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AGGRESSIVE LYMPHOMAS (NON –HODGKIN'S AND HODGKIN)

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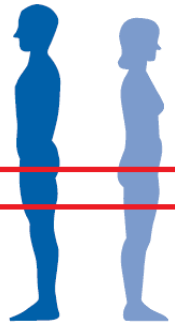
Epidemiology of Lymphomas

Figure 3. Leading Sites of New Cancer Cases and Deaths – 2019 Estimates

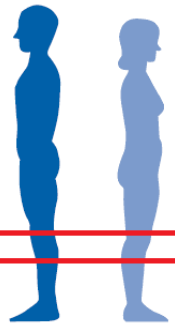
Estimated New Cases

Male			Female		
Prostate	174,650	20%	Breast	268,600	30%
Lung & bronchus	116,440	13%	Lung & bronchus	111,710	13%
Colon & rectum	78,500	9%	Colon & rectum	67,100	7%
Urinary bladder	61,700	7%	Uterine corpus	61,880	7%
Melanoma of the skin	57,220	7%	Melanoma of the skin	39,260	5%
Kidney & renal pelvis	44,120	5%	Thyroid	37,810	4%
Non-Hodgkin lymphoma	41,090	5%	Non-Hodgkin lymphoma	33,110	4%
Oral cavity & pharynx	38,140	4%	Kidney & renal pelvis	29,700	3%
Leukemia	35,920	4%	Pancreas	26,830	3%
Pancreas	29,940	3%	Leukemia	25,860	3%
All sites	**870,970**		**All sites**	**891,480**	



Estimated Deaths

Male			Female		
Lung & bronchus	76,650	24%	Lung & bronchus	66,020	23%
Prostate	31,620	10%	Breast	41,760	15%
Colon & rectum	27,640	9%	Colon & rectum	23,380	8%
Pancreas	23,800	7%	Pancreas	21,950	8%
Liver & intrahepatic bile duct	21,600	7%	Ovary	13,980	5%
Leukemia	13,150	4%	Uterine corpus	12,160	4%
Esophagus	13,020	4%	Liver & intrahepatic bile duct	10,180	4%
Urinary bladder	12,870	4%	Leukemia	9,690	3%
Non-Hodgkin lymphoma	11,510	4%	Non-Hodgkin lymphoma	8,460	3%
Brain & other nervous system	9,910	3%	Brain & other nervous system	7,850	3%
All sites	**321,670**		**All sites**	**285,210**	

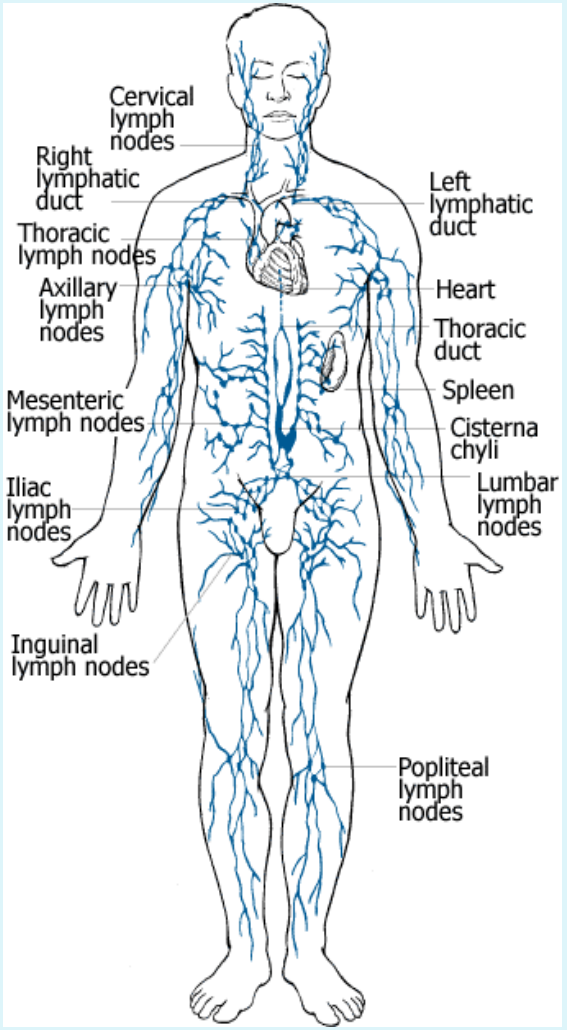


Estimates are rounded to the nearest 10, and cases exclude basal cell and squamous cell skin cancers and in situ carcinoma except urinary bladder. Estimates do not include Puerto Rico or other US territories. Ranking is based on modeled projections and may differ from the most recent observed data.

