CLINICAL PRACTICE GUIDELINES

An ESMO Product

Hodgkin lymphoma

ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up

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Diagnostic work-up in Hodgkin Lymphoma

† Disease is staged as limited, intermediate or advanced, according to the Ann Arbor classification

‡ including presence of B symptoms (fever, drenching night sweats, unexplained weight loss > 10% over 6 months) and disease-related symptoms

§ If available. If PET-CT is not available, BM biopsy is required

* If PET-CT scan is not available at initial staging

Diagnostic work-up in Hodgkin Lymphoma	
Diagnosis	Excisional lymph node biopsy or surgical specimen (WHO classification) Hodgkin and Reed–Sternberg cells define cHL NLPHL is characterised by LP cells
Staging and risk stratification†	Medical history and physical examination‡ X-ray of the chest Contrast-enhanced CT scan of the neck, chest and abdomen PET§ Full blood cell count and blood chemistry, ESR HBV, HCV and HIV screening
Pretreatment examinations	ECG Echocardiography Pulmonary function test Reproductive counselling (in patients of reproductive age) Serum pregnancy test (in female patients of reproductive age) Consultation of an ear, nose and throat specialist including a fiberoptic nasolaryngoscopy*

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Definition of HL Risk groups

According to the EORTC/LYSA and the GHSG

	EORTC/LYSA	GHSG
Treatment group		
Limited stages	CS I–II without risk factors (supradiaphragmatic)	CS I–II without risk factors
Intermediate stages	CS I–II with ≥ 1 risk factors (supradiaphragmatic)	CS I, CS IIA with ≥ 1 risk factors CS IIB with risk factors C and/or D, but not A/B
Advanced stages	CS III–IV	CS IIB with risk factors A and/or B CS III/IV
Risk factors		
	A: Large mediastinal mass* B: Age ≥ 50 years C: Elevated ESR† D: ≥ 4 nodal areas‡	A: Large mediastinal mass* B: Extranodal disease C: Elevated ESR† D: ≥ 3 nodal areas‡

*Large mediastinal mass: Mediastinum-to-thorax ratio ≥ 0.35 (EORTC/LYSA); mediastinal mass larger than one-third of the maximum thoracic width (GHSG)

†Elevated ESR: > 50 mm/h without B symptoms; > 30 mm/h with B symptoms (B symptoms: Fever, night sweat, unexplained weight loss > 10% over 6 months)

‡Nodal areas: Involvement of ≥ 4 out of 5 supradiaphragmatic nodal areas (EORTC/LYSA); involvement of ≥ 3 out of 11 nodal areas on both sides of the diaphragm (GHSG)

