HODGKIN LYMPHOMA

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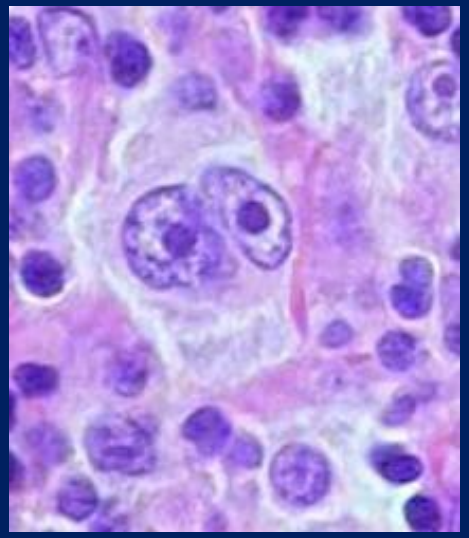
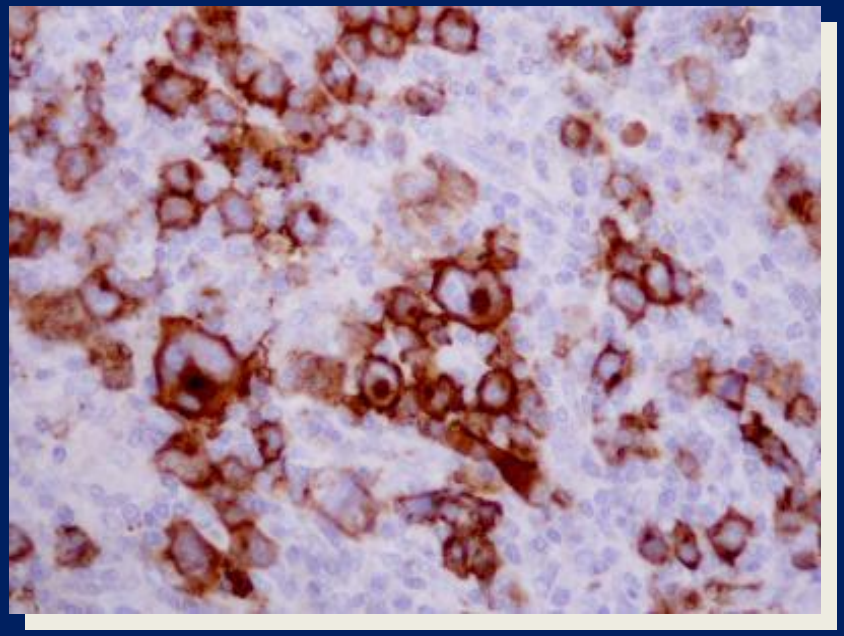
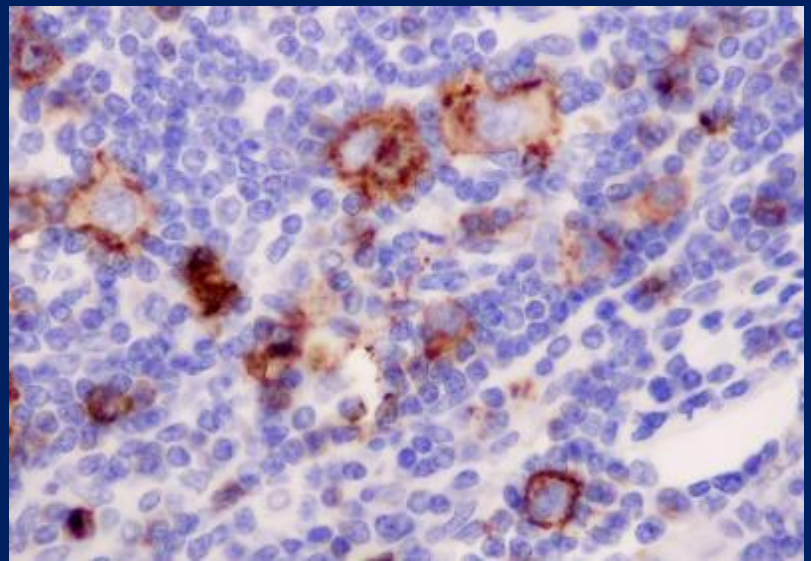
Characteristics

- Usualy arise in lymph nodes (cervical, mediastinum), axial progression
- Majority manifest in young adults
- 1/3 B symptoms
- Tumor cells (GC B lymphocytes) Hodgkin´s and RS cells – minority of tumor tissue, 1-3%
- HL account 15% of all lymphomas
- Excelent outcome, curability 85%