What is Lymphoma

- Cancer affecting the lymphatic system and usually develops in the lymph nodes and lymphatic tissue.

- Malignant transformation of lymphocyte (clone(s)) in the lymphatic system.



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What causes lymphoma ?

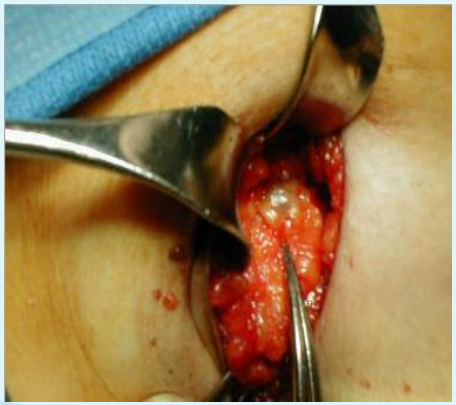
- The cause for malignant transformation is unclear
- Activation of cancer causing genes
- Inactivation of cancer suppressing genes
- Infection by certain virus that are known to cause cancer (HTLV -1, EBV, HHV- 8 etc)
- ? Hereditary causes

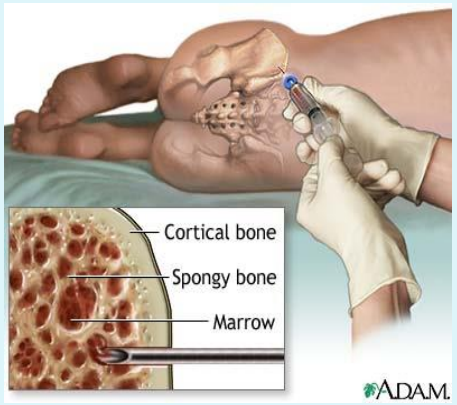
How do lymphoma present

- Currently no screening test exists
- Rapidity of clinical signs and symptoms depends upon the type of lymphoma (days – years)
- Enlarged lymph glands
- B symptoms- fever, weight loss, drenching sweats.
- Abnormal blood counts.
- Shortness of breath (Mass or blood counts)
- Abdominal pain or discomfort and back pain- enlarging liver, spleen and lymph nodes.

How do we diagnose Lymphoma

- Excisional Lymph node biopsy
- Bone marrow biopsy (Biopsy of other sites)





Investigations

- Other tests that influence treatment
- Cardiac testing – ECHO/MUGA
- Kidney and Liver function
- Hepatitis B and HIV testing.
- Pregnancy and fertility preservation.

Types of Lymphomas

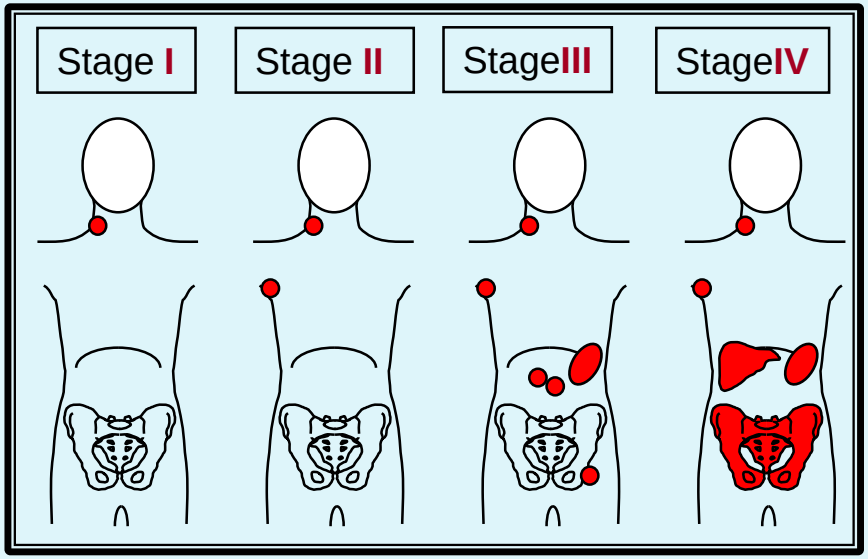
- NonHodgkin Lymphoma (NHL)
  - B- cell
  - T-cell

