content/search.do>
5. <http://chemoregimen.com/Lymphoma-c-44-55.html>
6. <http://chemoregimen.com/Dosage-for-Renal-Dysfunction-c-59-68.html>
7. Baxter Oncology - Selected Schedules of Therapy for Malignant Tumors, 11th edition.
8. 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

Kaohsiung Veterans General Hospital
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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。

2020/04/21 第一版

Diffuse large B cell lymphoma

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Diagnosis	Staging Work-up
<p>requirement :</p> <ul style="list-style-type: none">* 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. <p>※IHC panel : CD20, CD3 (as description of the pathologist)</p> <p>Useful under certain circumstances :</p> <ul style="list-style-type: none">※IHC panel : CD30,CD5,CD10,CD45,BCL2,BCL6,Ki-67, IRF4/MUM1※Cell surface marker analysis by flow cytometry : 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)	<p>requirement :</p> <ul style="list-style-type: none">* 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 <p>選擇性 :</p> <ul style="list-style-type: none">* HIV* Discussion of fertility issues and sperm banking* Lumbar puncture* Beta2- microglobulin

Diffuse large B cell lymphoma

INTERNATIONAL PROGNOSTIC INDEX^a

ALL PATIENTS:

- Age >60 years
- Serum LDH > normal
- Performance status 2–4
- Stage III or IV
- Extranodal involvement >1 site

INTERNATIONAL INDEX, ALL PATIENTS:

- Low 0 or 1
- Low-intermediate 2
- High-intermediate 3
- High 4 or 5

AGE-ADJUSTED INTERNATIONAL PROGNOSTIC INDEX^a

PATIENTS ≤60 YEARS:

- Stage III or IV
- Serum LDH > normal
- Performance status 2–4

INTERNATIONAL INDEX, PATIENTS ≤60 YEARS:

- Low 0
- Low-intermediate 1
- High-intermediate 2
- High 3

STAGE-MODIFIED INTERNATIONAL PROGNOSTIC INDEX^b

STAGE I OR II PATIENTS:

- Age >60 years
- Serum LDH > normal
- Performance status 2–4
- Stage II or IIE

INTERNATIONAL INDEX, STAGE I OR II PATIENTS:

- Low 0 or 1
- High 2–4

NCCN-IPI^c

Risk Group

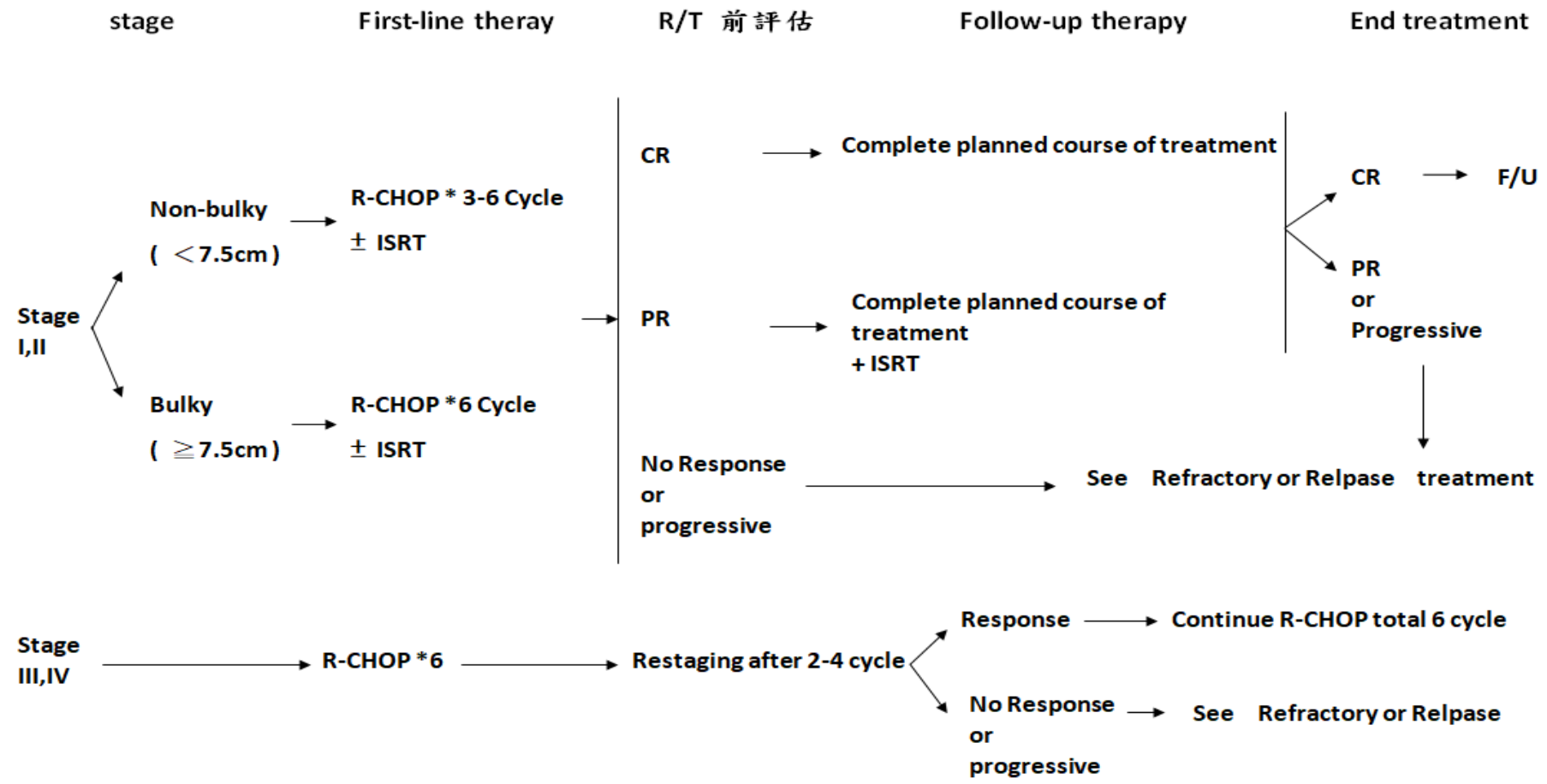
- | | | | |
|------------------------|---|---------------------|-----|
| Age, years | | <u>Risk Group</u> | |
| >40 to ≤60 | 1 | • Low | 0–1 |
| >60 to <75 | 2 | • Low-intermediate | 2–3 |
| ≥75 | 3 | • High-intermediate | 4–5 |
| LDH, normalized | | • High | ≥6 |
| >1 to ≤3 | 1 | | |
| >3 | 2 | | |
| Ann Arbor stage III-IV | 1 | | |
| Extranodal disease* | 1 | | |
| Performance status >2 | 1 | | |

*Disease in bone marrow, CNS, liver/GI tract, or lung.

