

高雄榮民總醫院

淋巴瘤診療原則

2022年04月26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：2021/04/21

本共識與上一版的差異

上一版	新版
<ul style="list-style-type: none">1. Prognostic model to assess the risk of CNS disease2. DLBCL治療指引流程圖3. 一線化療(適用於年紀大或心臟功能不好病人)regimen3. HL治療指引流程圖p36-43	<ul style="list-style-type: none">→更新圖表p. 19→更新流程圖p. 20→新增R-mini-CHOP p24→刪除HL summary p36→流程圖p37-38統整更新為p. 39→流程圖p40-41統整更新為p42→流程圖p43統整更新為p44

PROTOCOLS FOR TREATMENT OF MALIGNANT LYMPHOMA

Version 1. 2022

MALIGNANT LYMPHOMA

Kaohsiung Veterans General Hospital
Clinical Practice Guideline **Version 1.2022**

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%.

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

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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Staging of gastric MALT LYMPHOMA : comparison of different systems

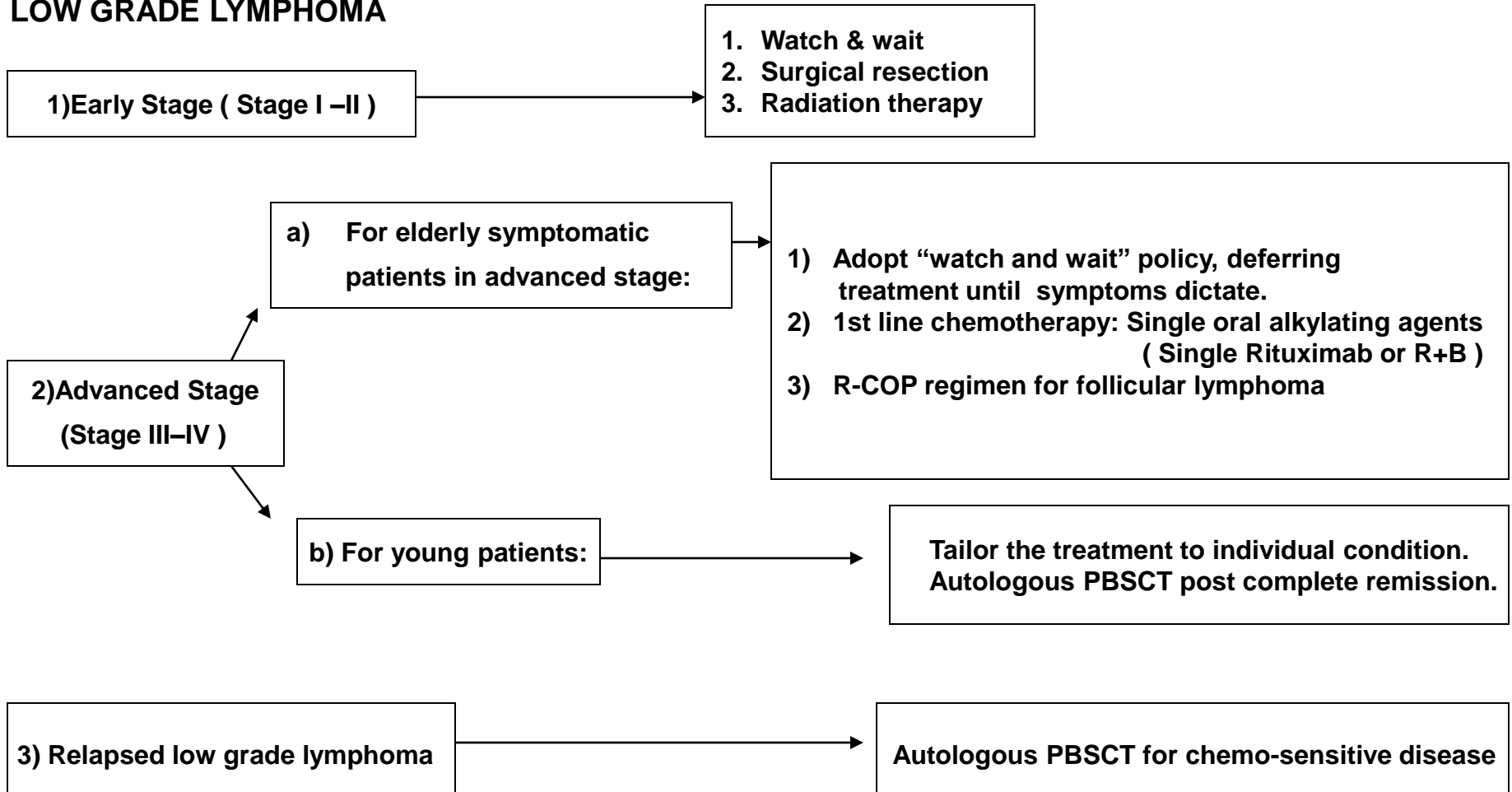
Lugano Staging System for Gastrointestinal Lymphomas		Lugano Modification of Ann Arbor Staging System	TNM Staging System Adapted for Gastric Lymphoma	Tumor Extension
Stage I	Confined to GI tract ^a			
	I ₁ = mucosa, submucosa	I _E	T1 N0 M0	Mucosa, submucosa
	I ₂ = muscularis propria, serosa	I _E	T2 N0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