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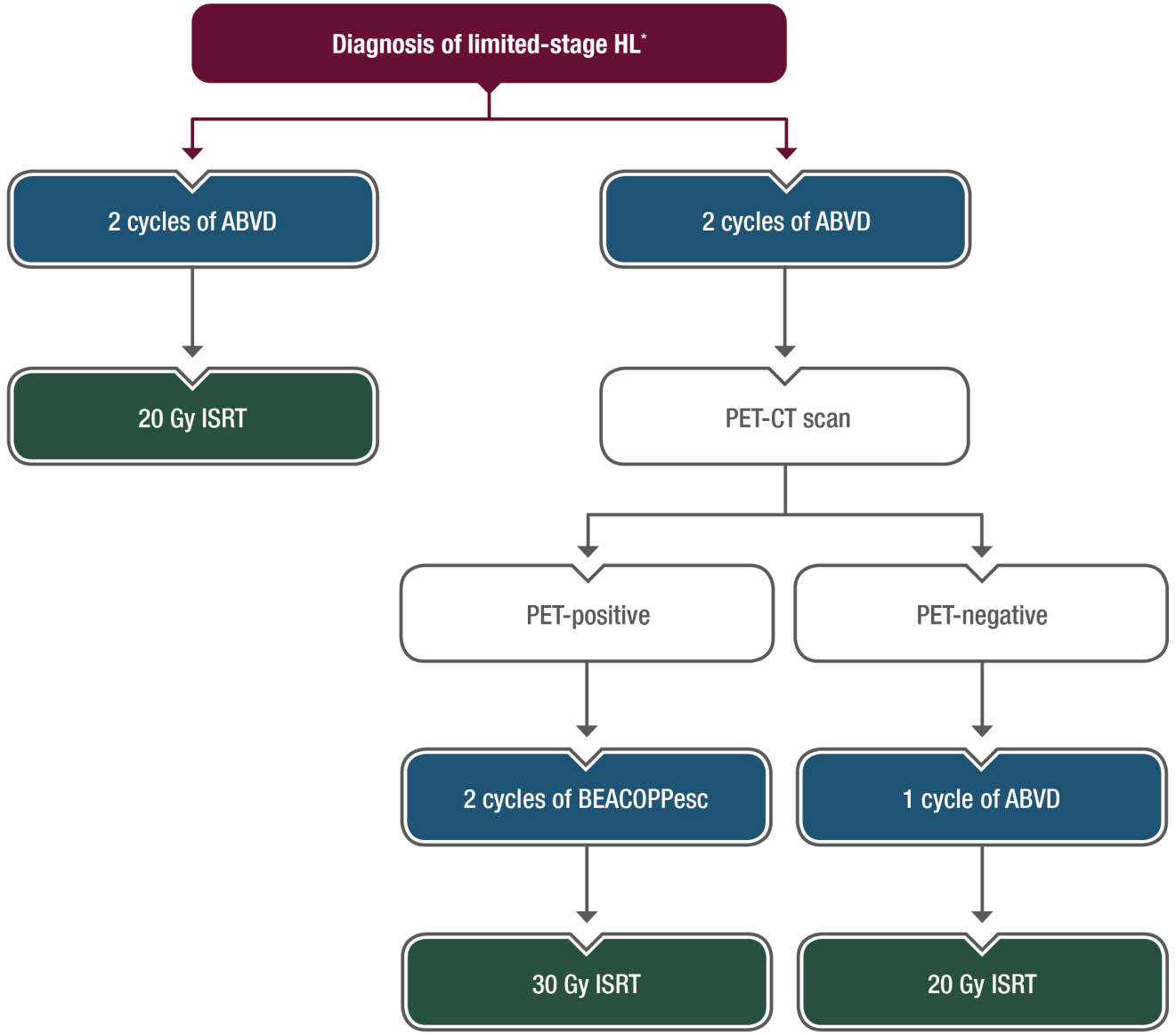
Diagnosis & treatment of limited-stage HL

Newly diagnosed patients ≤ 60 years

*Except for stage IA NLPHL without risk factors (treated with ISRT alone)

The figure includes one approach not guided by interim PET, based on the GHSG HD10 study (left) and one PET-guided approach based on the EORTC/LYSA/FIL H10 study (right)



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Treatment of cHL

The ABVD and BEACOPPescalated regimens

ABVD REGIMEN – Recycle: Day 29			
	Dose (mg/m^2)	Administration	Days
Doxorubicin	25	IV	1 + 15
Bleomycin	10	IV	1 + 15
Vinblastine	6	IV	1 + 15
Dacarbazine	375	IV	1 + 15

BEACOPPescalated REGIMEN – Recycle: Day 22			
	Dose (mg/m^2)	Administration	Days
Bleomycin	10	IV	8
Etoposide	200	IV	1 – 3
Doxorubicin	35	IV	1
Cyclophosphamide	1250	IV	1
Vincristine	1.4*	IV	8
Procarbazine	100	PO	1 – 7
Prednisone	40	PO	1 – 14
G-CSF		SC	From day 8