Hodgkin, RS cell







CD30+,CD15+ (až 70%)
CD20 -/+, BSAP+, fascin+,
BCL6-, CD45-,
Oct-2 a BOB.1 -

Classification

- Lymphocyte predominant HL (5%)
- Classical Hodgkin lymphoma (95%)
  - lymphocyte rich CHL
  - nodular sclerosis CHL
  - mixed cellularity CHL
  - lymphocyte-depleted CHL

Etiology

- Incidence 2-3/100.000 = 200-300 newly dg./year
- Male:Female 3:2
- median of incidence age 20-35 y
- EBV 75% MC CHL , 10-40% NS CHL
- EBV infection of B cells affect genetic alterations – lymhomagenesis
- HIV

Clinical stage, prognosis = treatment choice

- CT or better **PET/CT**

- Trephan biopsy only if PET result is uncertain

- KO, biochemistry, FW, serology (hepatitis, EBV, HIV)
- ECHO, ECG, spiromety

A : without symptoms
B: with symptoms = wight loss (more than 10% in 6m), non infectious febrile, sweats

Prognostic factors: for early and advanced stages, reflects tumor volume (bulky mass), agressivity of the disease (extranodal involvement, FW, leukocytosis, anemia, lymfopenia)

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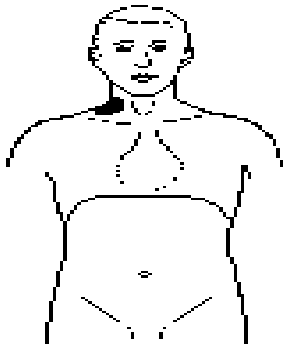
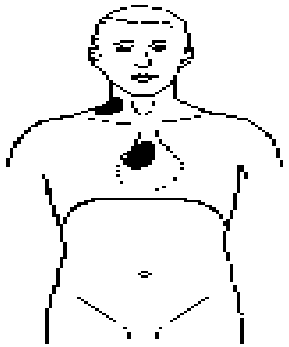


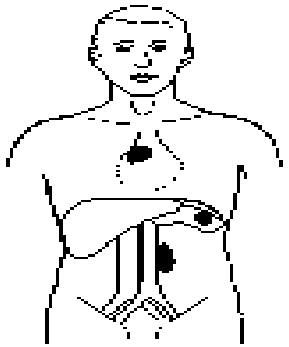
Stage I

single lymph node region or single extralymphatic site (Ie)



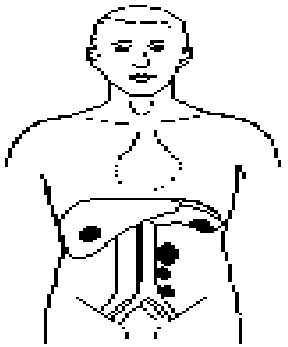
Stage II

two or more sites, same side of diaphragm or ē contiguous extralymphatic site (IIe)



Stage IIIs

both sides of diaphram or ē spleen (IIIs) or contiguous extralymphatic site (IIIe)



Stage IV

diffuse involvement of extralymphatic sites ± nodal disease

Stage subdivision: A-asymptomatic B-unexplained weight loss>10% in 6m and/or fever and/or night sweats

Extralymphatic = tissue other than lymph nodes, thymus, spleen, Waldeyer's ring, appendix & Peyer's patches

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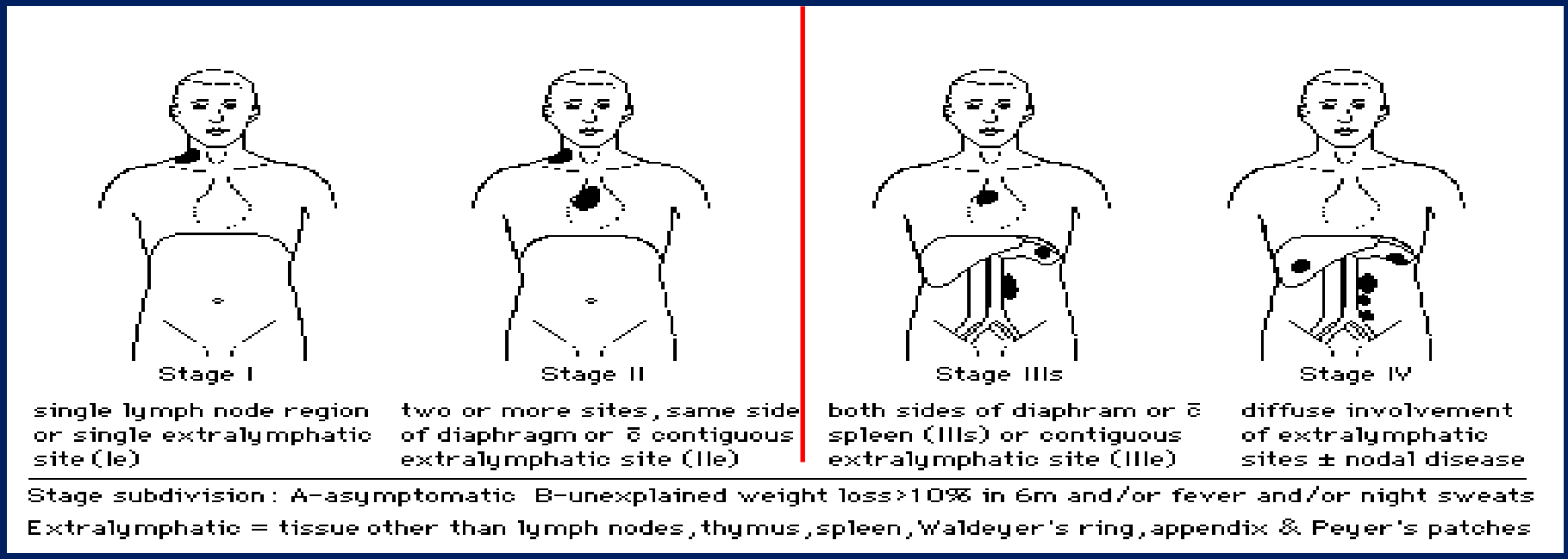