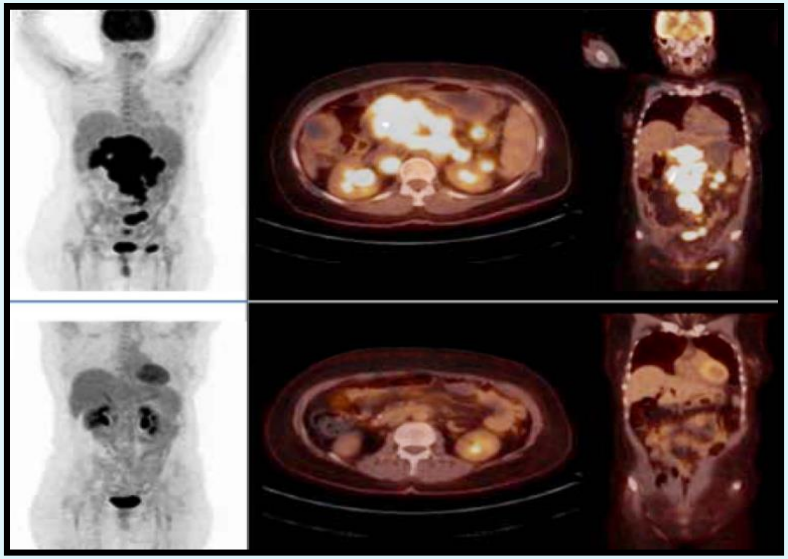
- Hodgkin Lymphoma
  - Classical
  - Non classical

Staging of Lymphoma

- Clinical Staging.

- Imaging Studies (CT Scan or PET scan)





A- Without B symptoms
B- With B symptoms (fever, weight loss, night sweats)