Prognostic Model to Assess the Risk of CNS Disease^d

- | | | |
|-------------------------|-------------------|--|
| • Age >60 years | Low risk | 0–1 |
| • Serum LDH > normal | Intermediate-risk | 2–3 |
| • Performance status >1 | High-risk | 4–6 or kidney or adrenal gland involvement |
- Stage III or IV
 - Extranodal involvement >1 site
 - Kidney or adrenal gland involvement
- Additional indications for CNS prophylaxis independent of CNS risk score
 - HIV lymphoma
 - Testicular lymphoma
 - High-grade B-cell lymphomas (HGBLs) with translocations of *MYC* and *BCL2* and/or *BCL6* HGBL, NOS
 - Primary cutaneous DLBCL, leg type
 - Stage IE DLBCL of the breast
- Suggested CNS prophylactic therapy (Optimal management is uncertain)
 - Intrathecal methotrexate and/or cytarabine (4–8 doses) during the course of treatment
 - or
 - Systemic methotrexate (3–3.5 g/m² for 2–4 cycles) during the course of treatment

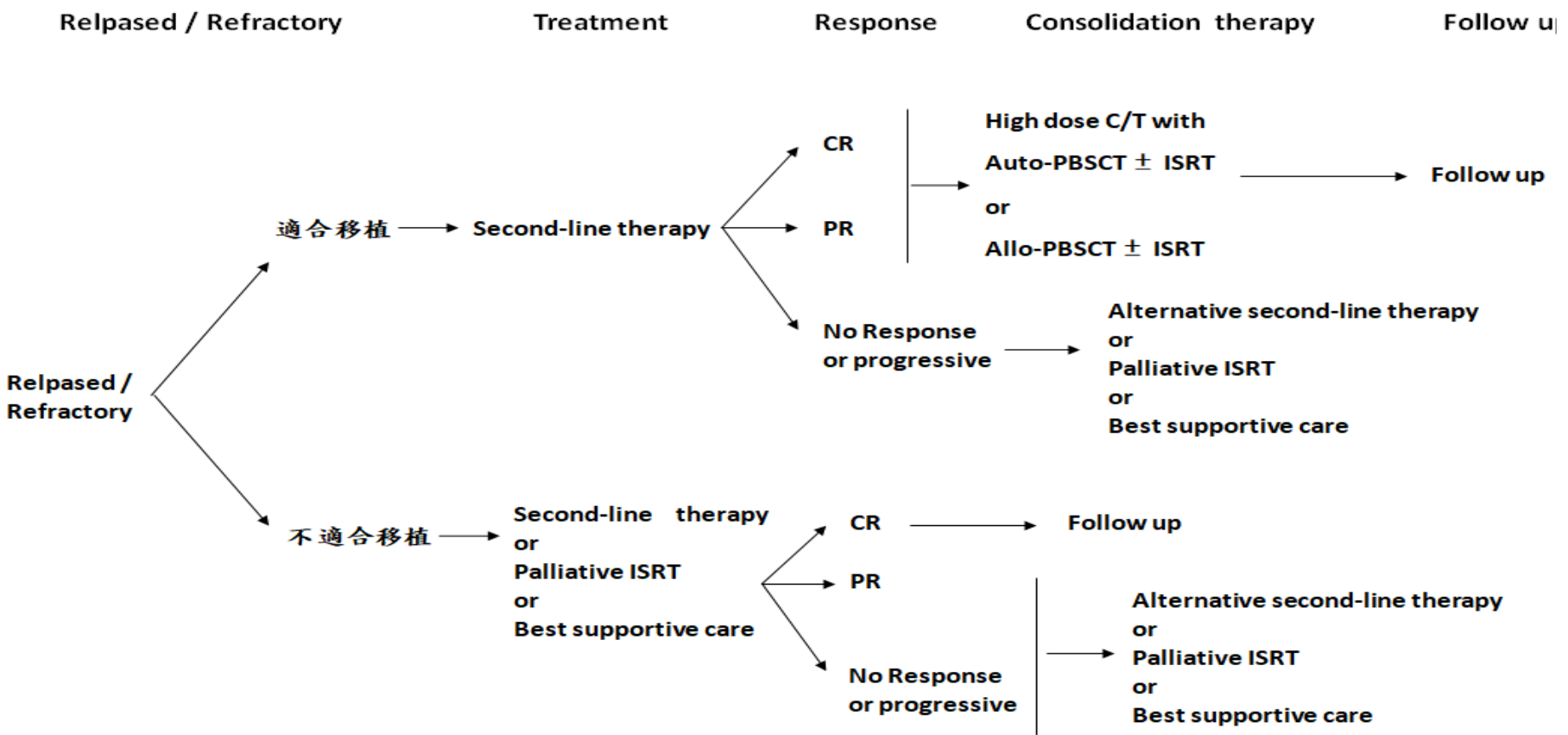
Diffuse large B cell lymphoma



追蹤:
 臨床 → 五年內每 3-6 個月追蹤一次 H&P 和 labs，然後每年追蹤或根據臨床表徵
 影像 → 完成治療後 2 年每 6 個月追蹤一次或根據臨床表徵重新評估影像

Diffuse large B cell lymphoma

➤ Relapsed / Refractory disease treatment



追蹤:
 臨床 → 五年內每 3-6 個月追蹤一次 H&P 和 labs，然後每年追蹤或根據臨床表徵
 影像 → 完成治療後 2 年每 6 個月追蹤一次或根據臨床表徵重新評估影像

Diffuse large B cell lymphoma

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

一線化療	
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
(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

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

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

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
- High-grade lymphoblastic lymphoma
- High-grade small noncleaved cell lymphomas (eg, Burkitt)
- HIV-related lymphoma
- Primary CNS lymphoma
- Patients with neurologic signs and symptoms
- breast lymphoma
- CNS IPI ≥ 4**

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 l'Adulte. J Clin Oncol 2005;23:4117-4126.
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- 4.Zaja F, Tomadini V, Zaccaria A,et al.CHOP-rituximab with pegylated liposomal doxorubicin for the treatment of elderly patients with diffuse large B-cell lymphoma. Leuk Lymphoma 2006;47:2174-2180.
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- 6.Velasquez WS, McLaughlin P,Tucker S, ET AL. ESHAP-an effective chemotherapy 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

Kaohsiung Veterans General Hospital
Clinical Practice Guideline **Version 1.2020**

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

2020/04/21 第一版

Hodgkin Lymphoma

Kaohsiung Veterans General Hospital
Clinical Practice Guideline **Version 1.2020**

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, II₃).

