Aggressive lymphomas

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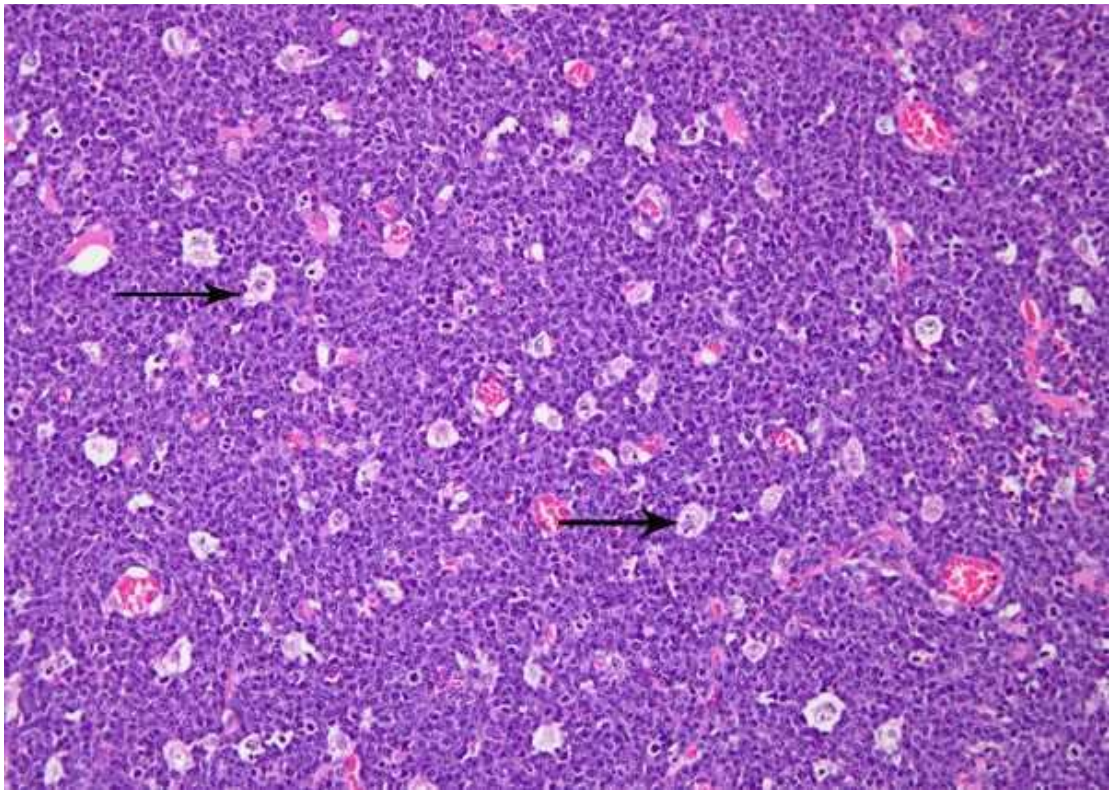
Burkitt lymphoma: diagnosis

Monomorphic medium size cells , very high prolipheration rate (Ki67 near 100%), «starry sky» appearance (scattered macrophages containg apoptotic tumour cells)



The fastest growing human tumour (cell doubling time 24-48 h)