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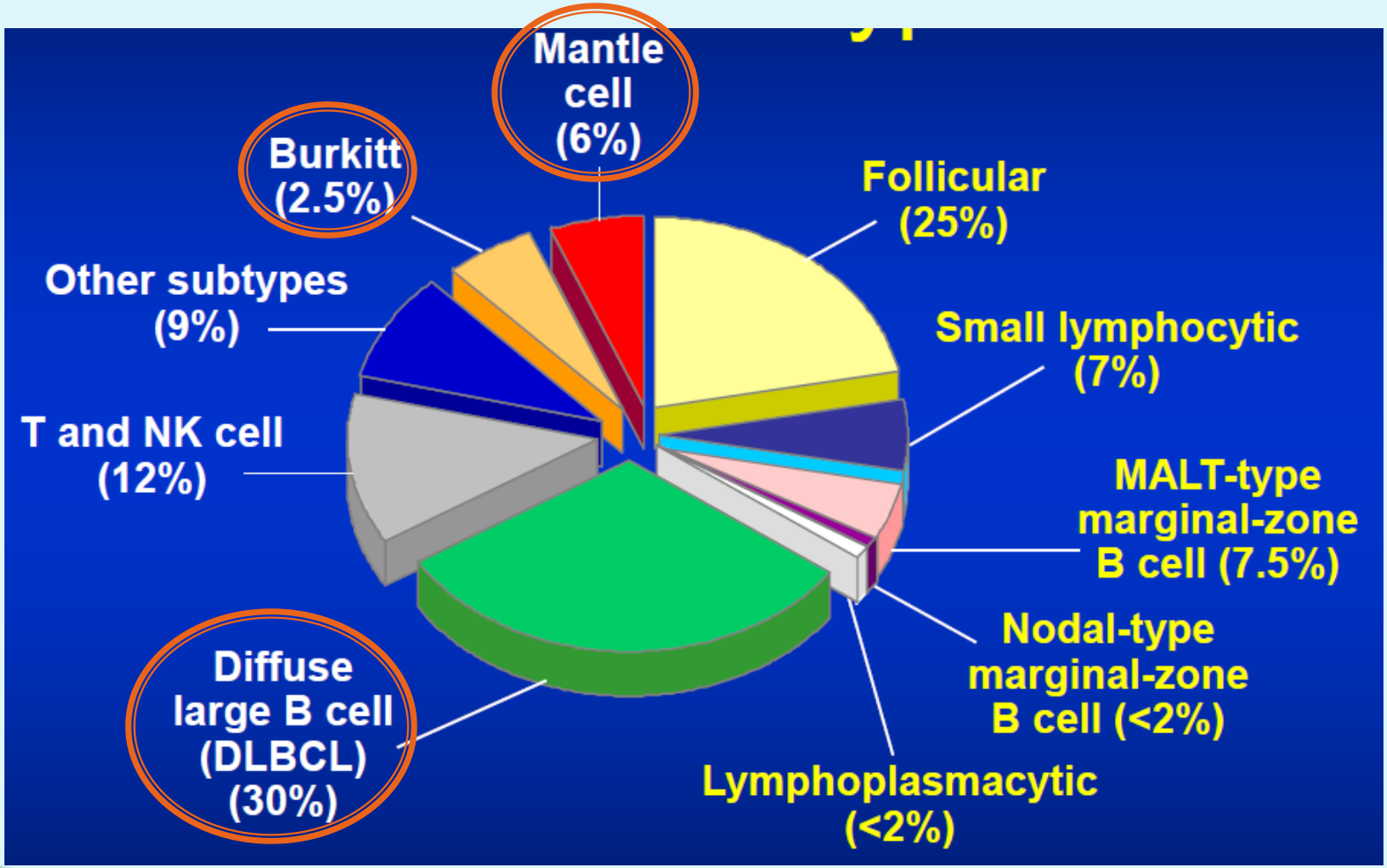
Frequency of common types of NHL



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Lymphomas behave differently

- **Indolent Lymphomas**
  - These lymphomas grow slowly.
  - The majority of NHLs are considered indolent.
  - Indolent lymphomas are generally considered incurable with chemotherapy and/or radiation therapy.

- **Aggressive Lymphomas**
  - These lymphomas have a rapid growth pattern.
  - This is the second most common form of NHL
  - Generally curable with chemotherapy.

- **Very Aggressive**
  - These lymphomas grow very rapidly.
  - They account for a small proportion of NHLs
  - Can be treated with chemotherapy.
  - Unless treated rapidly, these lymphomas can be life threatening.

Aggressive B Cell Lymphoma

- Follicular Lymphoma (Grade III)
- Diffuse Large B cell Lymphoma

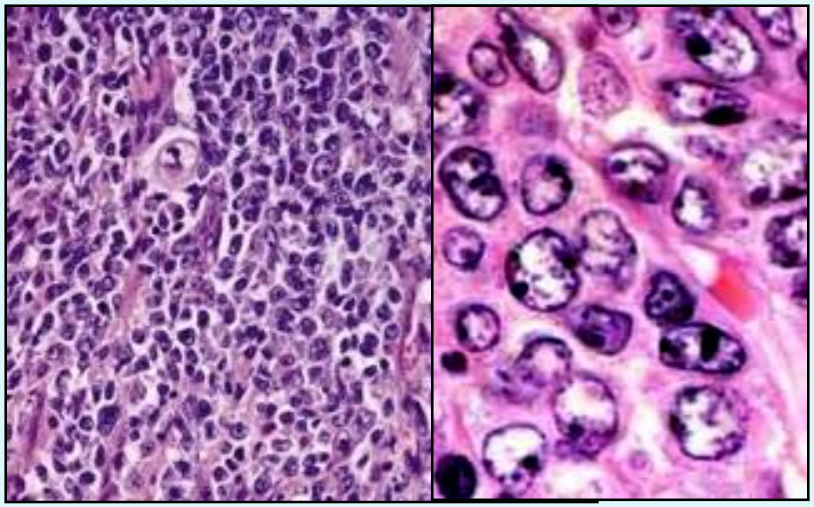
- Mantle cell Lymphoma

- Burkitt's lymphoma

DLBCL (Diffuse Large B Cell Lymphoma)