*The maximum absolute dose of vincristine is 2 mg

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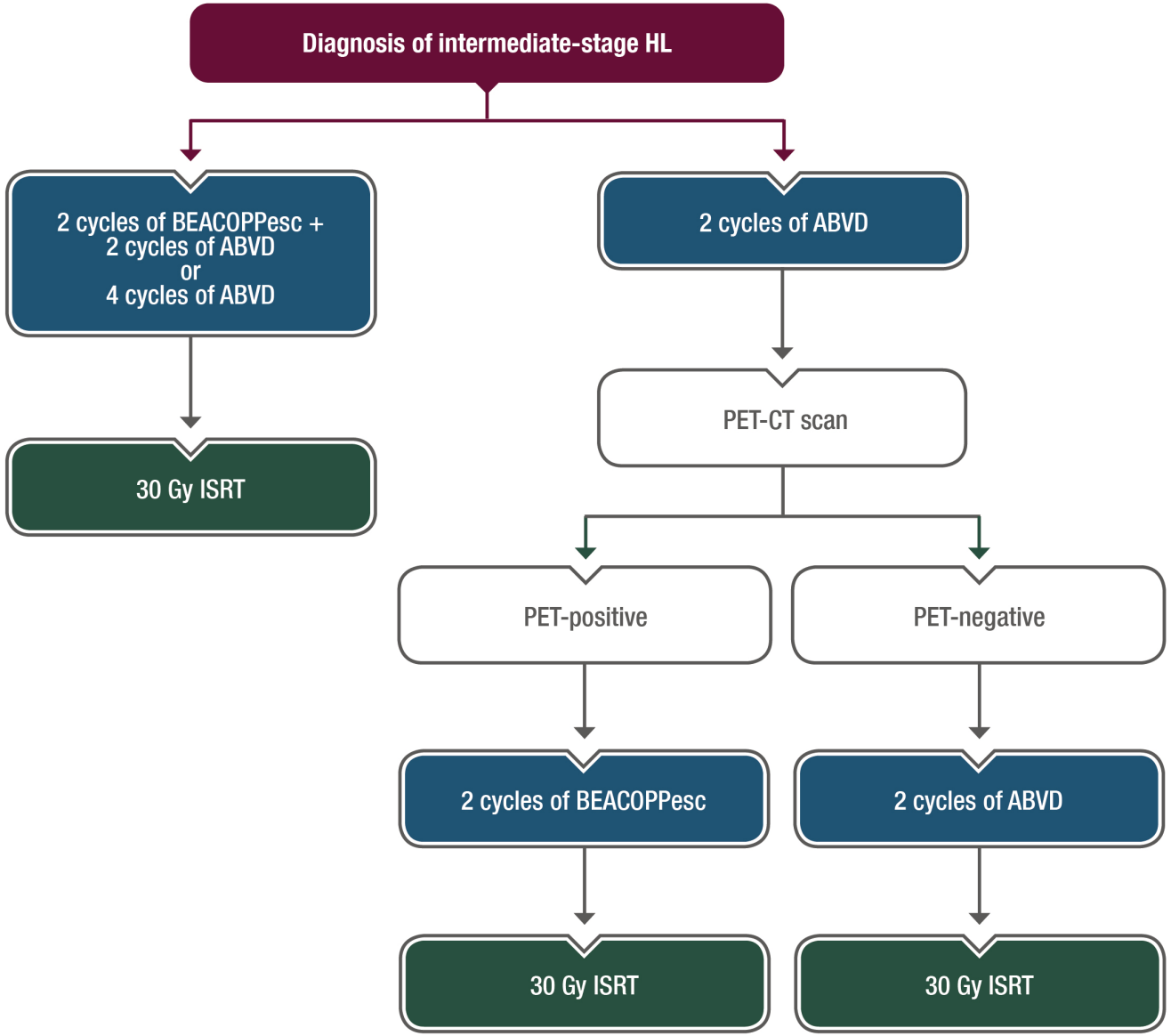
Diagnosis & treatment of intermediate-stage HL

Newly diagnosed patients ≤ 60 years

The figure includes one approach not guided by interim PET, based on the GHSG HD14 study (left) and one PET-guided approach based on the EORTC/LYSA/FIL H10 study (right)

In patients > 60 years, bleomycin should be discontinued after the second ChT cycle