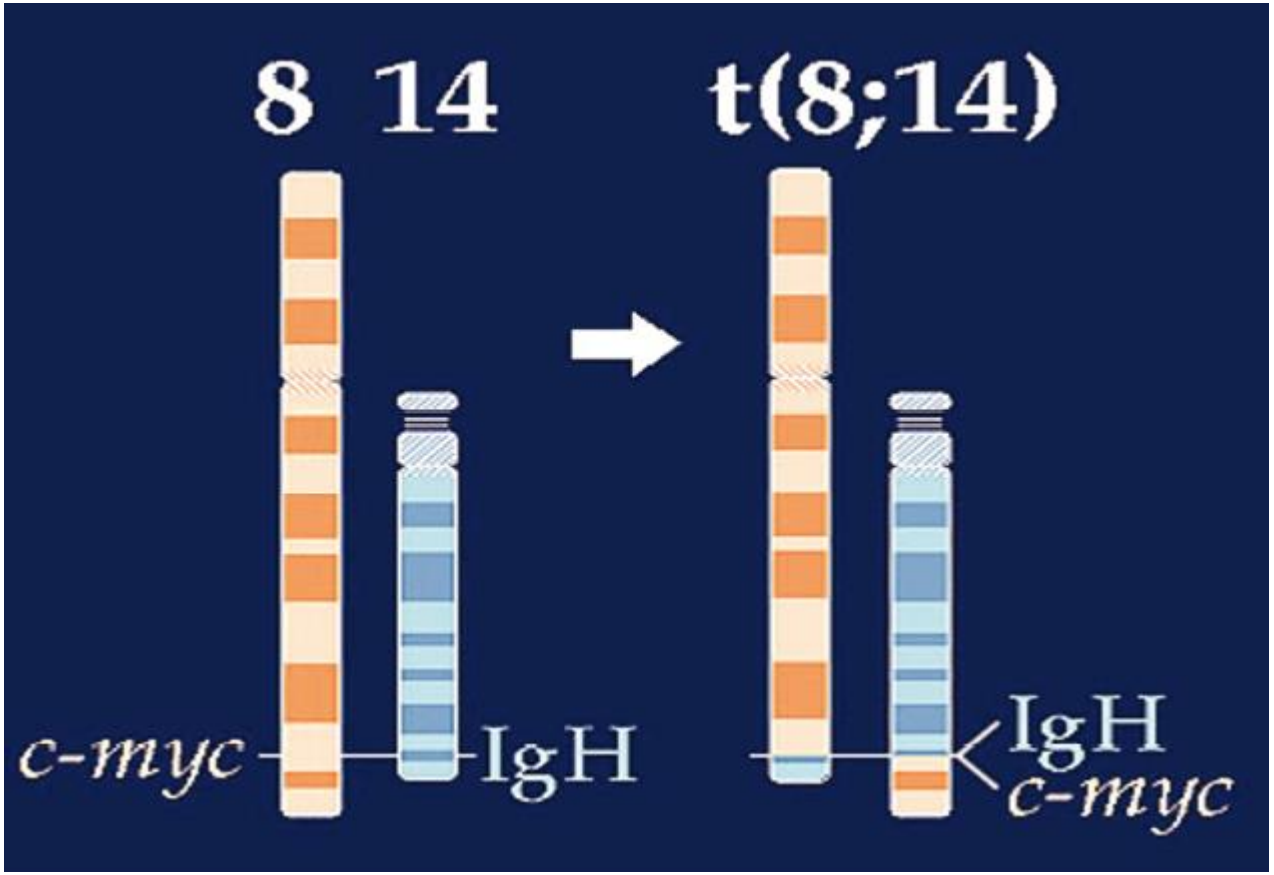
Always B-lineage (CD20+, CD79a +)

Usually CD10+, Bcl-6+

Usually Bcl-2 –

Note: «Burkitt-like lymphoma» is now «B-cell lymphoma unclassifiable, with features between DLBCL and BL»

Genetic background



80% of cases:

t(8;14)