- Most common type of NHL (25 %- 30%)

- DLBCL is a neoplasm of large B lymphoid cells with nuclear size equal to or exceeding normal macrophage nuclei that has a diffuse growth pattern



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Diffuse Large B cell Lymphoma (DLBCL)

- DLBCL is the most common lymphoma and accounts for approximately 30 % of all NHLs in the developed world
- Median onset at about 6th decade of life and more common in men.
- Majority present with rapidly enlarging symptomatic mass with B symptoms.
- May involve extranodal organs such as bone marrow, stomach, CNS, testis and skin.
- Curable in majority of cases.
- Median survival in weeks to months if not treated.

Over the course of years things have changed

- Not all DLBCL are the same.
- Certain DLBCL had more aggressive course.
- Lower response rate response to chemotherapy.
- Impact survival. (adjusted to stage and clinical risk)
- Need for a better risk stratification ….

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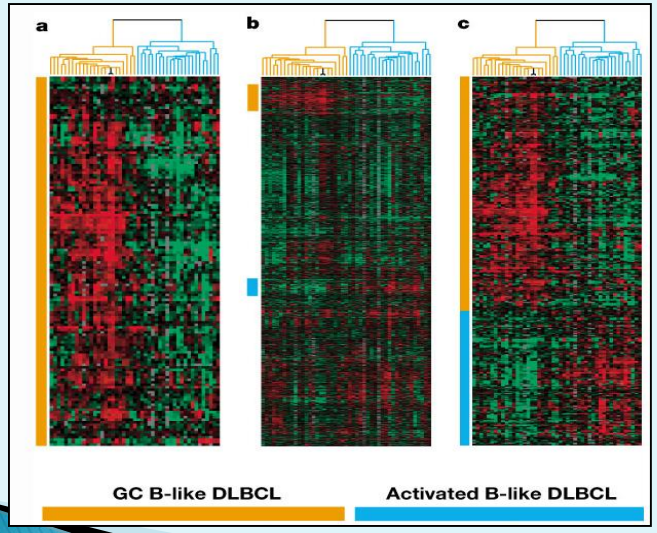
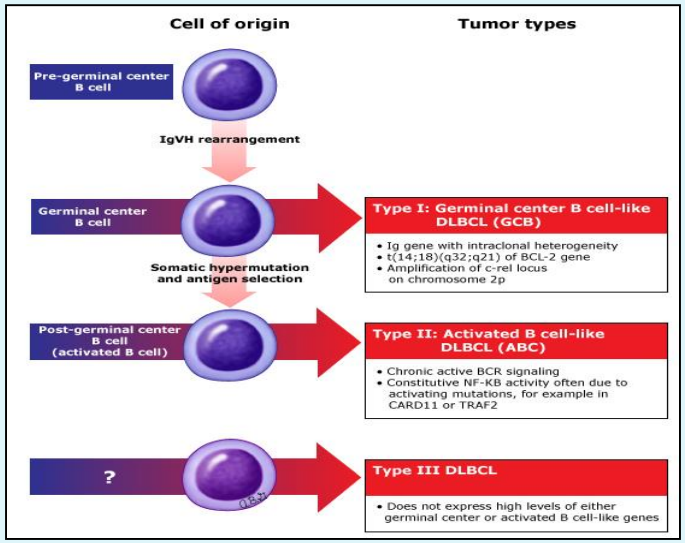
Advances in diagnostic testing

- Not all DLBCL are the same.
- Importance of cell of origin (COO)
- 3 distinct subtypes (Gene expression Profile)
  - Germinal center subtype (GCB)
  - Activated B cell subtype (ABC)
  - Unclassified (?)