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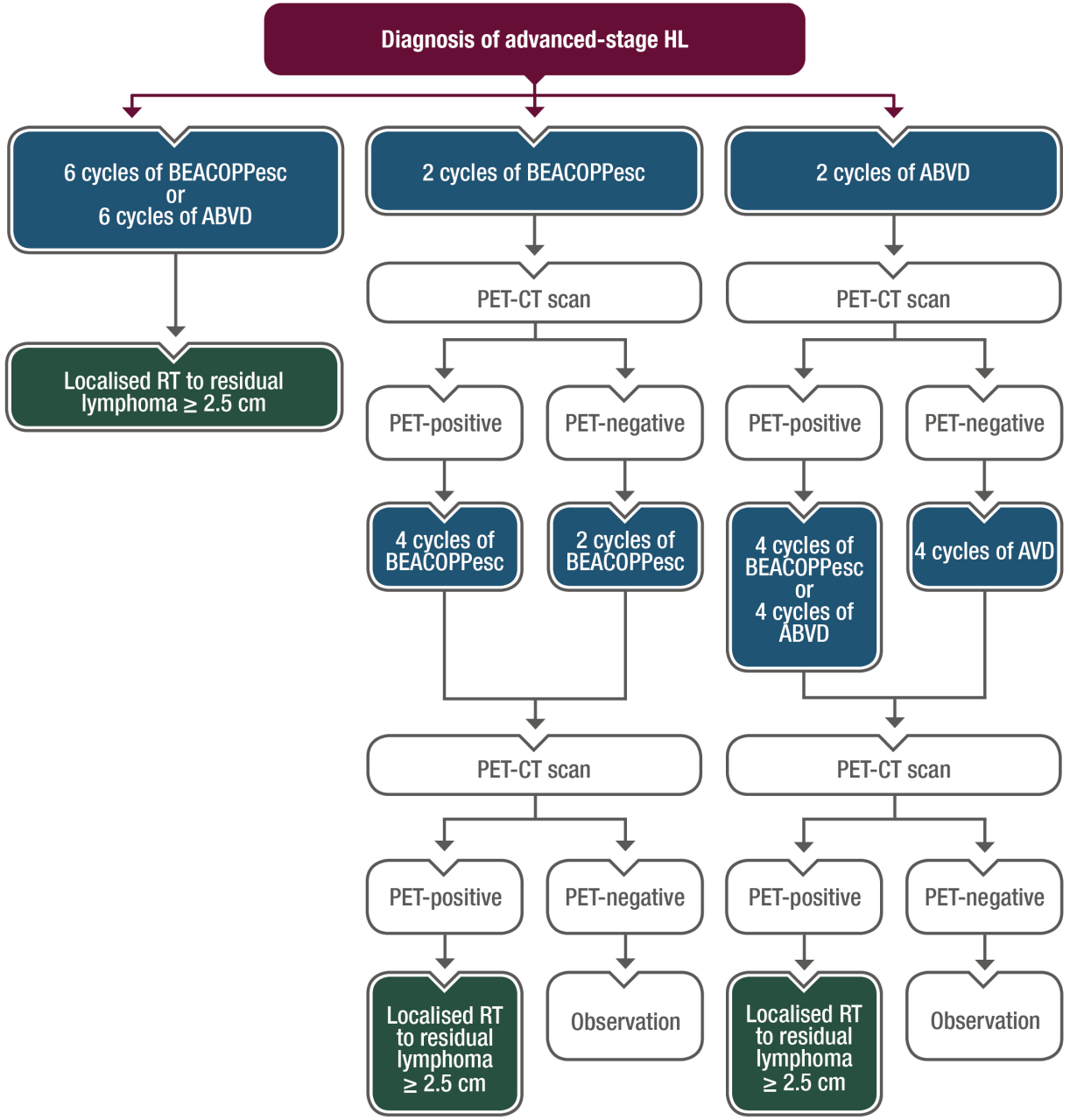
Diagnosis & treatment of advanced-stage HL

Newly diagnosed patients ≤ 60 years

The figure includes one approach not guided by interim PET (left) and two PET-guided approaches based on the GHSG HD18 study (middle) and the RATHL study (right)

ABVD is the standard of care for older patients fit enough for multiagent ChT, with discontinuation of bleomycin after the second cycle of ChT



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Treatment of relapsed disease