20% of cases

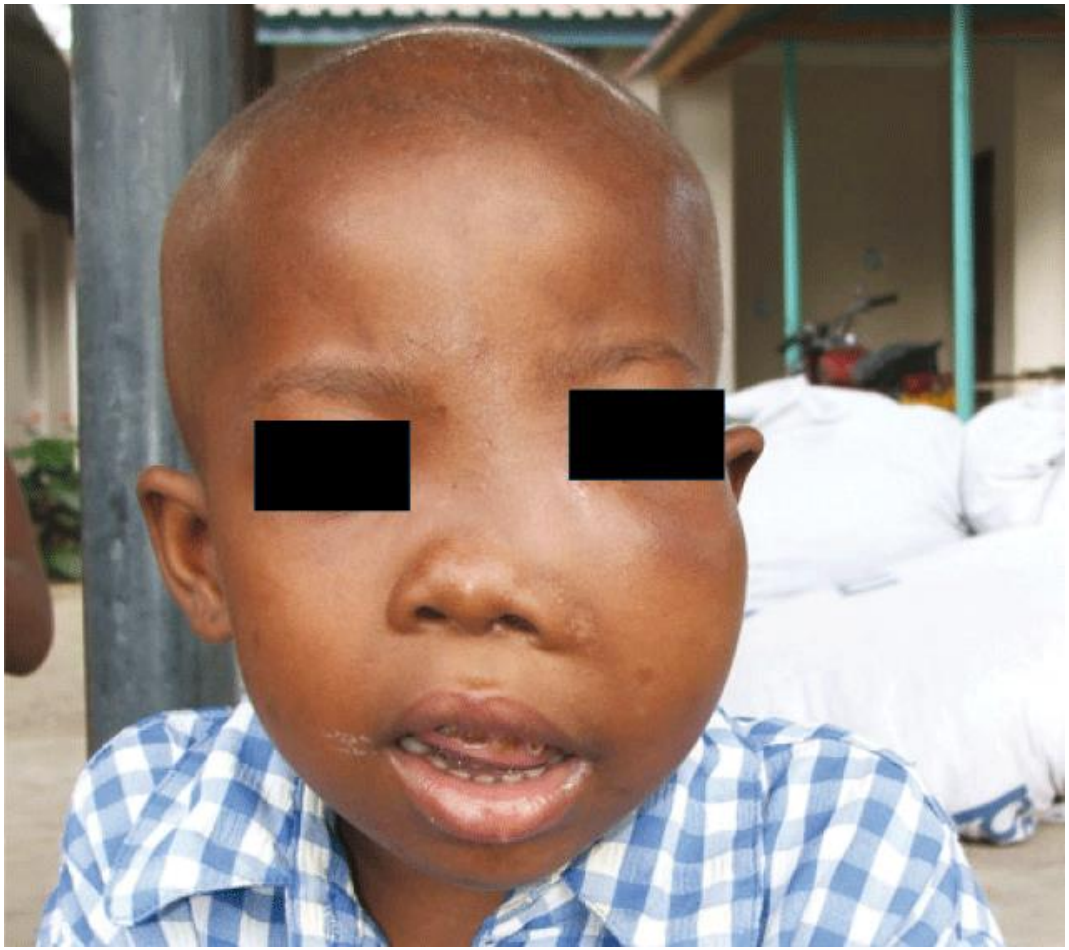
t(2;8)
t(8;22)

MYC activated by Ig gene

The 3 clinical variants

- Endemic
  - Associated with malaria (same geographical distribution)
  - EBV found in all cases
- Sporadic
  - 30-40% childhood NHL
  - 1-2% adult NHL
- Immunodeficiency related
  - Usually HIV+ patients, much less post-transplant
  - Patients have high CD4 cell counts

Endemic variant



Affects the face bones (jaw)