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 (III_E), 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

Kaohsiung Veterans General Hospital
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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
- Immunohistochemistry 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

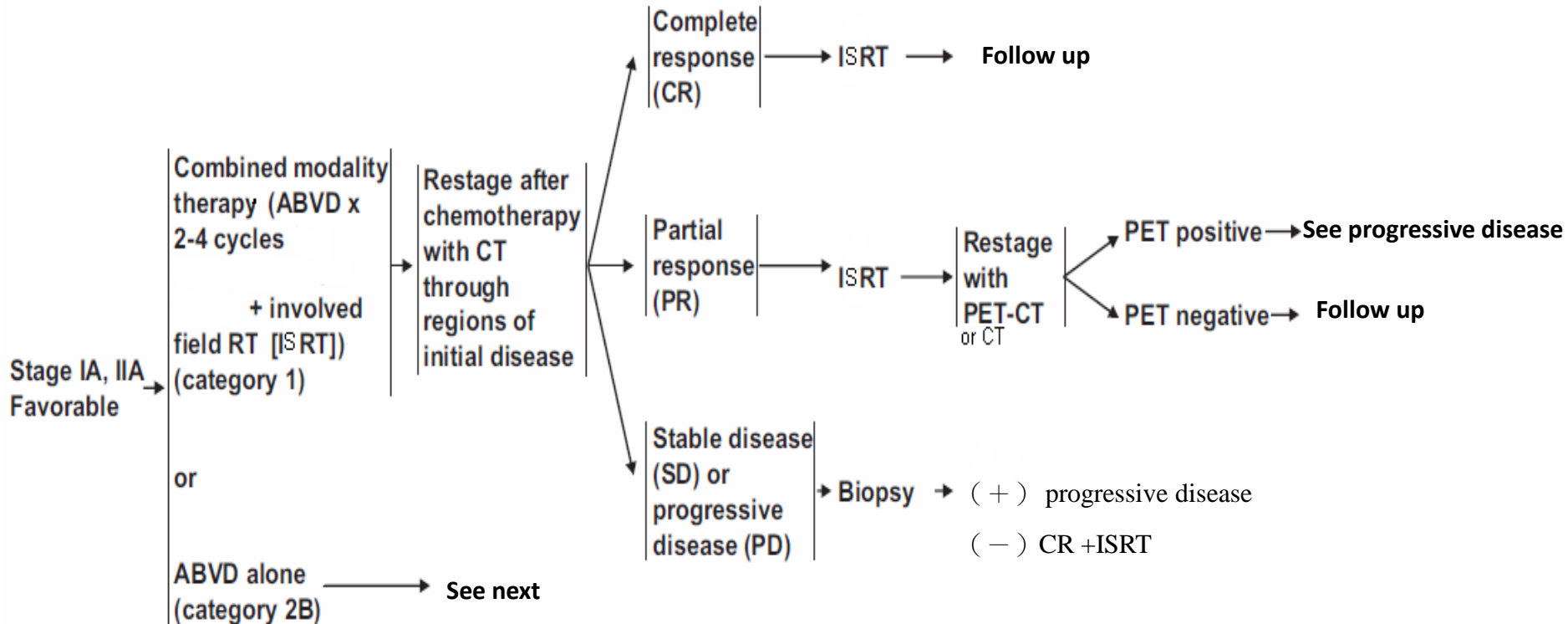
Summary

- 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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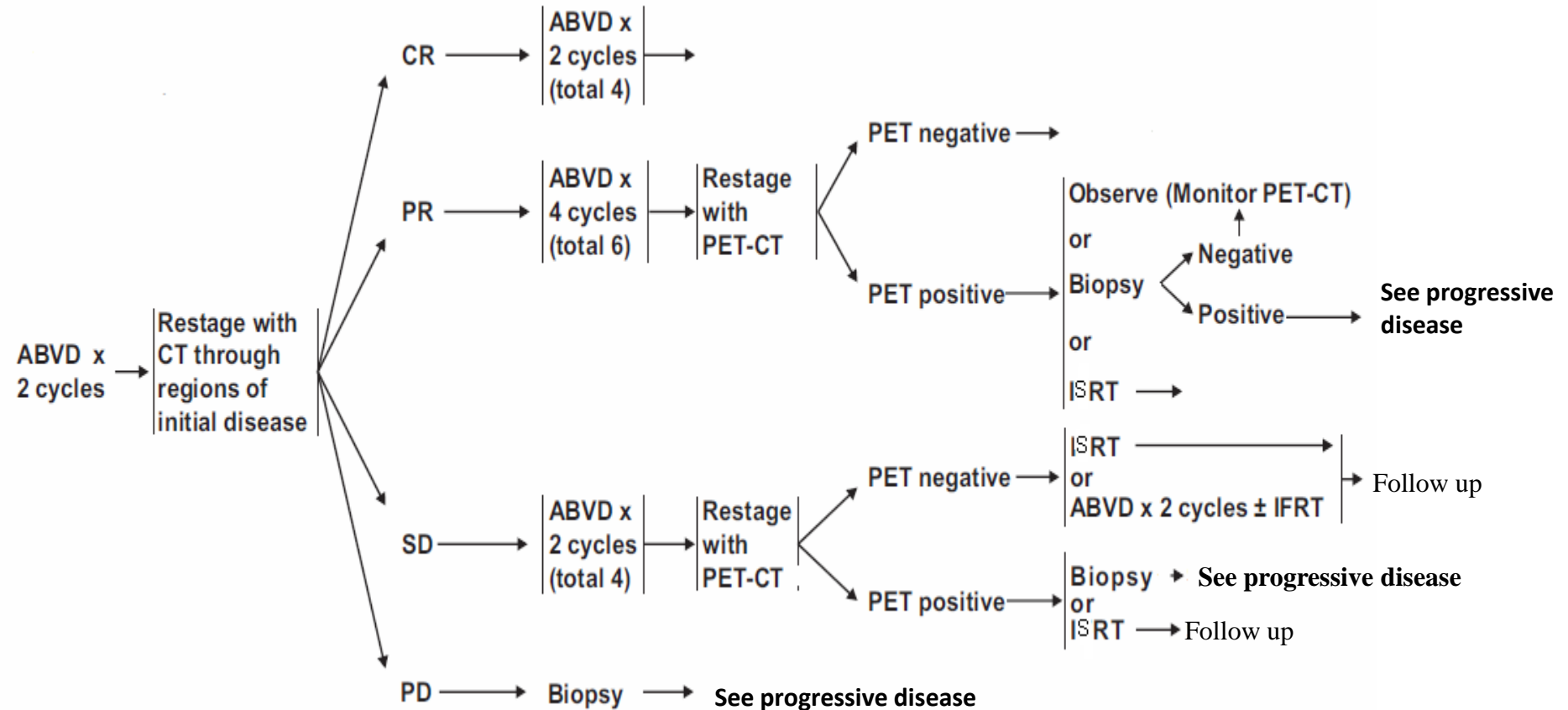
Classical Hodgkin Lymphoma Stage IA-IIA Favorable