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

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

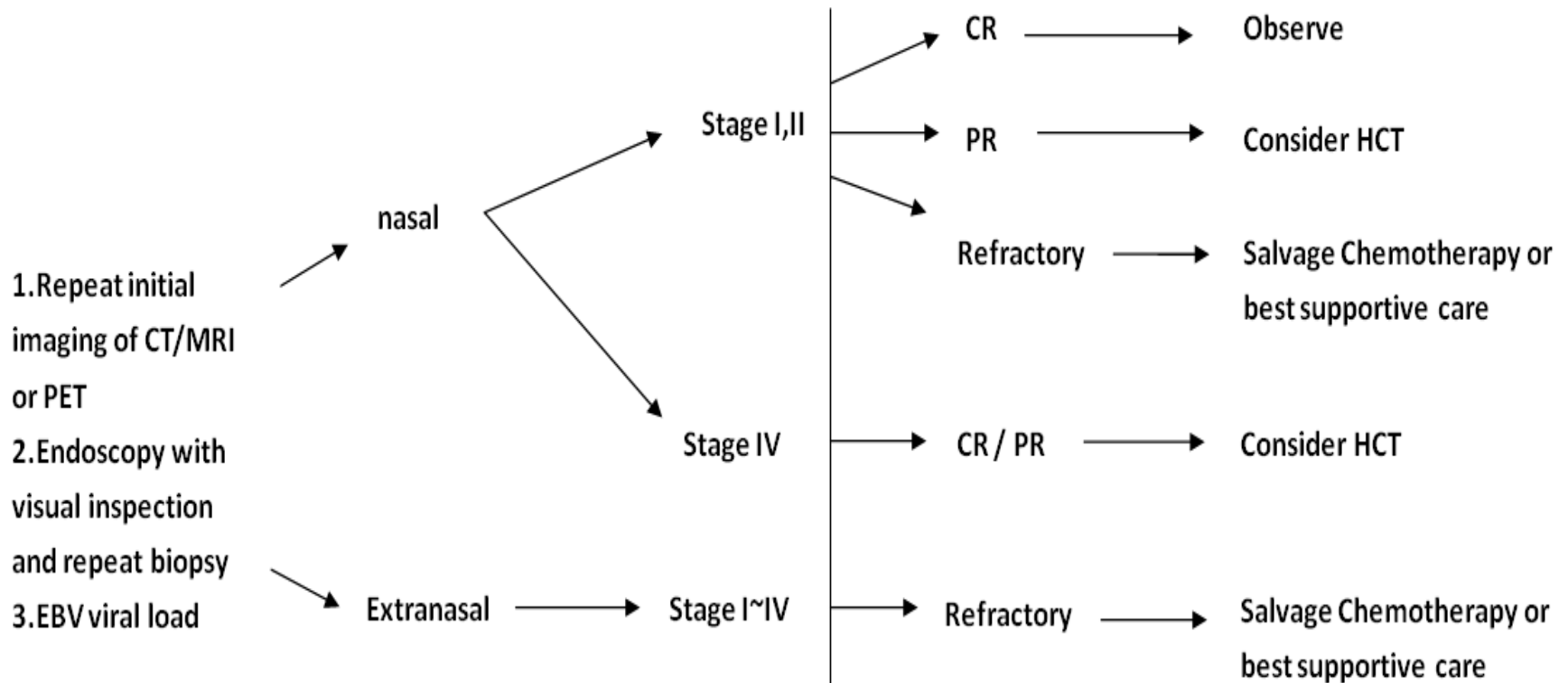
Diffuse aggressive NHL with

- 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)
- HIV-related lymphoma
- Primary CNS lymphoma
- Patients with neurologic signs and symptoms
- breast lymphoma

MALIGNANT LYMPHOMA

Extranodal NK/T cell lymphoma , nasal type

End-Of-Treatment evaluation



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 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.
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10. <https://www.uptodate.com/contents/treatment-of-extranodal-nk-t-cell-lymphoma-nasal-type> 7. Baxter Oncology - Selected Schedules of Therapy for Malignant Tumors, 11th edition.
11. Chan TSY, Li J, Loong F, et al. PD1 blockade with low-dose nivolumab in NK/T cell lymphoma failing L-asparaginase: efficacy and safety. *Ann Hematol* 2018; 97:193.
12. Kim SJ, Hyeon J, Cho I, et al. Comparison of Efficacy of Pembrolizumab between Epstein-Barr Virus-Positive and -Negative Relapsed or Refractory Non-Hodgkin Lymphomas. *Cancer Res Treat* 2019; 51:611
13. Li X, Cheng Y, Zhang M, et al. Activity of pembrolizumab in relapsed/refractory NK/T-cell lymphoma. *J Hematol Oncol* 2018; 11:15

MALIGNANT LYMPHOMA

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References:

14. NCCN guidelines of Non-Hodgkin's lymphomas, V.2 2022

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CHOP較單用化療處方CHOP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CHOP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CHOP。

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。

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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.※ IHC panel : CD30,CD5,CD10,CD45,BCL2,BCL6,Ki-67, IRF4/MUM1,MYC※ Cell surface marker analysis by flow cytometry : kappa/lambda, CD45,CD3,CD5,CD19,CD10,CD20 <p>Useful under certain circumstances :</p> <ul style="list-style-type: none">* Additional immunohistochemical studies to establish lymphoma subtype※ IHC panel : Cyclin D1, kappa/lambda,CD30,CD138,EBV-ISH ,ALK,HHV8,SOX-11* Karyotype or FISH for BCL2,BCL6 rearrangements if MYC positive	<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

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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 | | | |
| >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.

Diffuse large B cell lymphoma

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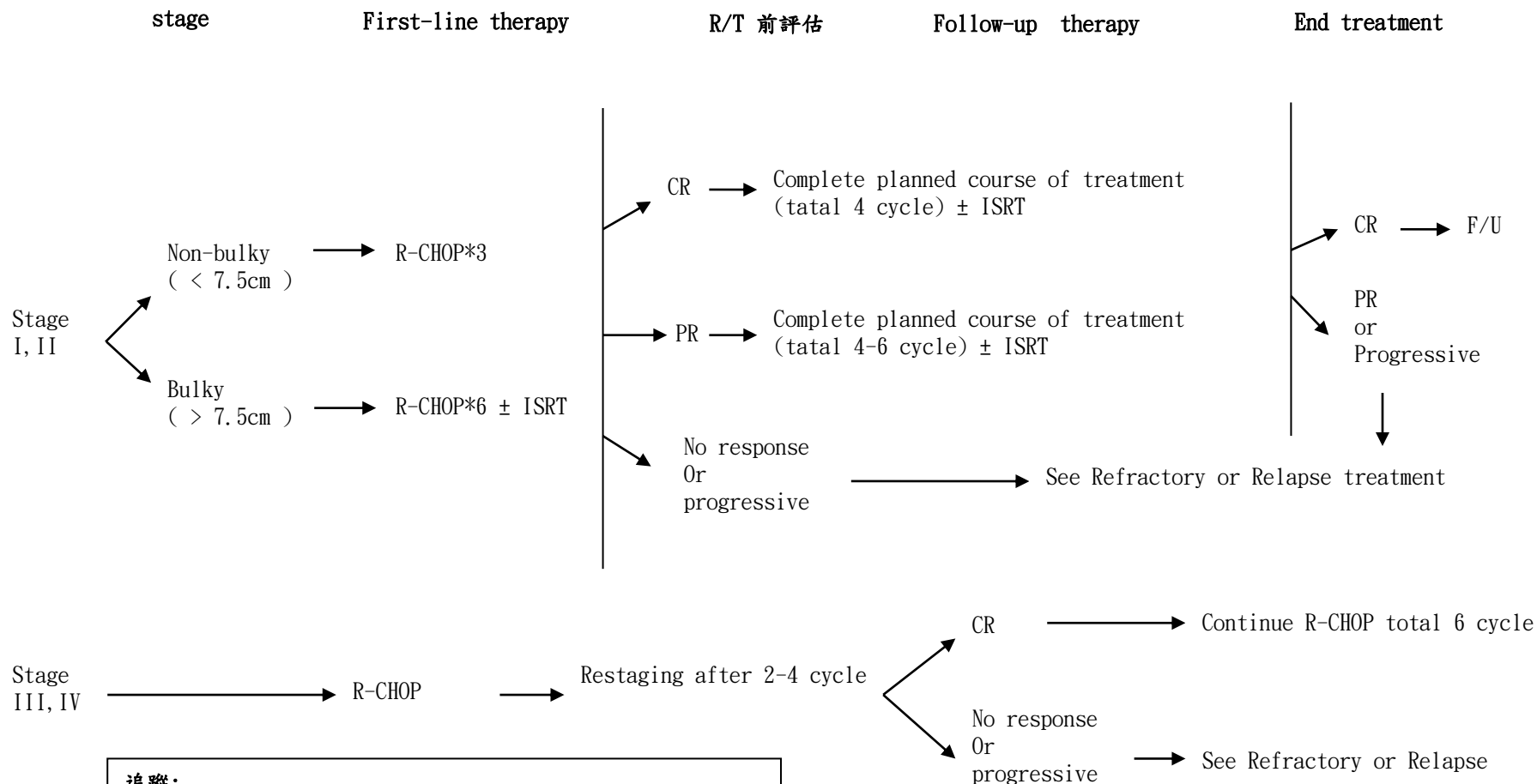
PROGNOSTIC MODEL TO ASSESS THE RISK OF CNS DISEASE^d