Malaria associated, most frequent children cancer in these areas

EBV + in >90% of cases

Interaction between plasmodium and EBV is probaly causative

Peak age: 6 years

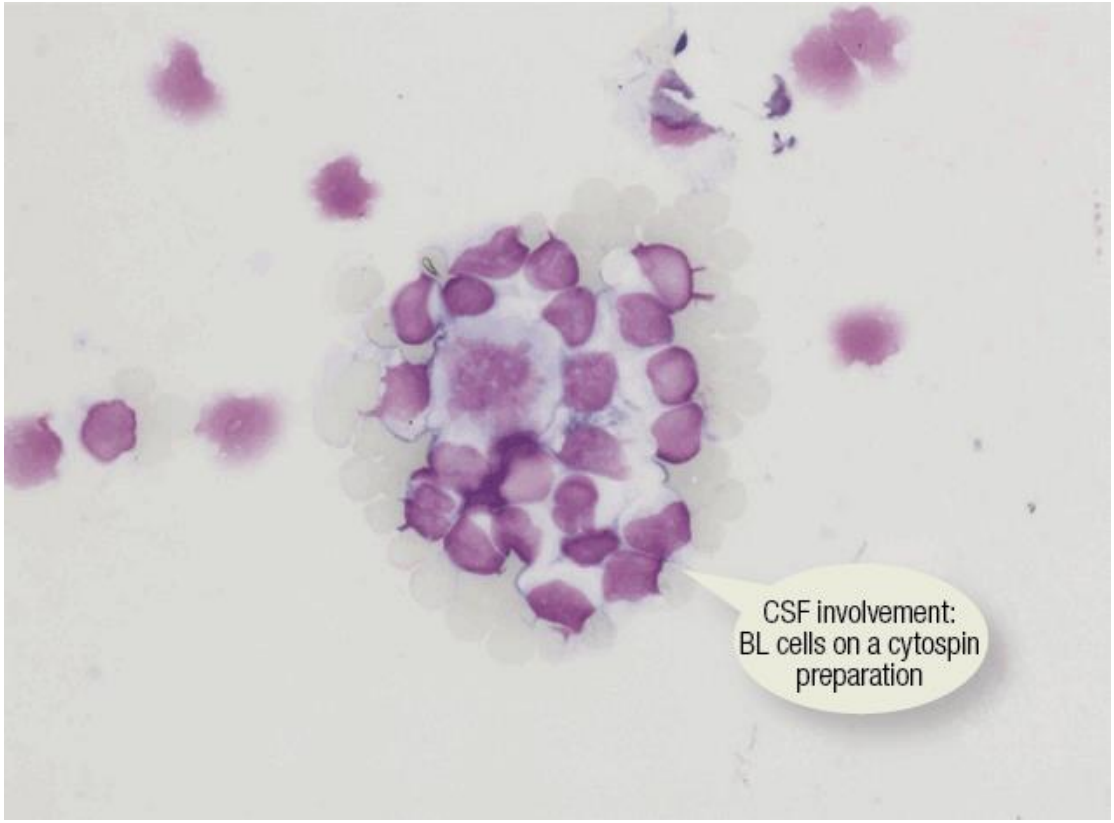
Immunodeficiency related BL

- 30-40% of HIV lymphomas
- Risk proportional to viral load
- Higher incidence when CD4>200