Hodgkin Lymphoma

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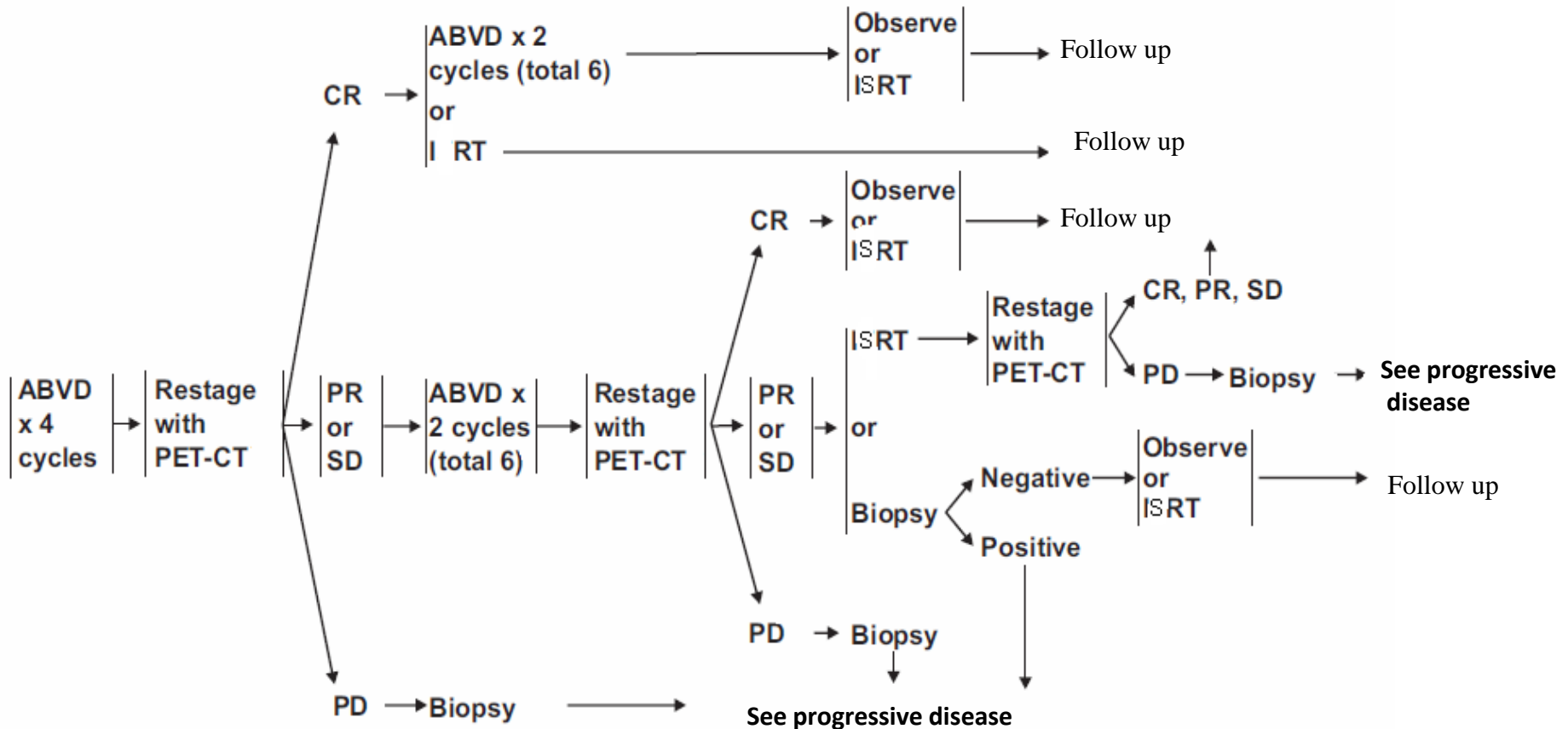
Classical Hodgkin Lymphoma Stage IA-IIA Favorable (C/T alone first)



Hodgkin Lymphoma

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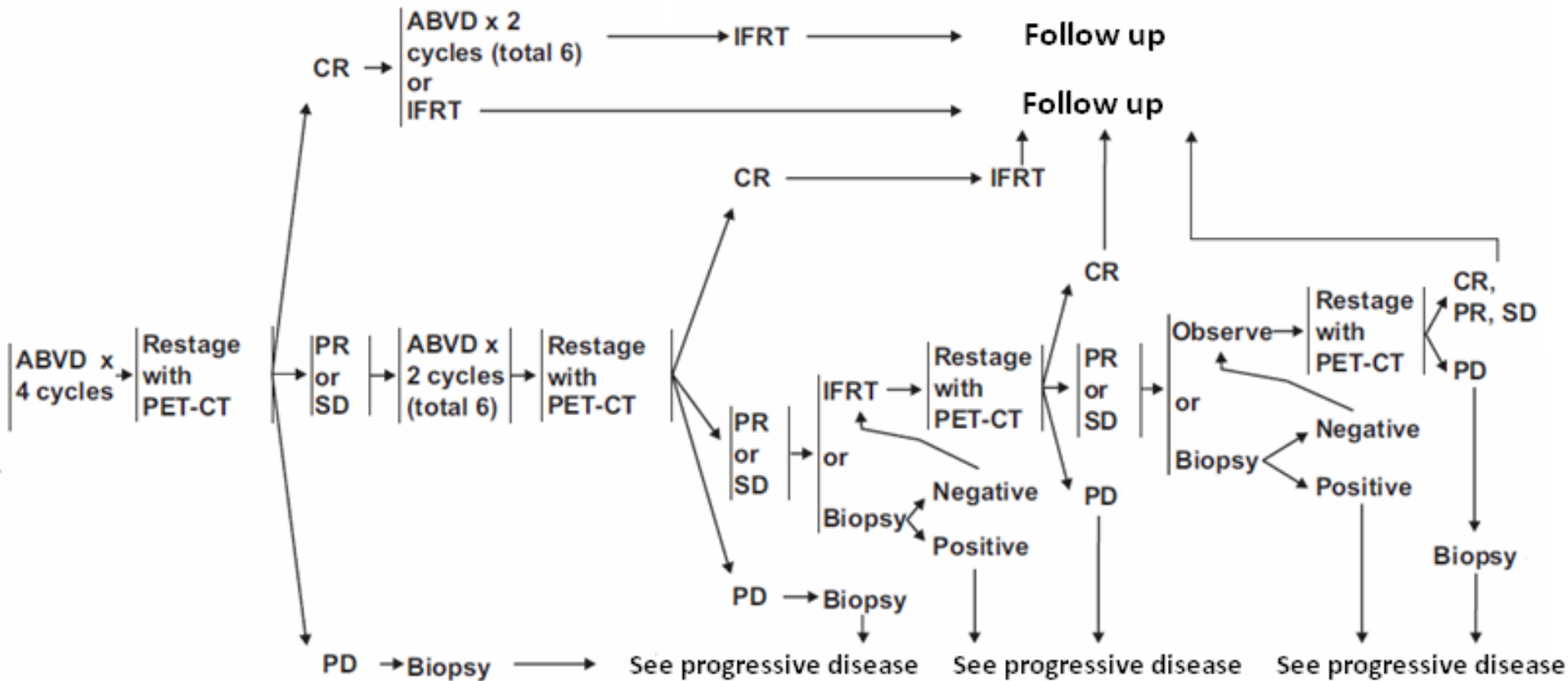
Classical Hodgkin Lymphoma Stage I-II Unfavorable (Non-bulky, C/T alone first)