• 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**
 - 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
 - Kidney or adrenal gland involvement
- **Role of CNS prophylaxis remains controversial but can be considered in patients with high-risk factors based on the aforementioned criteria. If CNS prophylaxis is used, options include:**
 - Systemic high-dose methotrexate (3–3.5 g/m² for 2–4 cycles) during or after the course of treatment and/or
 - Intrathecal methotrexate and/or cytarabine (4–8 doses) during or after the course of treatment

Diffuse large B cell lymphoma

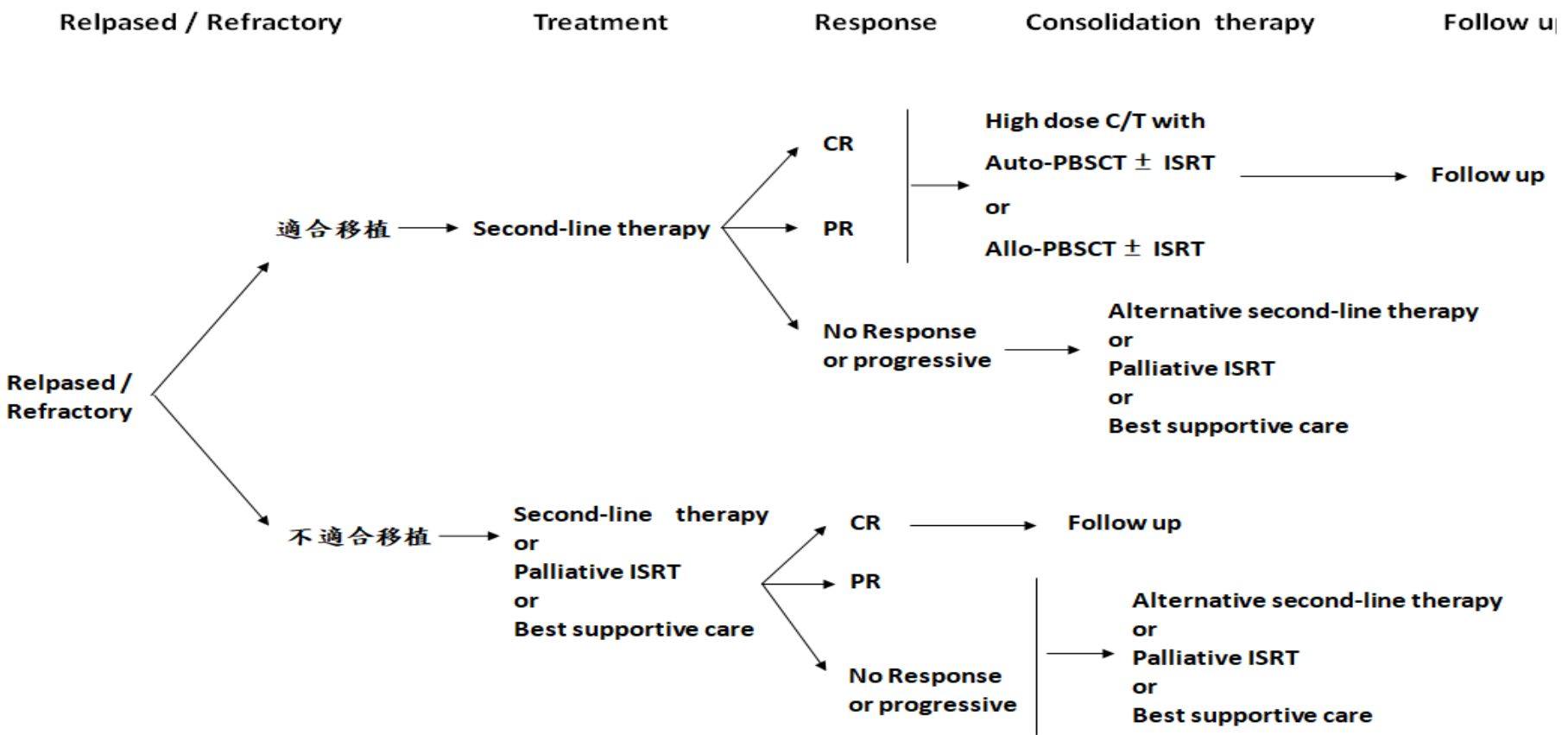
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追蹤:
 臨床→五年內每3-6個月追蹤一次
 影像→完成治療後每6個月追蹤一次或根據臨床表徵重新評估影像

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

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建議治療療程

一線化療	
R-CHOP	± Rituximab 375MG/M2 IVA or Rituximab 1400mg SC on D1
	Cyclophosphamide 750MG/M2 IVA on D1 or D2
	Doxorubicin 50MG/M2 IVA on D1 or D2
	Vincristine 2MG IVA on D1 or D2
	Prednisone 5MG 10TAB BID po for 5days
	References:NO 2.4
R-CEOP	± Rituximab 375MG/M2 IVA or Rituximab 1400mg 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 3

Diffuse large B cell lymphoma

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一線化療	
EPOCH-R (DA)EPOCH-R	Etoposide 50MG/M2 IVA D1-4
	Prednisone 10TAB PO BID for 5days
	Vincristine 0.4MG/M2 IVA D1-4
	Epincin 15MG/M2 IVA D1-4
	Cyclophosphamide 750MG/M2 IVA D5
	± Rituximab 375MG/M2 IVA or Rituximab 1400mg SC D1

References: NO 5

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 Rituximab 1400mg 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 6
R-COP	± Rituximab 375MG/M2 IVA or Rituximab 1400mg 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 6
R-mini-CHOP	References : NO 6

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 AUCx 5MG IVA on D1
	Cytarabine 2000MG/M2 IVA Q12H on D2
	註：CCr < 60 使用 Carboplatin References : NO7
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 : NO8

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	註:maximum dose 1750mg
	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 : NO9
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 : NO9
ICE	Etoposide 100MG/M2 IVD on D1-3	
	Carboplatin AUCx5MG IVA on D2	
	Ifosfamide 1GM/M2 IVA on D2	References : NO9