- Treatment same as sporadic BL
- Use G-CSF and antibiotic prophylaxis

Adult sporadic BL

Most commonly involved sites: terminal ileum, caecum, intra-abdominal LN



30% BM involved

15% CNS involved

High-risk of CNS relapse without CNS prophylaxis

Treatment principles

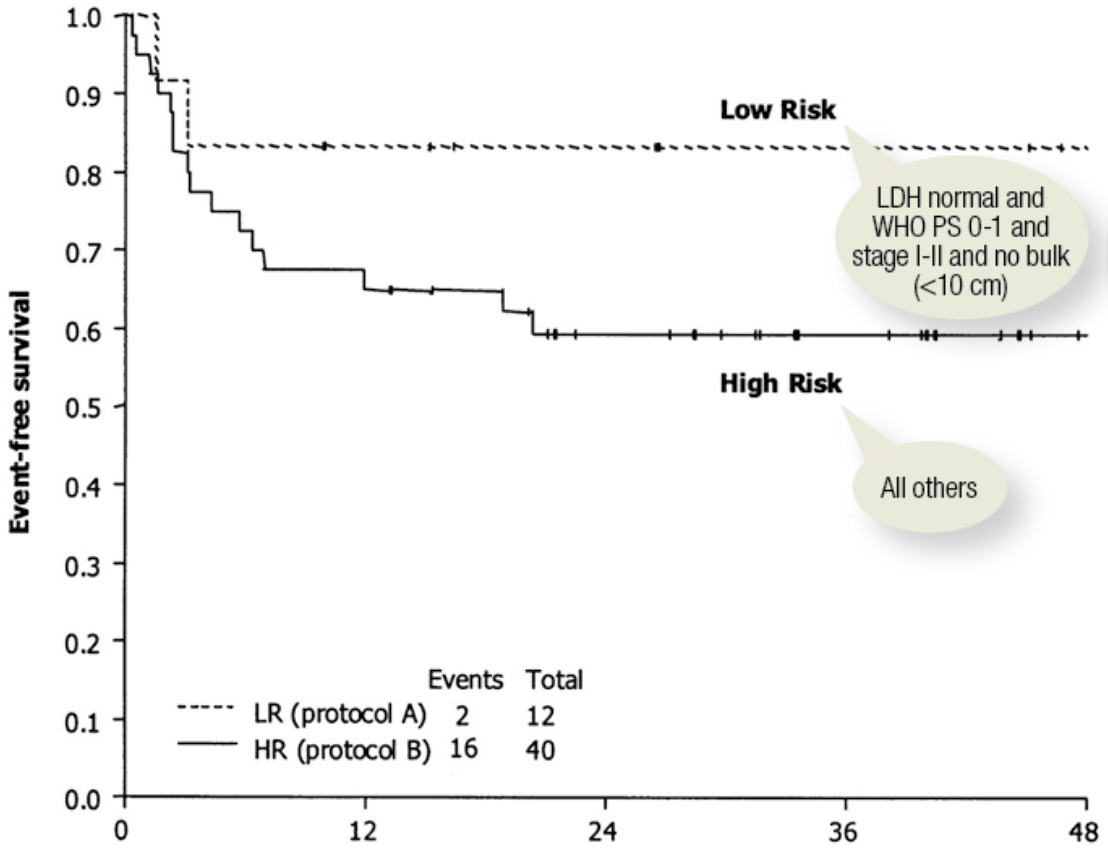
- Start treatment within 48h from diagnosis
- Prevent TLS with hydration and rasburicase
- Keep intervals between cycles as short as possible

  (ANC>1 and Pl >75 x 10^9/L)
- Give CNS prophylaxis
- Fractionate alkylating agents (CTX)

The Magrath regimen

CODOX Cycle 1+3	Cycloph	iv	800 mg/m2 200 mg/m2	D1 D2-5
	VCR	iv	1.5 mg/m2	D1 + D8
	DOX	iv	40 mg/m2	D1
	MTX	iv	3 g/m2	D10 in 24h
	AraC MTX	it it	70 mg 12 mg	D3 D15
IVAC Cycle 2 +4	Etoposide Ifosfamide AraC	iv iv iv	60 mg/m2 1.5 g/m2 2 g/m2 x 2	D1-5 D1-5 D1 + D2
	MTX	it	12 mg	D5

Prognosis according to risk factors



EFS of patients treated according to the Magrath protocoll (CODOX-M / IVAC)