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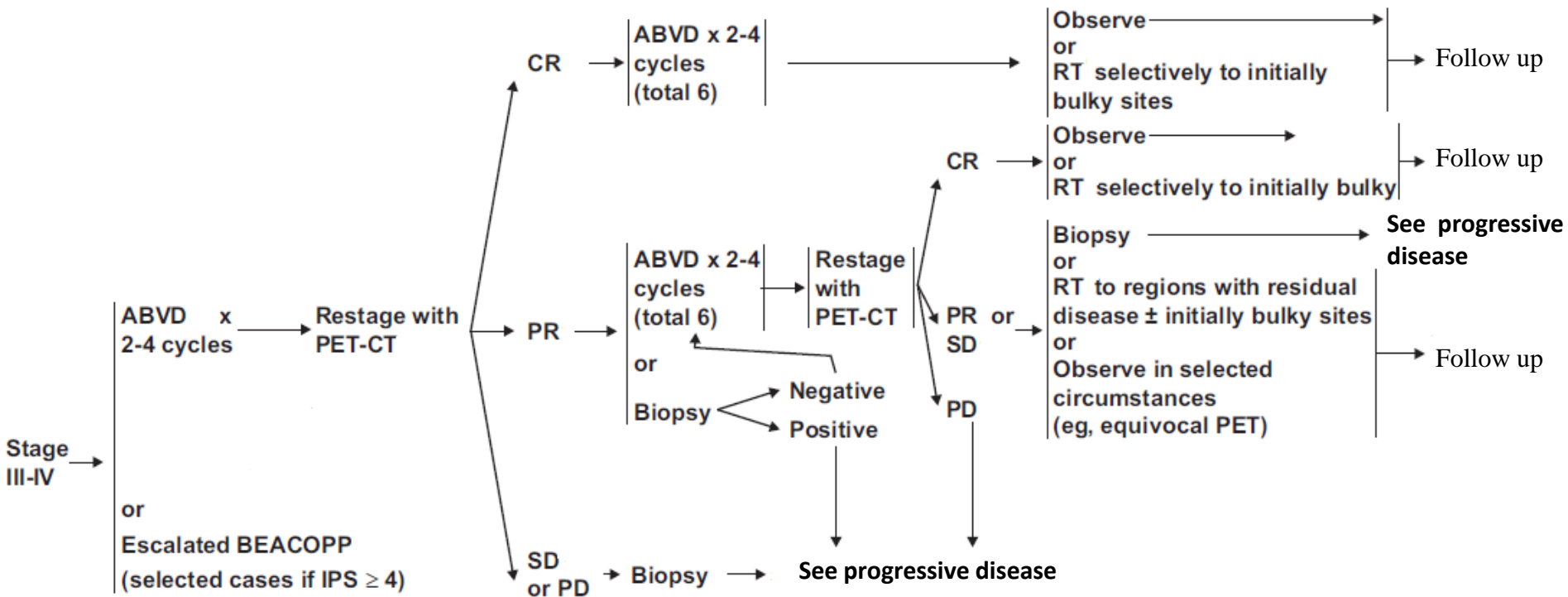
Classical Hodgkin Lymphoma Stage I-II Unfavorable (Bulky, C/T alone first)



Hodgkin Lymphoma

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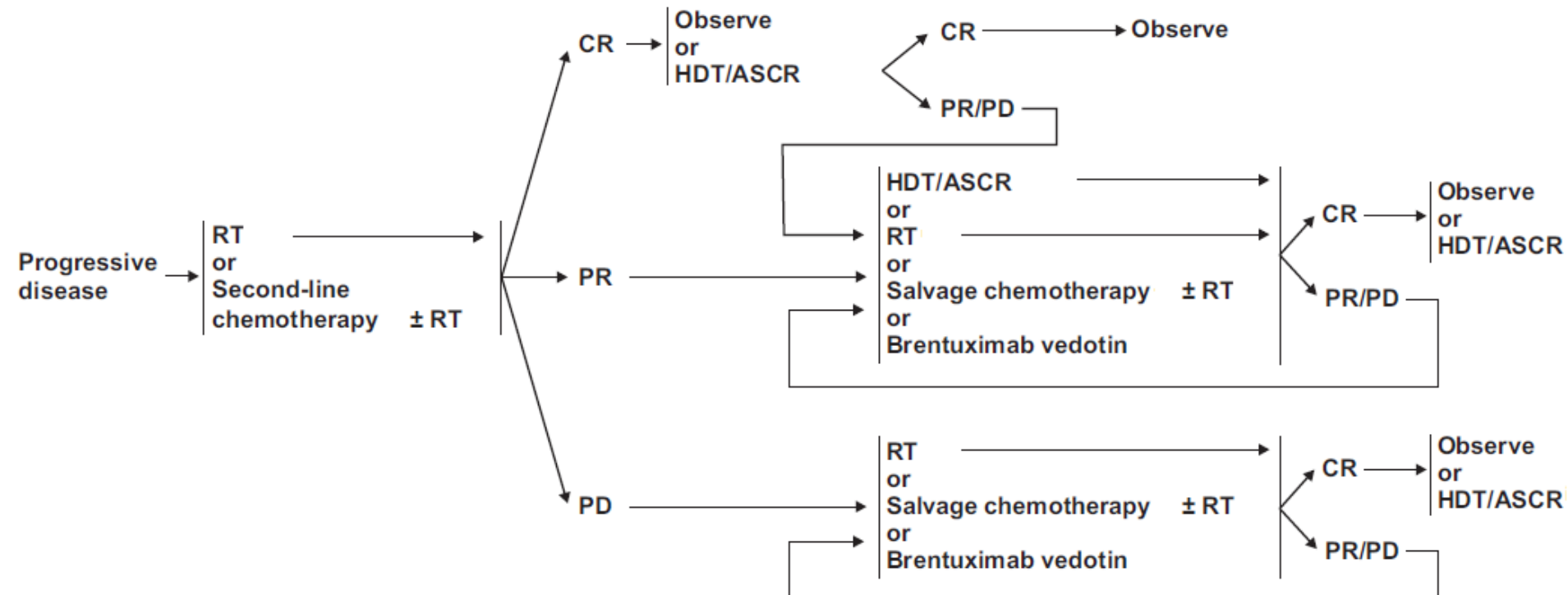
Classical Hodgkin Lymphoma Stage III-IV