Patient types	Treatment
Most patients with refractory or relapsed HL	HDCT followed by ASCT
High-risk patients	HDCT followed by tandem ASCT
Patients with ≥ 1 risk factors*	Consolidation with BV after HDCT and ASCT
Patients with single PET-positive lymph nodes after salvage therapy	RT before HDCT and ASCT
Patients failing ASCT	BV is an option
Patients with disease recurrence†	Anti-PD-1 antibodies
Patients failing HDCT and ASCT	Allogeneic stem cell transplantation‡
Patients with multiple relapses	Enrolled in clinical trials whenever possible Gemcitabine-based palliative chemotherapy and/or regional RT

The goal of salvage therapy, with regimens including DHAP, IGEV or ICE, is a negative PET prior to HDCT and ASCT. In some patients, single-agent BV is a sufficient salvage therapy

* Primary disease progression, early disease recurrence < 12 months after the end of first-line treatment and extranodal disease at relapse

† After HDCT followed by ASCT and BV

‡ For young, chemosensitive patients in good general condition

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Treatment of NLPHL

Summary of recommendations	
Stage IA without risk factors	• Standard treatment: ISRT 30 Gy • The ISRT fields for single-modality RT are larger than those for combined-modality RT
Other stages	• NLPHL treated identically to cHL • Addition of an anti-CD20 antibody (e.g. R-CHOP) may improve treatment efficacy
Relapsed NLPHL	• New biopsy in patients with suspected NLPHL before salvage therapy (excludes transformation into aggressive non-hodgkin lymphoma) • Localised NLPHL relapses can be effectively treated with single-agent anti-CD20 antibodies* • More aggressive ChT, possibly combined with an anti-CD20 antibody, may be required† • Salvage therapy should be tailored to the individual‡ • BV is not a treatment option

* Such as rituximab or ofatumumab

† For patients with more disseminated disease at relapse and additional poor-risk features

‡ Based on factors including time to relapse, disease extent at relapse and prior treatment

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Response evaluation

Type of treatment	Response Evaluation	Final staging
No PET-guided treatment	Interim contrast-enhanced CT before RT in limited-and intermediate-stage disease, and after 4 cycles of ChT as well as before RT in advanced stages	Mandatory after completion of treatment: • Physical examination • Laboratory analyses • Contrast-enhances CT (or PET-CT if available)
Interim-PET-guided treatment (only for patients receiving ABVD)	Interim PET-CT scan after 2 cycles of ChT Patients with advanced disease: PET-CT scan after the end of ChT	
BEACOPPescalated (patients with advanced HL)	Interim PET-CT scans should be carried out after 2 cycles of ChT and after the end of ChT	

Prognosis:

With modern treatment strategies, 80–90% of HL patients can be considered cured

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Follow-up, long-term implications and survivorship

Surveillance and follow-up

Summary of recommendations
History, physical examination and laboratory analysis, including full blood cell count, ESR testing and blood chemistry*
CT scans and previously pathological radiographic tests needed to confirm remission status; thereafter, clinical follow-up is sufficient†
Thyroid function should be evaluated annually in patients undergoing neck irradiation
Testosterone and oestrogen levels should be monitored, particularly in younger patients who underwent intensive ChT
Patients should be asked about symptoms indicating long-term toxicity, especially those affecting the heart and lungs
Regular cancer screening is required • Female patients < 40 years old: annual mammogram, commencing 8–10 years after RT • Female patients ≤ 30 years old: breast MRI + annual mammogram, commencing 8–10 years after RT

* every 3 months for the first half-year, every 6 months until the fourth year and annually thereafter

† Surveillance scans only if clinical symptoms occur

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This slide set provides you with the most important content of the full ESMO Clinical Practice Guidelines (CPGs) on the management of Hodgkin Lymphoma. Key content includes diagnostic criteria, staging of disease, treatment plans and follow-up.

The ESMO CPGs are intended to provide you with a set of recommendations for the best standards of care, using evidence-based medicine. Implementation of ESMO CPGs facilitates knowledge uptake and helps you to deliver an appropriate quality of focused care to your patients.

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