Low risk: CODOX-M x 3

High risk: CODOX-M x 2
IVAC x 2
alternated

Mead et al, Ann Oncol 2002

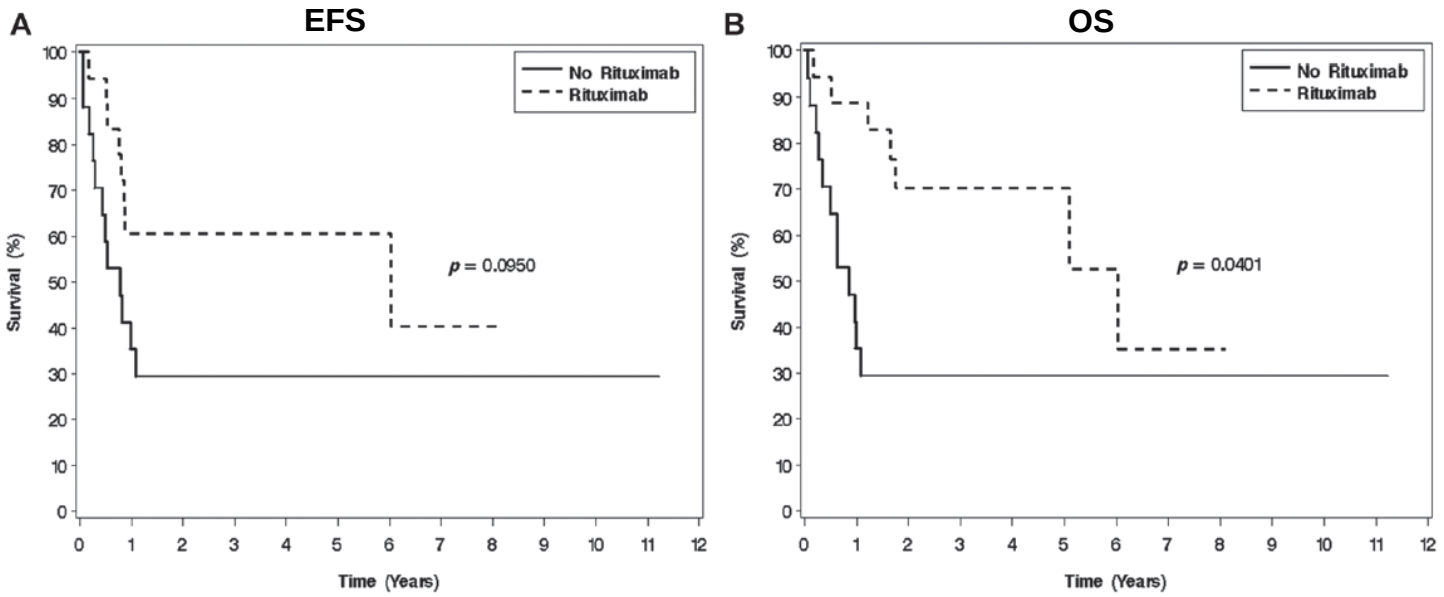
Treatment regimens for BL

Author	Regimen
Mead GM, et al	CODOX-M / IVAC
Rizzieri DA, et al	CALGB 9251
van Imhoff GW, et al	HOVON
Thomas DA, et al	R-Hyper CVAD
Hoelzer D, et al	GMALL
Dunleavy K, et al	DA-EPOCH

The contribution of rituximab

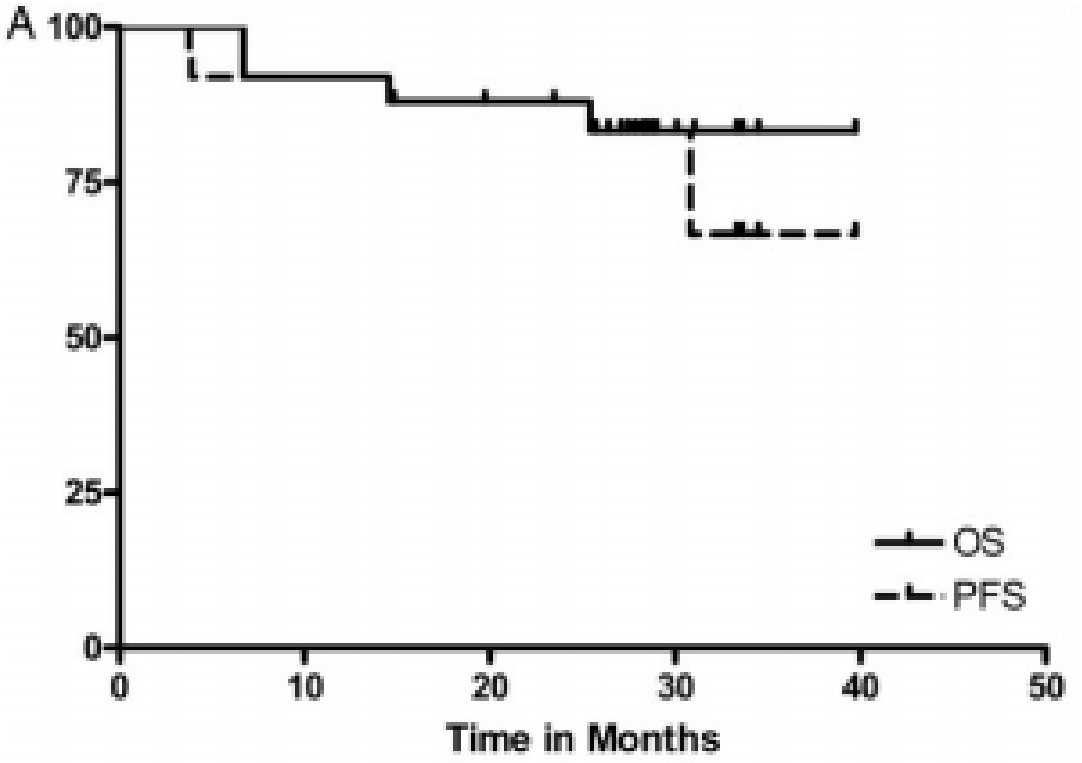
Washington and Wisconsin: 39 cases, half with and half without R