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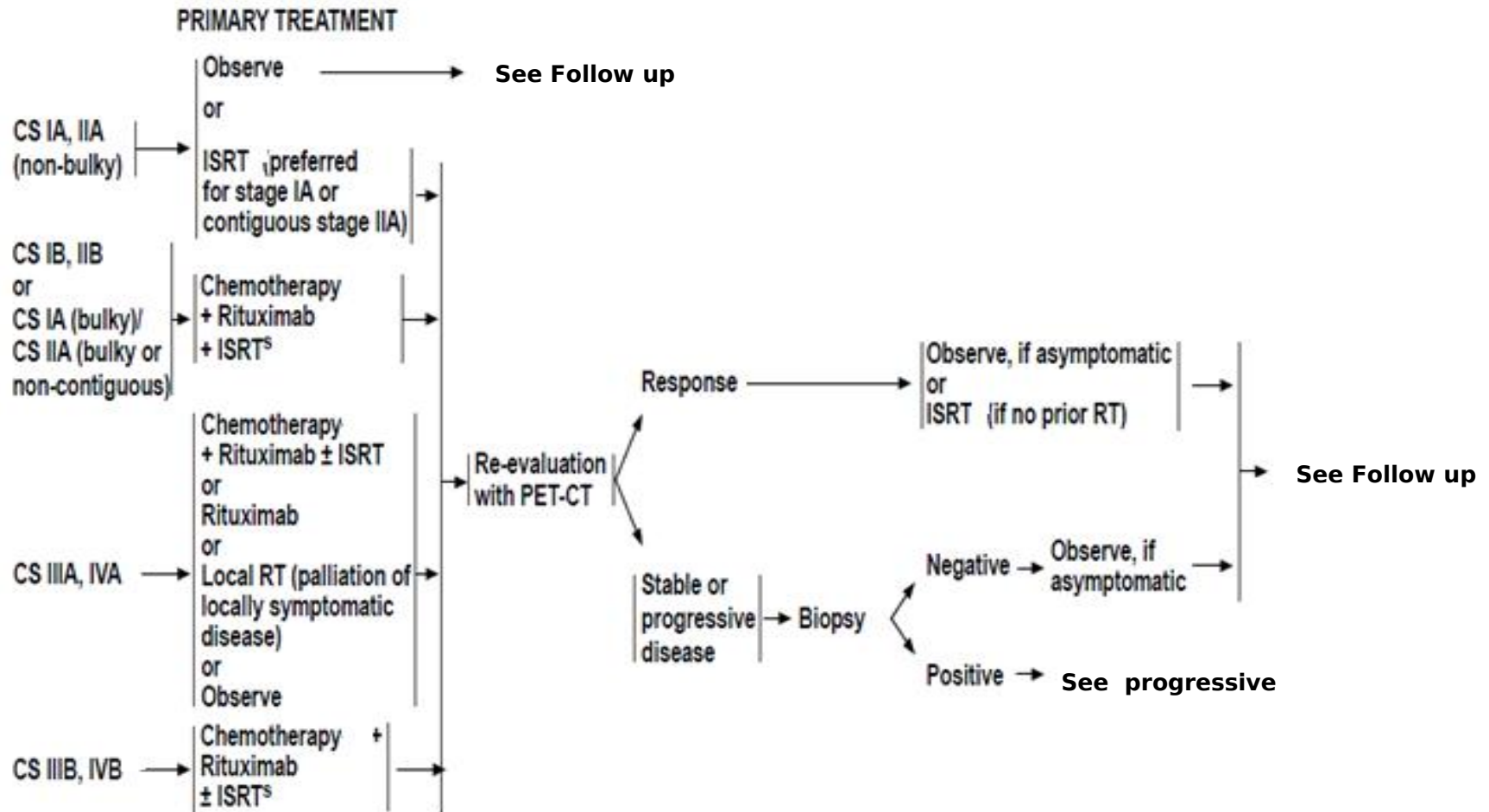
Classical Hodgkin Lymphoma (progressive disease or relapse)



Hodgkin Lymphoma

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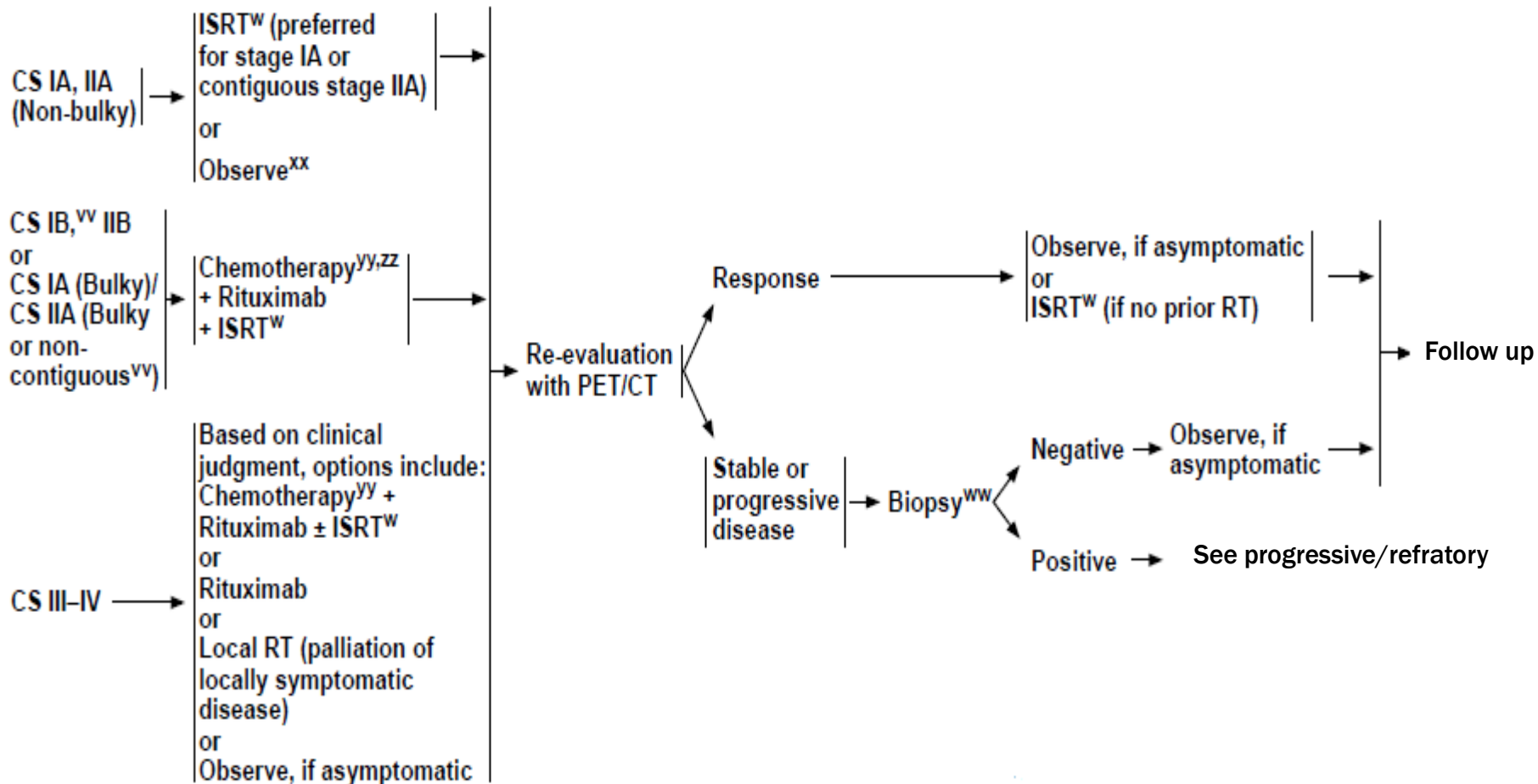
Lymphocyte-predominant Hodgkin Lymphoma