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3 groups of different treatment

Risk factors (GHSG)	**Stage** (Ann Arbor)		
	IA, IB, IIA	**IIB**	**III,IV**
No	**EARLY favorable**		**ADVANCED**
≥ 3 areas	**EARLY unfavorable**		
Hihg FW			
MMT			
Extranodal			

Treatment strategy

1. **Early stages ➡ combined modality treatment (CHT + RT**
2. **Advanced stages ➡ chemoterapy (RT only PET + rezidua)**

- regimens = ABVD or BEACOPP
- ABVD = adriamycin, bleocin, vinblastin, dacarbazin
- BEACOPP = bleocin, etoposid, adriamycin, cyklofosfamid, vinkristin, prokarbazin, prednison

RECENT RECOMMENDATIONS FOR 1st LINE TREATMENT OF HL

Early favorable stages

2xABVD + IF RT 20 Gy (8y EFS 87%, OS 95%)

Intermediate stages

2 BEACOPP esk. + 2 ABVD + IF RT 30 Gy or (5y EFS 86%, OS 95%)
4xABVD + IF RT 30 Gy

Advanced stages

6xBEACOPP esc (RT only for PET + residui)

(5 y PFS 90%, OS 95%)

How to treat refractory or relapsed disease?

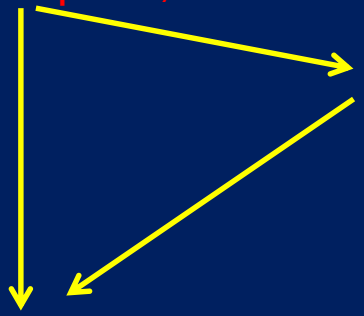
1. Risk stratification = primary resistant? Early relaps (up to 1 y)? late relaps?
   (further prognosis = advanced stage, anemia, EN, B symptoms)

2. If possible : salvage chemo, platinum based regimen (DHAP, ESAP, ICE)
   = ORR 60-85%, durable remission = 10-35%

3. If possible : salvage chemo + Auto SCT (BEAM), durable remission = 50%.
   high risk - tandem ASCT.

4. PET pos. residui = IF RT

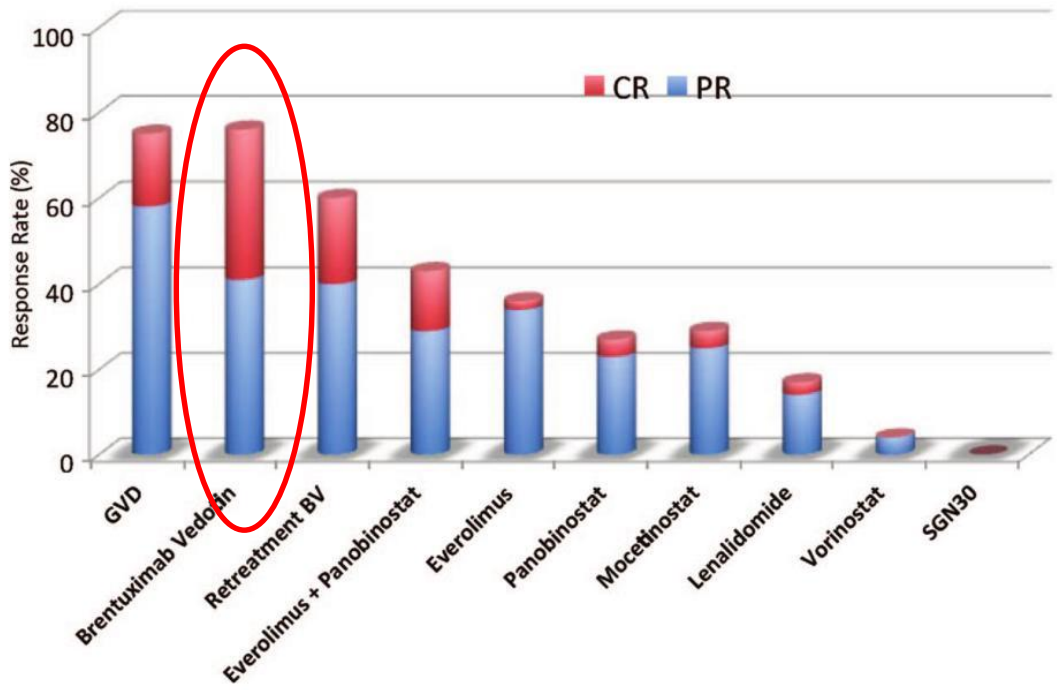
5. Multiple relapses, chemoresistent disease, young pts