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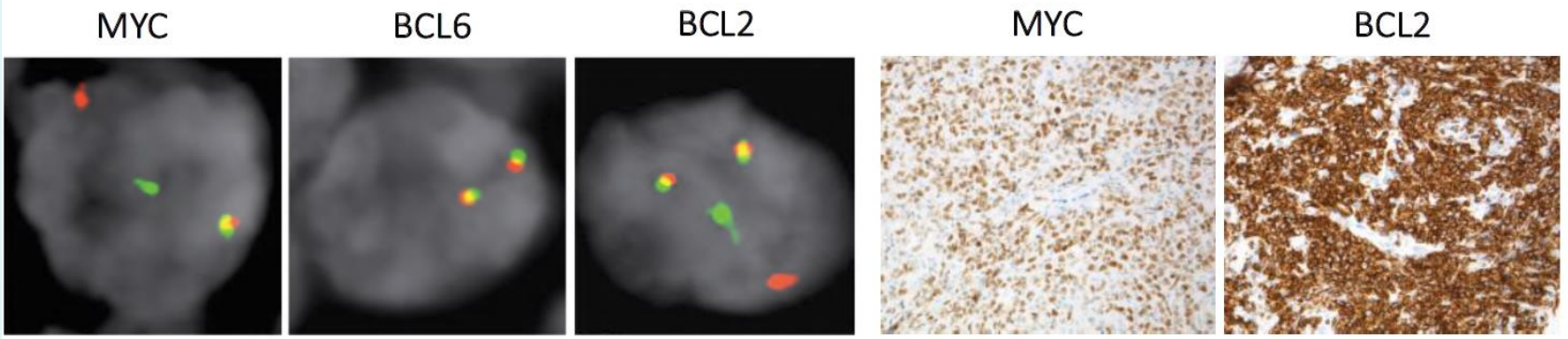
Double Hit (Expressor) DLBCL
Triple Hit (Expressor) DLBCL



- **DHL:** Detected by FISH, co-rearrangement is non-IgH in DLBCL with most common type BCL2, prognosis depended upon co-translocation
- **DEL/DPL:** Upregulated MYC expression can be from rearrangement, copy number gain or mutation within gene sequence
- MYC/BCL2 effect seems to cut across cell of origin

Green TM et al. J Clin Oncol. 2012 Oct 1;30(28):3460-7

Choosing treatment in DLBCL

- Cell of origin- now plays an important role
- Many algorithms are available to identify the cell of origin.
- Activated B cell origin, Double hit or triple hit lymphoma – tend to be more aggressive and hence would consider using more intense chemotherapy regimen.
- Emphasis on gene rearrangement or protein expression to diagnose double hit or double expresser DLBCL.

How do we treat Diffuse Large B cell Lymphoma

- Apart from biopsy- Surgery has no role in treatment.
- Combination chemotherapy + Immunotherapy (rituximab)
- With or without Radiation.
- Most commonly used regimen- R-CHOP
- (R- rituximab, C- Cyclophosphamide, H- Doxorubicin, O- Onco-vincristine, P- Prednisone)
- R+CHOP with additional drugs such as revlimid or etoposide
- Administered every 3 weeks for 6 cycles.

Management based on Cell of Origin

- Germinal center B cell subtype (GCB)
- R (rituximab) –CHOP (**C**ytoxan/**A**driamycin/**O**ncovincristine/**P**rednisone)

- Activated B cell subtype (ABC)/ DEL and DHT DLBCL
- R-CHOP (may still be an option)
- Revlimid + R-CHOP
- Intense chemotherapy regimens (EPOCH -R)

- Few patients based on risk stratification maybe recommended chemotherapy into spinal fluid to prevent disease in the central nervous system.