Hodgkin Lymphoma

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Lymphocyte-predominant Hodgkin Lymphoma



Hodgkin Lymphoma

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Hodgkin lymphoma-Commonly used chemotherapy regimen

ABVD (Q4W)	Doxorubicin (Adriamycin) 25 mg/m ² iv d1 and 15
	Bleomycin 10 U/m ² iv d1 and 15
	Vinblastine 6 mg/m ² iv d1 and 15
	Dacarbazine (DTIC) 375 mg/m ² iv d1 and 15
	References : NO3 、 4

HL used chemotherapy regimen for advance stage

AVD+BV (Q4W)	Doxorubicin (Adriamycin) 25 mg/m ² iv d1 and 15
	Vinblastine 6 mg/m ² iv d1 and 15
	Dacarbazine (DTIC) 375 mg/m ² iv d1 and 15
	Brentuximab(Adcetris) 1.8mg/Kg IV
	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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Second –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
Brentuximab	Brentuximab(Adcetris) 1.8mg/Kg IV	
Pembrolizumab	Pembrolizumab(Kytruda) 200mg IV	

Hodgkin Lymphoma

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Reference

- 1.NCCN guidelines of Hodgkin's lymphomas, V.3. 2018
- 2.Engert A et al. Two cycles of doxorubicin, bleomycin, vinblastine, and dacarbazine plus extended-field radiotherapy is superior to radiotherapy alone in early favorable Hodgkin's lymphoma: Final results of the GHSG HD7 trial. J Clin Oncol 2007; 25:3495
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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

2019/04/21修訂

Follicular lymphoma

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 node 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 cytometry : kappa/lambda, CD45,CD3,CD5,CD19,CD10,CD20
 - * Additional immunohistochemical studies to establish lymphoma subtype
 - * IHC panel : Cyclin D1, kappa/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

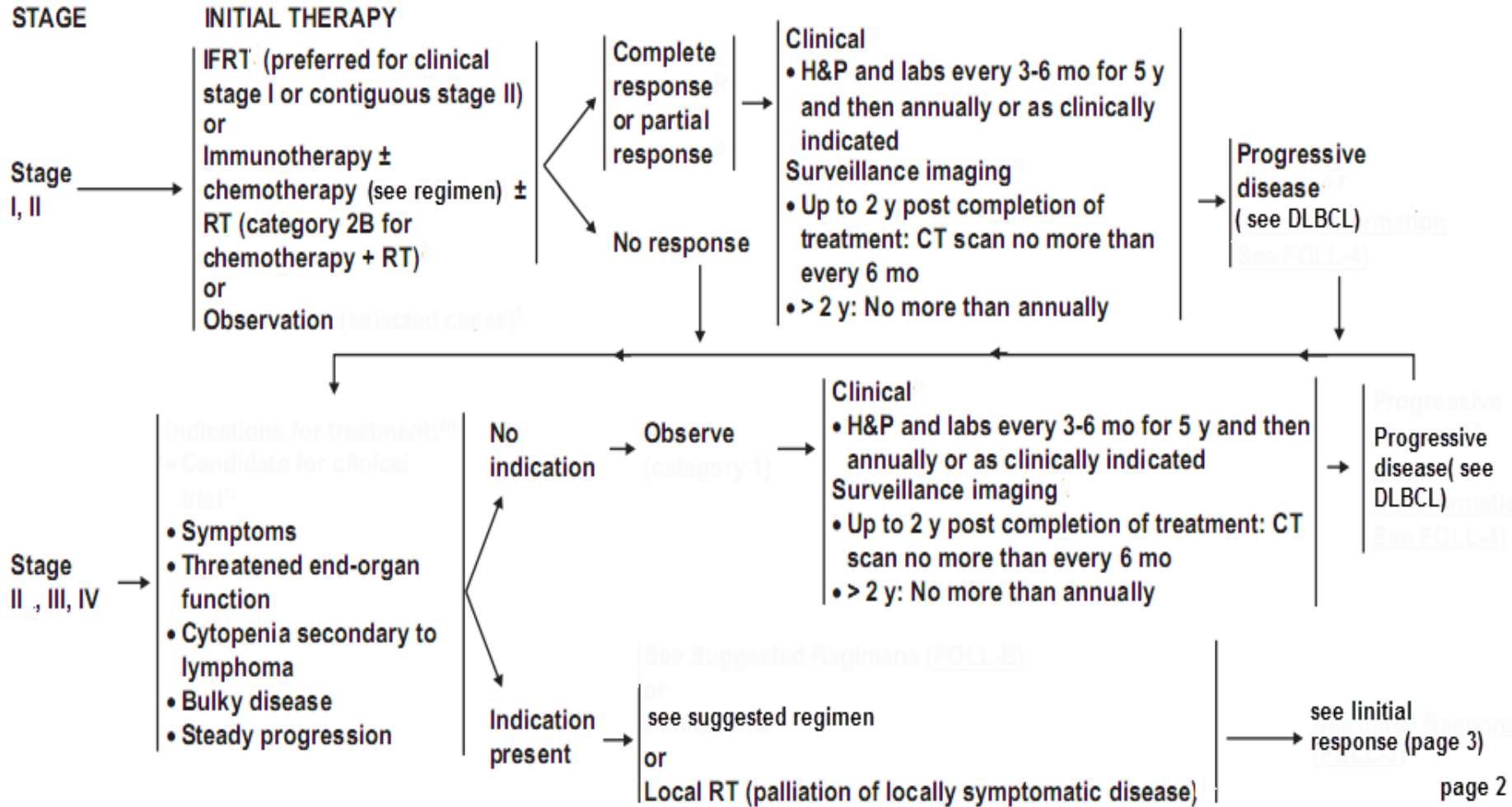
備註 : Follicular lymphoma grade 3 is commonly treated according to the DLBCL