EFS and OS for the entire cohort according whether treatment included rituximab



Wildes TM, et al, Ther Adv hematol 5(1). 2013

Modified Magrath regimen + Rituximab

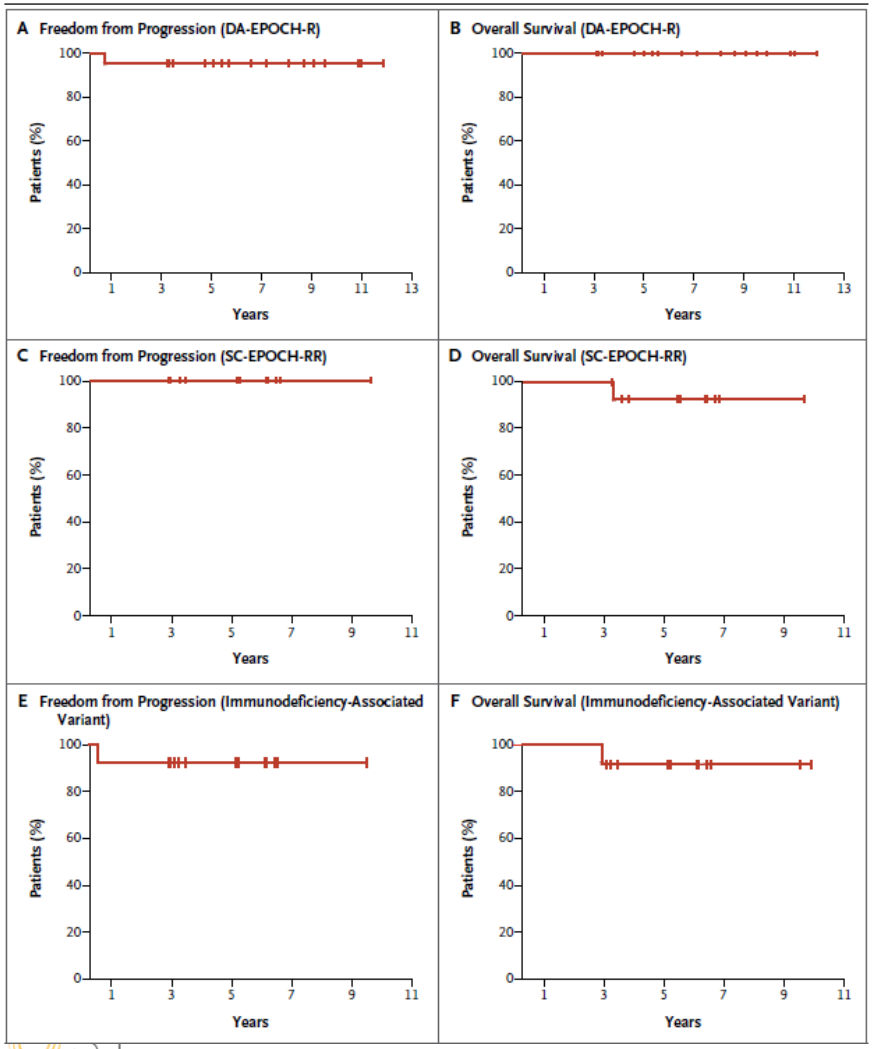


N = 25 BL

5 low risk
20 high risk

Evens et al, Ann Oncol 2013

Surprising data: NCI



DA-EPOCH-R in HIV- patients (n=19)