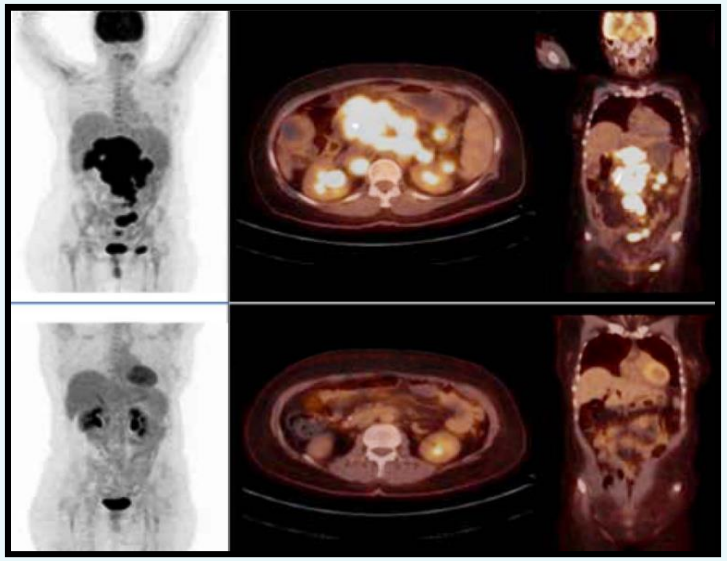
Based on stage of the disease

- Localized stage I/II disease:
  - Abbreviated course of chemotherapy with immunotherapy (rituximab)followed by radiation.
  - Or a full course of chemotherapy

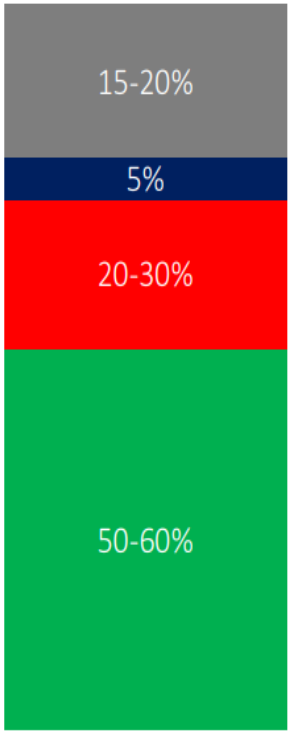
- Advanced-stage disease:
  - Chemotherapy in combination with immunotherapy (rituximab).

How do we follow patients after treatment

- After chemo-immunotherapy- PET CT, blood work and clinical exam – to confirm remission
- Once confirmed- there is no role for repeat PET CT unless there are new clinical symptoms
- Maintenance therapy with rituximab has no benefit.
- Lab work and clinical exam every 3 months for first year and then every 3- 6 months for the second year and annually after 3 years.



What Happens After First line Chemotherapy



Refractory to any chemotherapy

Partial Response

Relapse

CR and Cured with R-CHOP or 1st line immuno-chemotherapy

Generally people who respond quickly and achieve complete remission (CR) will have long term disease free survival

Patient who relapse late will do reasonably good.

Patients who have partial response (PR) or are refractory to chemotherapy- generally respond poorly to additional treatment.

Relapse disease

- Despite high rate of cure after treatment.
- About 30-40 % of patients do suffer from relapse
- Majority of them in the first year.
- Few after 3 years
- Most of the time relapse are symptomatic.
- Many of these patients will remain sensitive and will respond to second line of chemotherapy.

Treatment of relapsed disease

- Disease has to be confirmed with a biopsy.

- Treatment would be based on
  - Patients medical and physical status.
  - Time to relapse from initial therapy.
  - Initial chemotherapy regimen used.
  - Ability to undergo cellular therapy
    - CAR-T therapy
    - Autologous transplant (individuals own stem cells)
    - Allogeneic transplant (cells from a different individual of same species)

Treatment in the relapse (refractory) setting

- Generally Autologous transplant is preferred at first relapse.
  (Approach is changing with emergence of CAR-T)
- Abbreviated course of chemotherapy is administered.
- Response is assessed usually after 2 or 3 cycles.
- If in complete remission- then Autologous transplant is offered.
- If response is partial then further chemotherapy is administered and CAR-T or allogeneic transplant may be considered.
- Transplant (Auto/Allo) is generally not considered if complete response is not achieved.

Treatment options for DLBCL in relapsed setting

National Comprehensive Cancer Network®

NCCN Guidelines Version 4.2020
Diffuse Large B-Cell Lymphoma

NCCN Guidelines Index
Table of Contents
Discussion

SUGGESTED TREATMENT REGIMENS[a,b]

An FDA-approved biosimilar is an appropriate substitute for rituximab.