Stage I,II

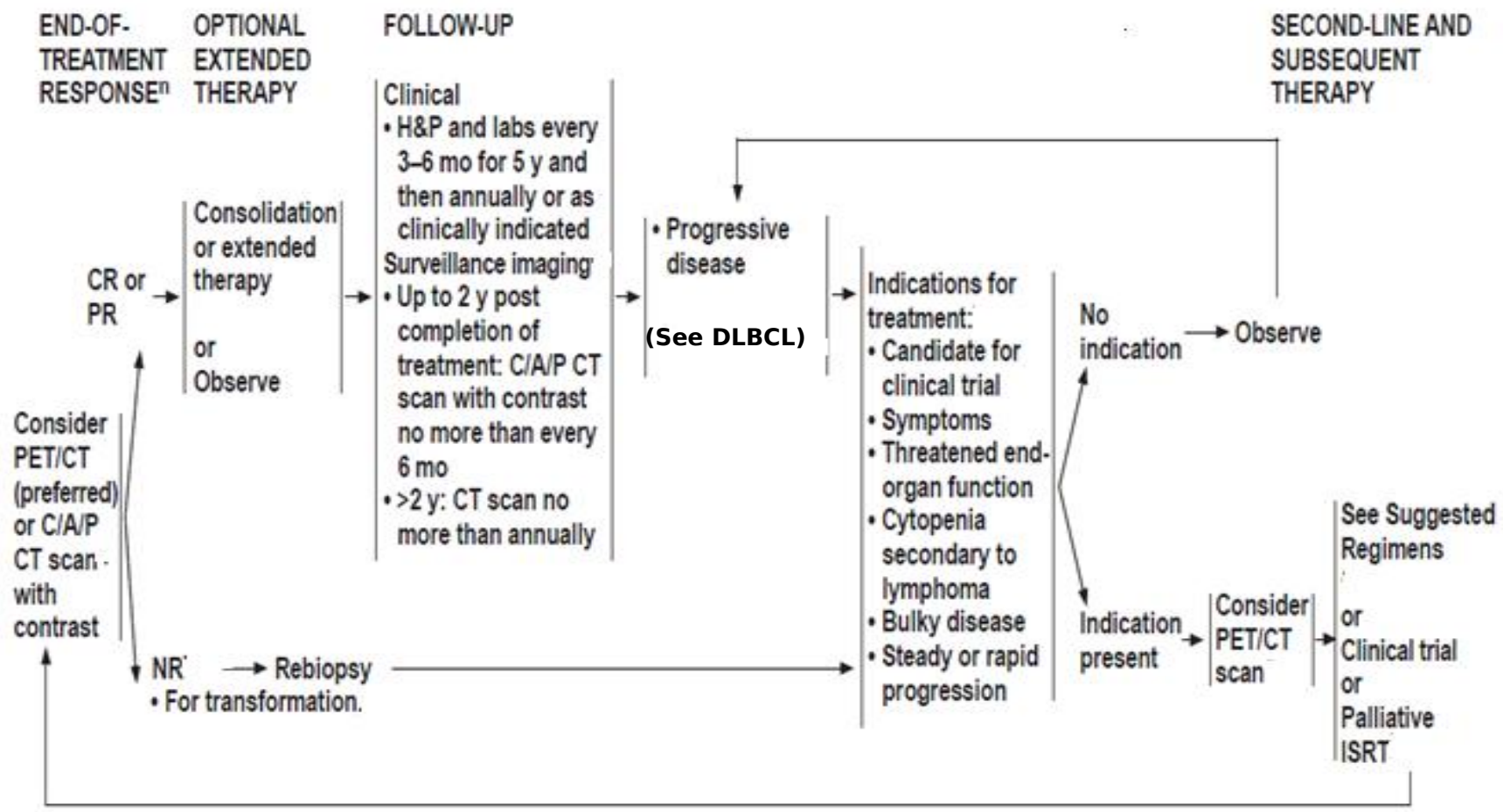
Stage III,IV

See
Page 2

Follicular lymphoma (grade 1-2)



Follicular lymphoma (grade 1-2)



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 $< 1.0 \times 10^9/L$ and/or platelets $< 100 \times 10^9/L$)
- Leukemia ($> 5.0 \times 10^9/L$ malignant cells)

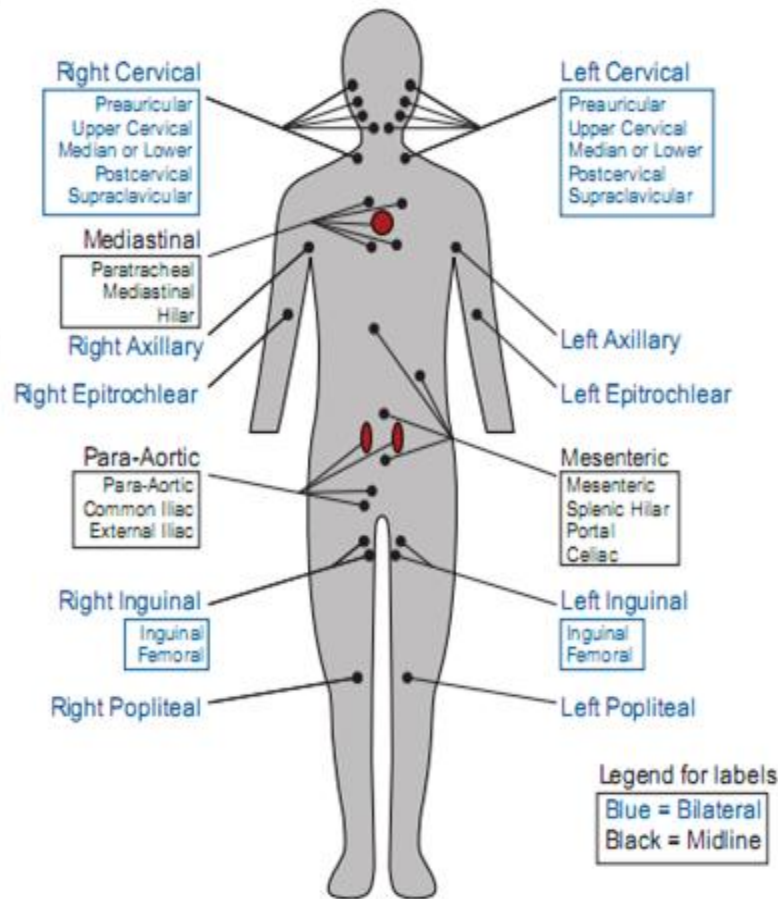
FLIPI - 1 CRITERIA

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/m² 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/m² 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/m² + Rituximab 375mg/m²

2. R-FCM (Rituximab 375mg/m², Fludarabine 25mg/m² D1-3, Cyclophosphamide 200mg/m² D1-3, Mitoxantrone 8mg/m² D1)

3. Fludarabine + Rituximab

4. Rituximab

5. RFND (Rituximab, Fludarabine, Mitoxantrone, Dexamethasone 20MG/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/m² one dose every 3 months up to 2 years

Reference: NO11

Follicular lymphoma (grade 1-2)

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references

- 1.NCCN guidelines of Non-Hodgkin's lymphomas, V.4 2018
- 2.Czuczman MS, Weaver R, Alkuzweny B, et al. Prolonged clinical and molecular remission in patients with low-grade or follicular non-Hodgkin's lymphoma treated with rituximab plus CHOP chemotherapy:9-year follow-up. J Clin Oncol 2004;22:4711-4716.
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Follicular lymphoma (grade 1-2)

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