Diffuse large B cell lymphoma

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建議治療療程

二線化療（適用於無法執行高劑量化療者）

R+B	± Rituximab 375mg/M2 IVA or Rituximab 1400mg SC on Day1	
	Bendamustine 50~150MG/M2 IVA	References : NO10.11
GemOx (2weeks/cycle)	Gemcitabine 1000MG/M2 IVA on Day1	
	Oxaliplatin 100mg/M2 IVA on Day1	
	± Rituximab 375mg/M2 IVA or Rituximab 1400mg SC on Day1	References : NO12
Lenalidomide	Revlimid Cap 25mg 1cap po QD x 21days	References : NO10.11

Diffuse large B cell 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
- 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.2 2021
- 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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- 11.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.
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Diffuse large B cell lymphoma

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References:

13. NCCN guidelines of Non-Hodgkin's lymphomas, V.2 2022

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

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Hodgkin Lymphoma

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Definitions of Stages in Hodgkin Lymphoma²

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 (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)

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
- Immunohistochemistry evaluation

Essential:

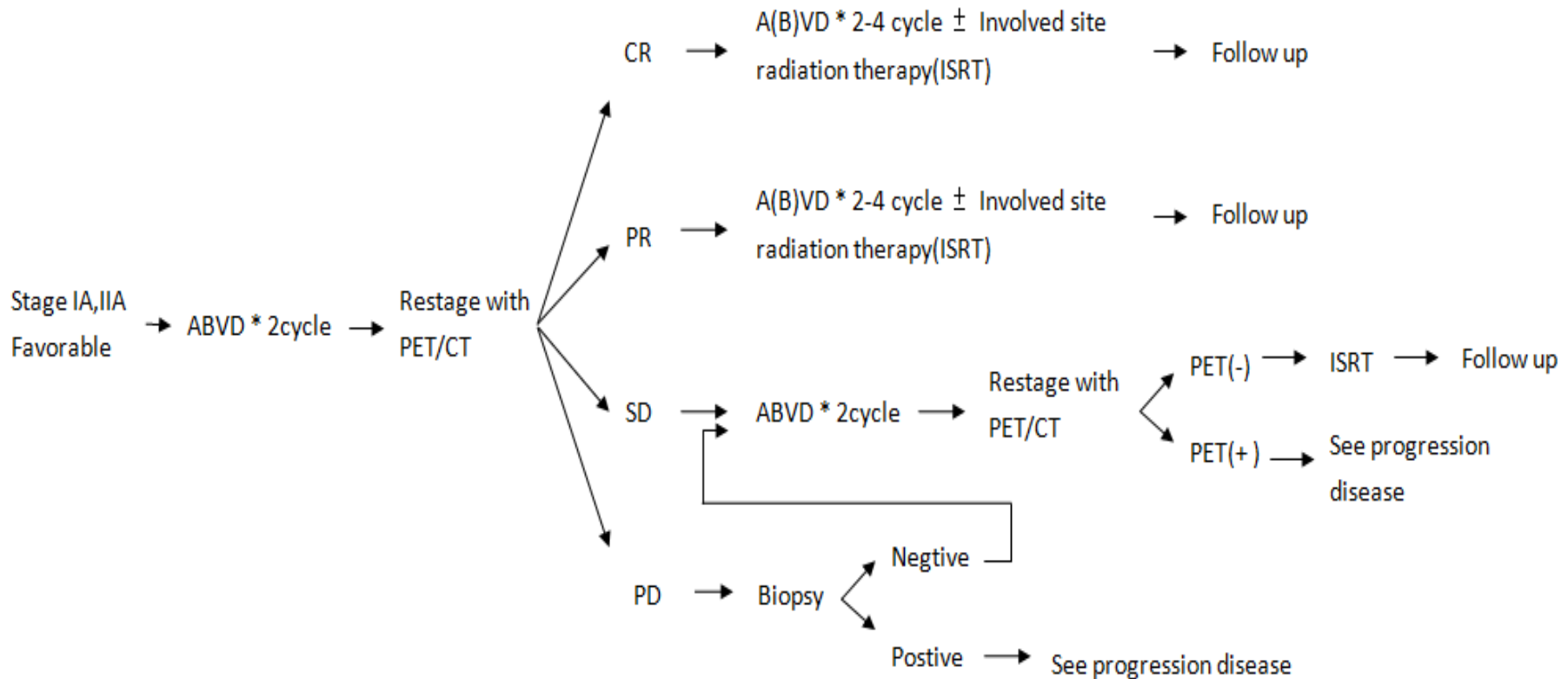
- H&P including: B symptoms (unexplained fever $>38^{\circ}\text{C}$; drenching night sweats; or weight loss $>10\%$ of body weight within 6 mo of diagnosis), alcohol intolerance, pruritus, fatigue, performance status, examination of lymphoid regions, spleen, liver
- CBC, differential, platelets
- Erythrocyte sedimentation rate (ESR)
- Comprehensive metabolic panel, lactate dehydrogenase (LDH), and liver function test (LFT)
- Pregnancy test for women of childbearing age
- ★ PET/CT scan (skull base to mid-thigh or vertex to feet in selected cases)
- Counseling: Fertility, smoking cessation, psychosocial

Useful in selected cases:

- Fertility preservation
- ★ Pulmonary function tests (PFTs incl. diffusing capacity [DLCO]) if ABVD or escalated BEACOPP are being used
- Pneumococcal, H-flu, meningococcal vaccines, if splenic RT contemplated
- HIV and hepatitis B/C testing (encouraged)
- Diagnostic CT (contrast-enhanced)
- Chest x-ray (encouraged, especially if large mediastinal mass)
- Adequate bone marrow biopsy if there are unexplained cytopenias other than anemia (eg, thrombocytopenia or neutropenia) and negative PET
- Evaluation of ejection fraction if anthracycline-based chemotherapy is indicated
- MRI to select sites, with contrast unless contraindicated
- PET/MRI (skull base to mid-thigh) without contrast