SC-EPOCH-RR in HIV+ patients (n=11)

It MTX for the 3 cases with CNS+

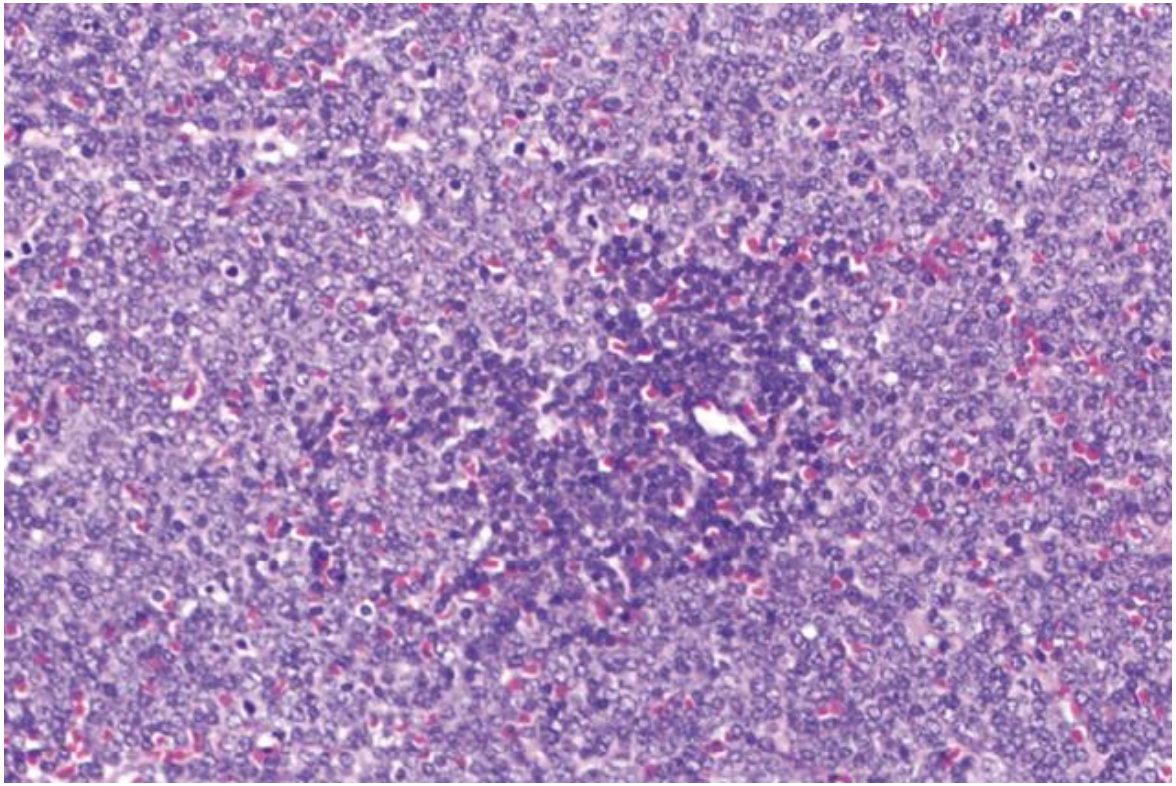
Only 13% BM involvement
Only 3% CNS involvement

Only 1 TLS

Dunleavy et al, NEJM 2013

Lymphoblastic lymphoma

Same disease as lymphoblastic leukemia . LL has enlarged LN and BM < 25% involved



10% are B-LBL
90% are T-LBL

Mainly a disease of Children and young

High risk of CNS infiltration

LL must be treated as ALL

Therapy	Age (range)	CR	5a DFS (range)
Conventional NHL	28-45	58%	26%
Modified NHL	14-22	92%	49%
High-grade NHL	25-34	67%	51%
ALL	22-37	80%	56%

Conclusions

BL and LL are rare very aggressive diseases needing immediate treatment in centres with experience in leukemia treatment