New drugs = Brentuximab vedotin, anti CD 30 + MAE
= Nivolumab, check point inhibitor

Allo SCT, ale TRM 15%, RR 60%, PFS 20%, OS 40%

New drugs tested for R/R HL

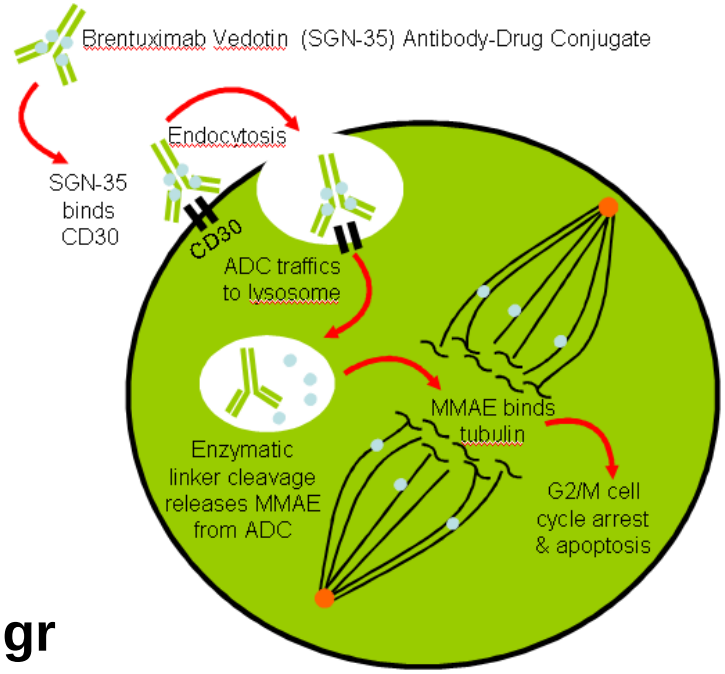


-Ab
- mTOR inhibitors
- JAK/STAT inhibitors
- epigenetic th

	Cíl	Podání	N	ORR	CR	
Brentuximab	CD 30	iv	102	75%	34%	Younes et al
Everolimus	mTOR	Po	19	47%	5%	Johnston et al
Vorinostat	I/II HDAC	po	25	4%	0%	Kirschbaum et al
Mocetinostat	HDAC 1,2	po	51	27%	4%	Younes et al
Panobinostat	I/II/IV HDAC	po	129	27%	4%	Younes et al
Entinostat	HDAC 1,3	po	49	16%	0%	Younes et al

Brentuximab vedotin for R/R HL

– Anti CD 30 + mikrotubulární toxin monomethyl auristatin E (MMAE)



- **after 4 decades new highly effective drug registered as target therapy for HL**
- **75% ORR for R/R HL heavily pretreated, poor prognostic pts**
- **specific toxicity, mainly polyneuropathy gr 1 a 2, typicaly after long terming use, mostly reversible**
- **contraindication of concurrent Bleomycinu**

Nivolumab u R/R HL

- **second new highly effective treatment developed in last few years for several malignancies, incl. HL**

- **anti-PD1 Ab stimulating T cell imune response**

- **R/ R HL (78 % after ASCT, 78 % after BV)**
  ORR 87 % !! 17 % CR 13 % SD

- **specific toxicity – autoagressive symptoms (skin, lung, liver)**

Summary and current trends

- **standard modalities have reached top of their power**

Even if most pts are cured, it costs a lot

<u>Late advers events</u>:

sec. Tumors after CHT i RT, infertility, cardiotoxicity, lung toxicity etc..

- **trends:**
  1. **adapted treatment (according to PET results)**
  2. **new (less toxic) drugs for early phase of th, not only for R/R**
  3. **further new drugs and approaches for R/R**