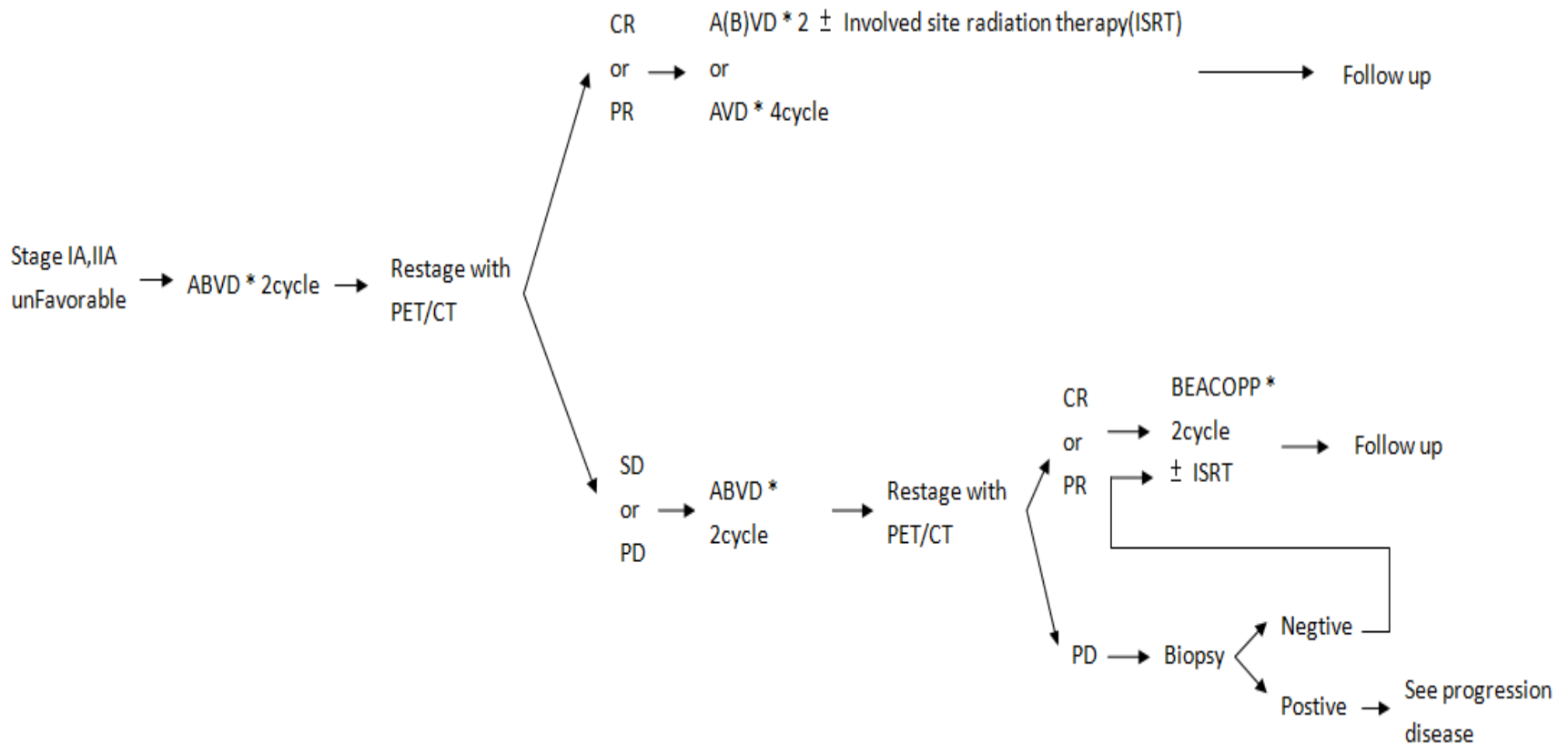
Hodgkin Lymphoma

Classical Hodgkin Lymphoma Stage IA-IIA Favorable



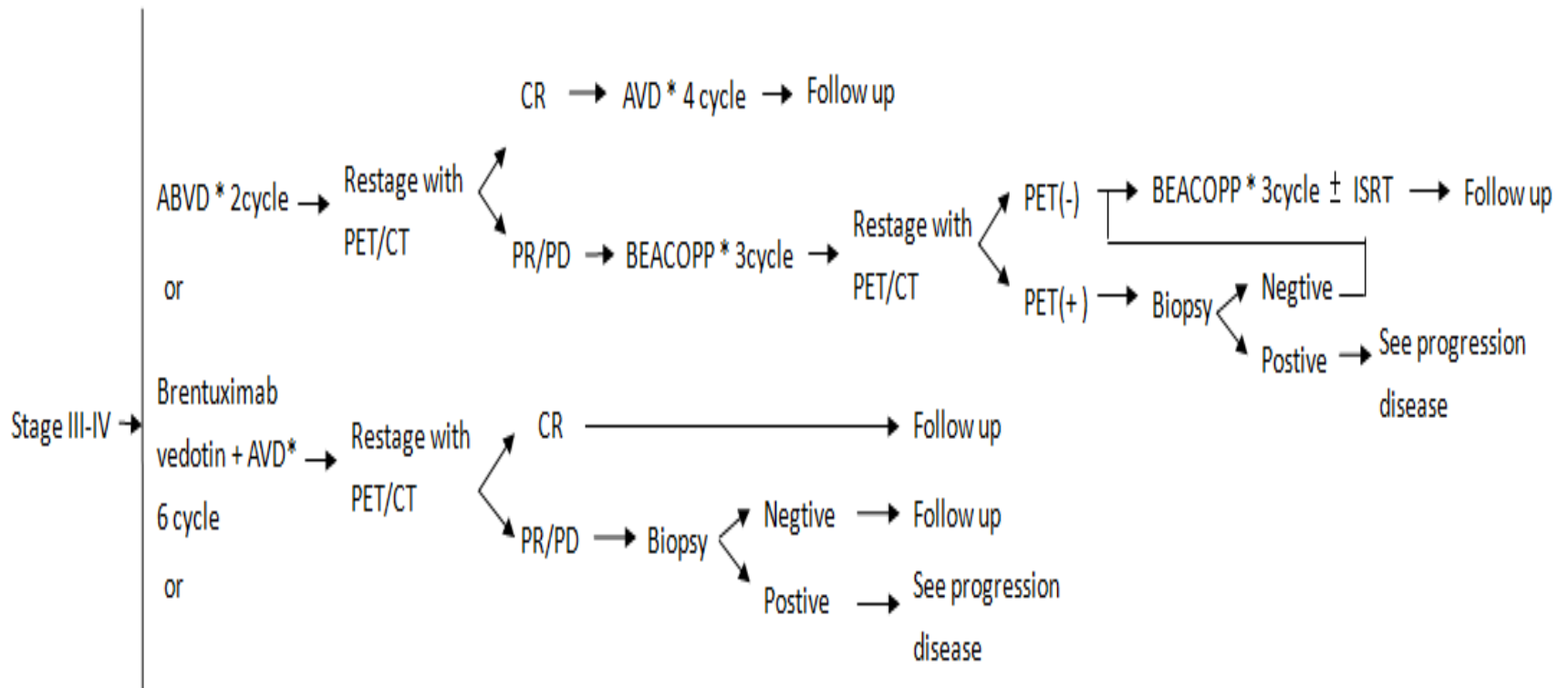
Hodgkin Lymphoma

Classical Hodgkin Lymphoma Stage I-II Unfavorable



Hodgkin Lymphoma

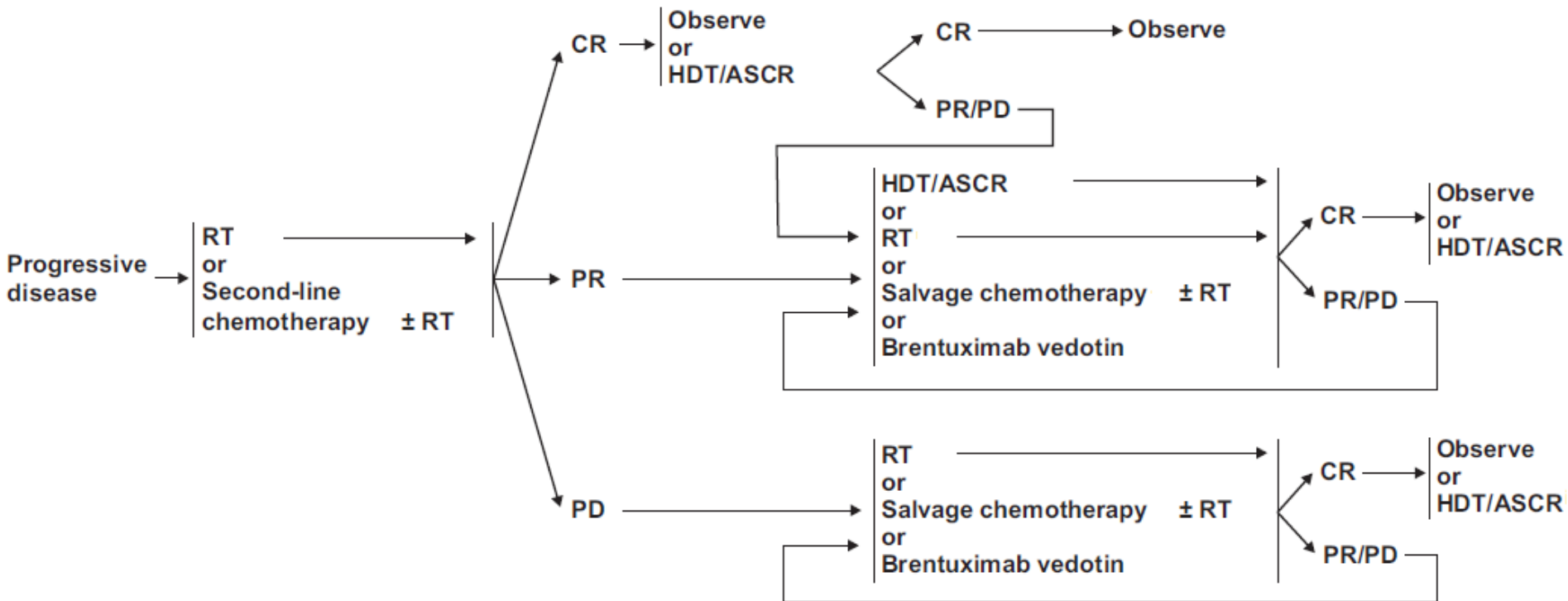
Classical Hodgkin Lymphoma Stage III-IV



Hodgkin Lymphoma

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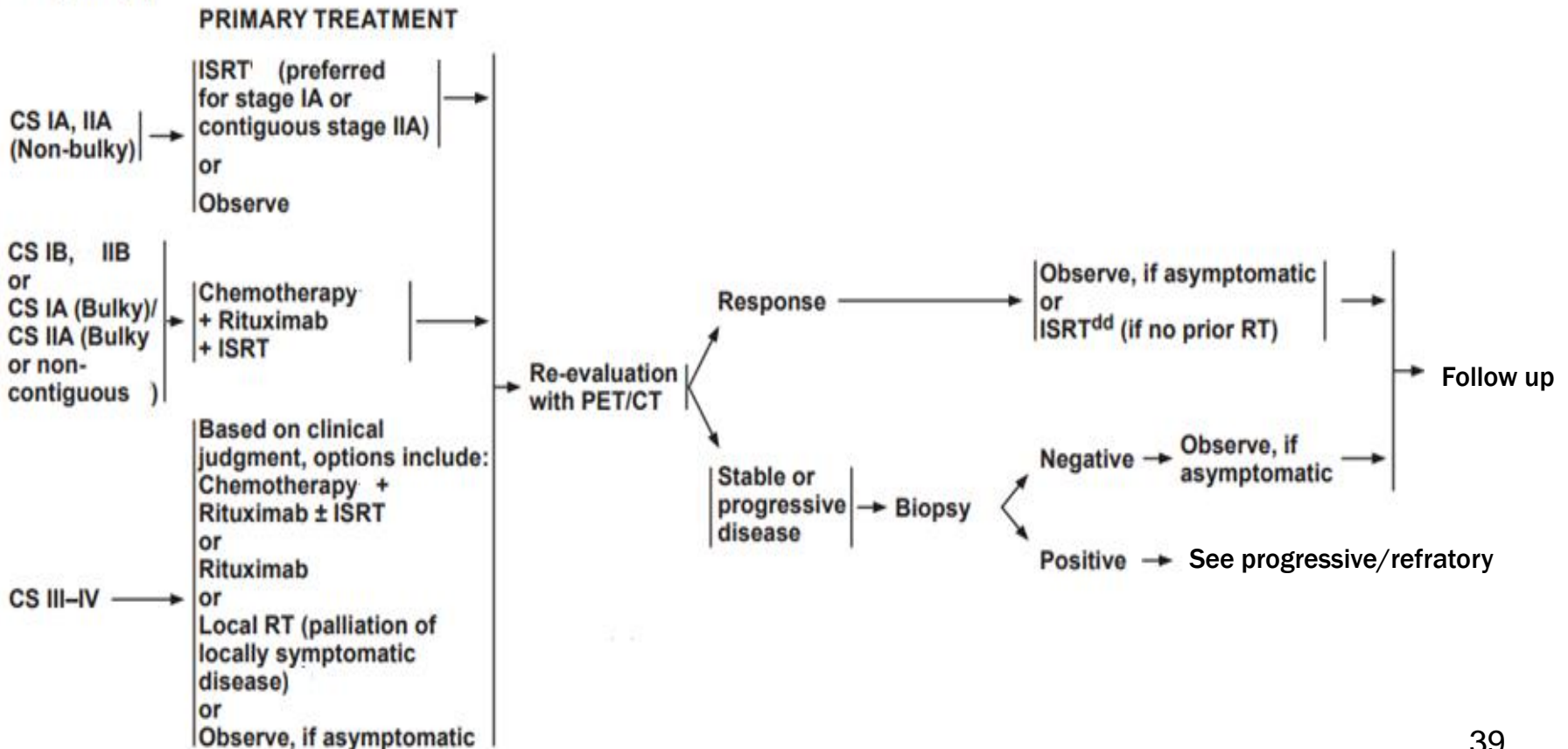
Classical Hodgkin Lymphoma (progressive disease or relapse)



Hodgkin Lymphoma

Lymphocyte-predominant Hodgkin Lymphoma

CLINICAL PRESENTATION:
Nodular Lymphocyte-Predominant
Hodgkin Lymphoma



Hodgkin Lymphoma

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Hodgkin lymphoma-Commonly used chemotherapy regimen

ABVD (Q4W)	Epirubicin 37.5mg/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)	Epirubicin 37.5mg/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 Vedotin(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 AUCx5MG 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 vetodin(Adcetris) 1.8mg/Kg IV	
Pembrolizumab	Pembrolizumab(Keytruda) 200mg IV	

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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- 5.Velasquez WS. Cabanillas F, Salvador P, et al. Effective salvage therapy for lymphoma with cisplatin in combination with high-dose Ara-C and dexamethasone(DHAP). Blood 988;71:177-122.
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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

2022/04/26 第一版

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.
- * Additional immunophenotyping to establish diagnosis:
 - IHC panel : CD20,CD3,CD5,CD10,BCL2,BCL6,CD21,CD23, with or without
 - Cell surface marker analysis by flow cytometry with peripheral blood and/or biopsy specimen : kappa/lambda,CD19,CD20,CD5,CD23,CD10
- * Useful under certain circumstances :
 - IHC panel : Ki-67, IRF4/MUM1 for FL,grade3 ,cyclin D1
 - Karyotype or FISH : t (14;18) ; BCL6, IRF4/MUM1 rearrangements
 - NGS panel

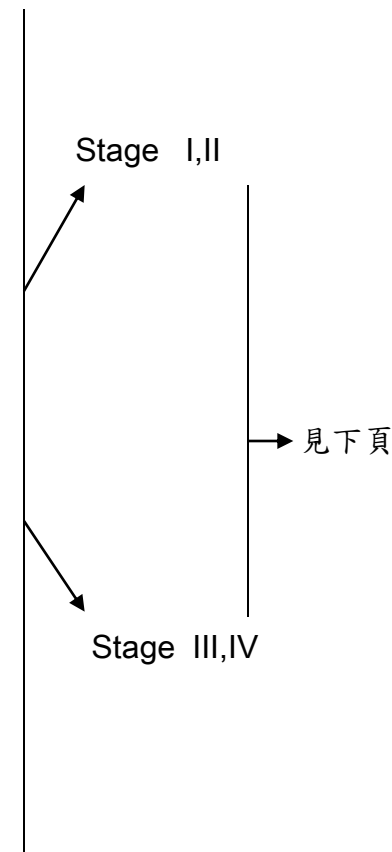
Work-up Essential :

- * 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

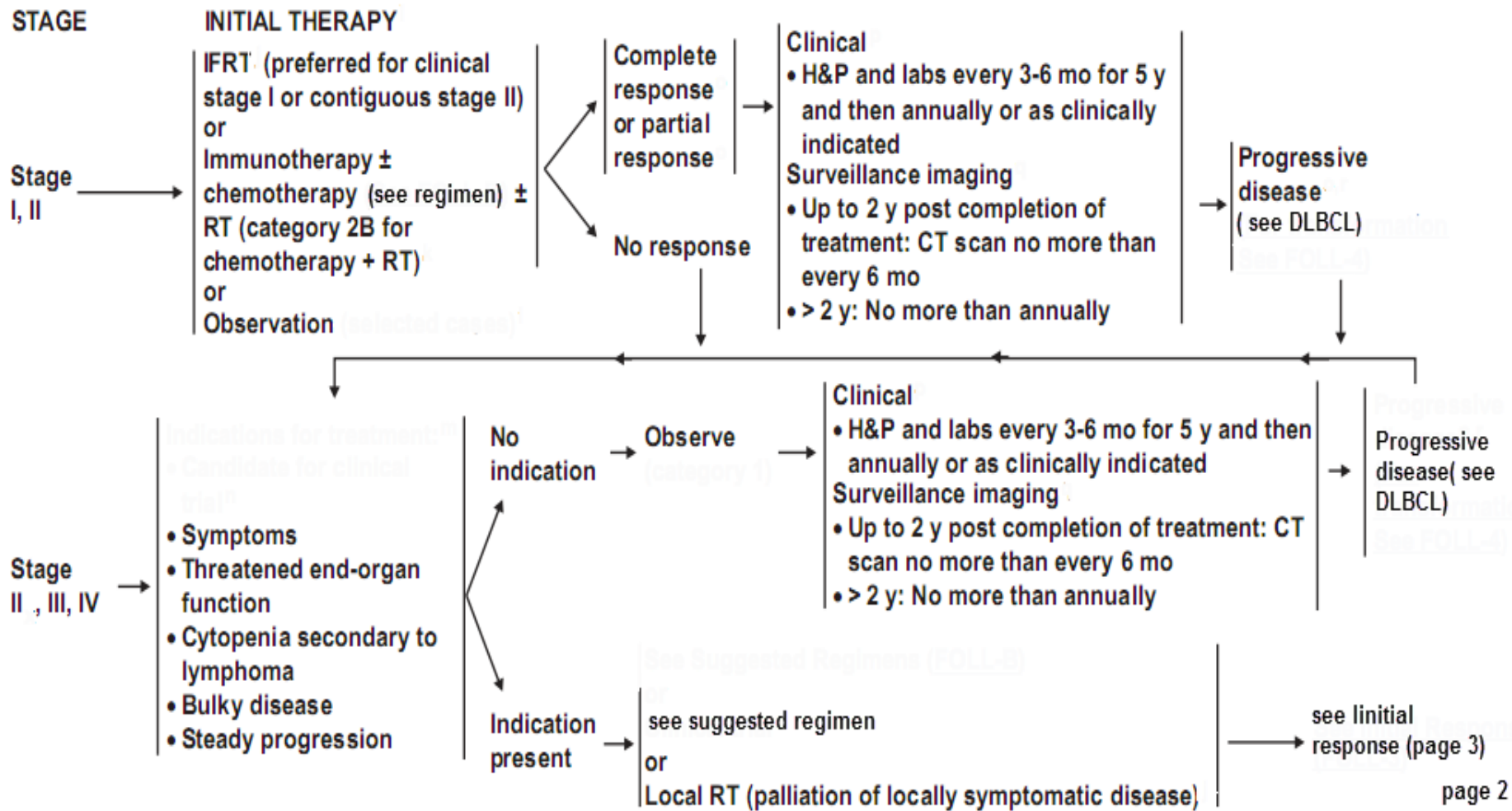
選擇性 :

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

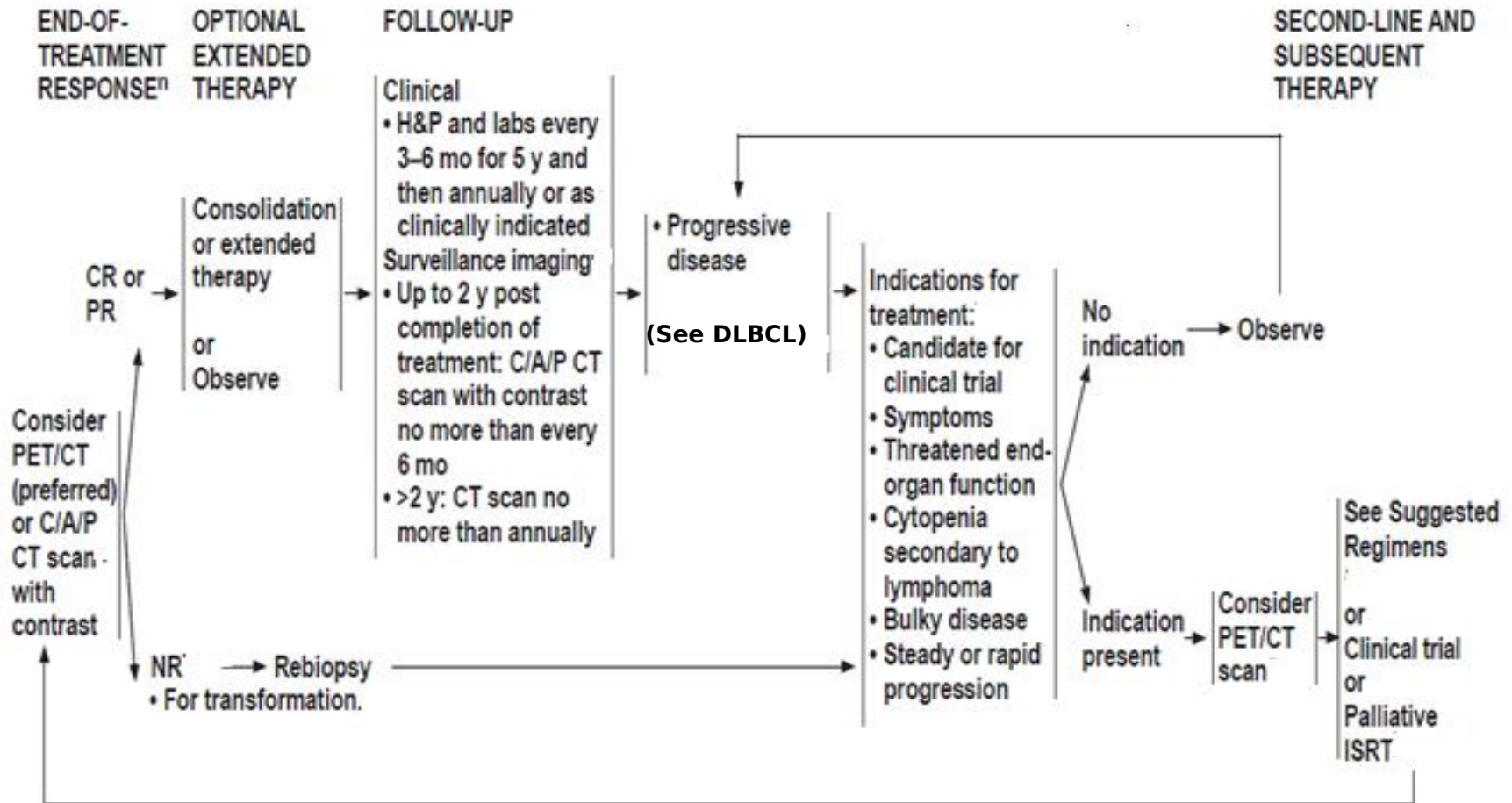
備註 : Follicular lymphoma grade 3 is commonly treated according to the DLBCL



Follicular lymphoma (grade 1-2)



Follicular lymphoma (grade 1-2)



Follicular lymphoma

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)

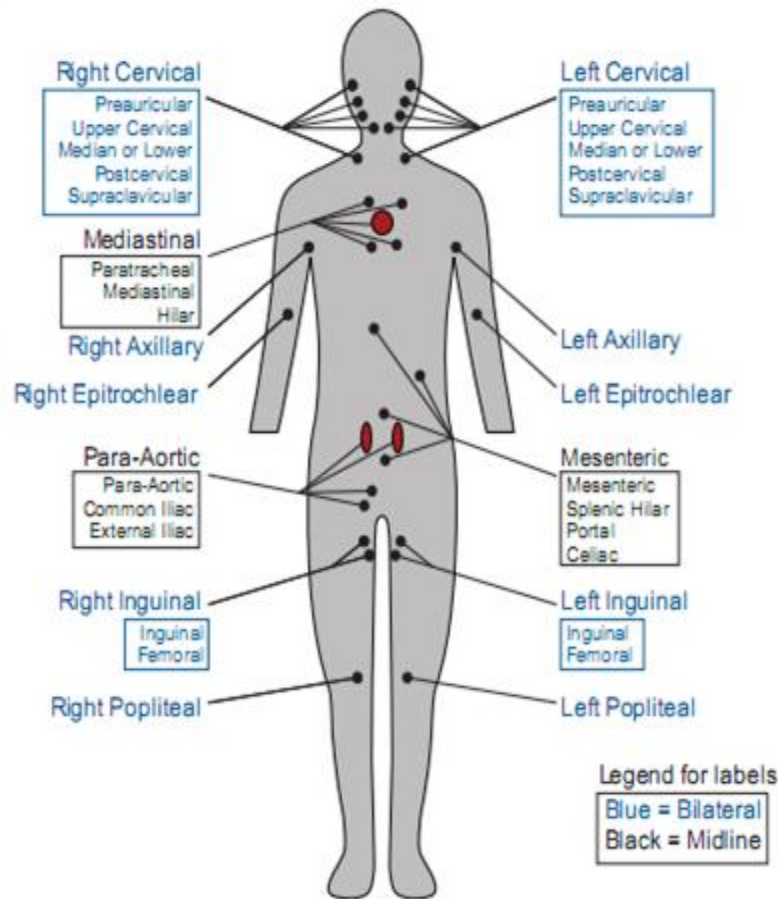
FLIPI - 1 CRITERIA

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)

First line regimen :

R-CHOP	± Rituximab 375mg/m ² IVA or Rituximab 1400mg SC on D1
	Cyclophosphamide 750mg/m ² IVA on D1 or D2
	Doxorubicin 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	
R-CEOP	± Rituximab 375mg/m ² IVA or Rituximab 1400mg 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 :

R-COP	±Rituximab 375mg/m ² IVA or Rituximab 1400mg 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
R+B	±Rituximab 375mg/m ² IVA or Rituximab 1400mg SC on D1	
	Bendamustine 50-150mg/m ² IVA on D1	Reference:NO6
Rituximab 375mg/m ² IVA or Rituximab 1400mg 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 Rituximab 1400mg SC weekly for 4 doses

2.Single-agent alkylators ± Rituximab 375mg/m²

Reference:NO7

First line consolidation or extended dosing (optional) :

1.Rituximab 375mg/m² one dose every 12weeks for 8doses

2.Obinutuzumab (Gazyva) 1000mg every 8weeks for 12 doses

3.If initially treated with single-agent Rituximab,consolidation with Rituximab 375mg/m² one dose every 8weeks for 4 doses

Reference:NO8

Follicular lymphoma (grade 1-2)

Second line and subsequent therapy :

1. Bendamustine 50~150mg/m ² + Rituximab 375mg/m ²
2. R-FCM (±Rituximab 375mg/m ² , Fludarabine 25mg/m ² D1-3, Cyclophosphamide 200mg/m ² D1-3, Mitoxantrone 8mg/m ² D1)
3. Fludarabine 25mg/m ² + Rituximab 375mg/m ²
4. Rituximab 375mg/m ²
5. RFN (±Rituximab 375mg/m ² , Fludarabine 25mg/m ² D1-3, Mitoxantrone 10mg/m ² D1 , Dexamethasone 20mg/m ²)
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 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
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Follicular lymphoma (grade 1-2)

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