Second-line and Subsequent Therapy[d,i,j] (intention to proceed to transplant)
- **Preferred regimens (in alphabetical order)**
  - **DHAP (dexamethasone, cisplatin, cytarabine) ± rituximab**
  - **DHAX (dexamethasone, cytarabine, oxaliplatin) ± rituximab**
  - **GDP (gemcitabine, dexamethasone, cisplatin) ± rituximab or (gemcitabine, dexamethasone, carboplatin) ± rituximab**
  - **ICE (ifosfamide, carboplatin, etoposide) ± rituximab**
- **Other recommended regimens (in alphabetical order)**
  - **ESHAP (etoposide, methylprednisolone, cytarabine, cisplatin) ± rituximab**
  - **GemOx (gemcitabine, oxaliplatin) ± rituximab**
  - **MINE (mesna, ifosfamide, mitoxantrone, etoposide) ± rituximab**

Anti-CD19 CAR T-cell therapy[n,o]
- **Axicabtagene ciloleucel**
- **Tisagenlecleucel**

See First-line Therapy on BCEL-C 1 of 4.

Consider prophylaxis for tumor lysis syndrome (See NHODG-B)
See monoclonal antibody and viral reactivation (NHODG-B)

Second-line and Subsequent Therapy[d,i,j] (non-candidates for transplant)
- **Preferred regimens (in alphabetical order)**
  - **GemOx ± rituximab**
  - **Polatuzumab vedotin ± bendamustine ± rituximab (after ≥2 prior therapies)[k,l]**
- **Other recommended regimens (in alphabetical order)**
  - **CEPP (cyclophosphamide, etoposide, prednisone, procarbazine) ± rituximab - PO and IV**
  - **CEOP (cyclophosphamide, etoposide, vincristine, prednisone) ± rituximab**
  - **DA-EPOCH ± rituximab**
  - **GDP ± rituximab or (gemcitabine, dexamethasone, carboplatin) ± rituximab**
  - **Gemcitabine, vinorelbine ± rituximab (category 3)**
  - **Rituximab**
  - **Tafasitamab[p] + lenalidomide**
- **Useful in certain circumstances**
  - **Brentuximab vedotin for CD30+ disease**
  - **Bendamustine[k] ± rituximab (category 2B)**
  - **Ibrutinib[m] (non-GCB DLBCL)**
  - **Lenalidomide ± rituximab (non-GCB DLBCL)**

Third-line and Subsequent Therapy (including patients with disease progression after transplant or CAR T-cell therapy)
- **Selinexor (only after at least two lines of systemic therapy)[q]**

[a] See references for regimens BCEL-C 3 of 4 and BCEL-C 4 of 4.
[b] Rituximab and hyaluronidase human injection for subcutaneous use may be substituted for rituximab after patients have received the first full dose of rituximab by intravenous infusion. This substitution cannot be made for rituximab used in combination with ibritumomab tiuxetan.
[d] Inclusion of any anthracycline or anthracenedione in patients with impaired cardiac functioning should have more frequent cardiac monitoring.
[i] If additional anthracycline is administered after a full course of therapy, careful cardiac monitoring is essential. Dexrazoxane may be added as a cardioprotectant.
[j] Rituximab should be included in second-line therapy if there is relapse after a reasonable remission (>6 mo); however; rituximab should often be omitted in patients with primary refractory disease.
[k] In patients intended to receive CAR T-cell therapy, bendamustine should be used with caution unless immediately prior to CAR T-cell therapy, since it could impact the success of the patient's T-cell collection.
[l] Bendamustine, rituximab, and polatuzumab vedotin-piiq is indicated for the treatment of adult patients with relapsed or refractory DLBCL and HGBL with translocations of *MYC* and *BCL2* and/or *BCL6* after ≥2 prior therapies.
[m] See Special Considerations for Use of Small-Molecule Inhibitors (NHODG-E).
[n] See Guidance for Treatment of Patients with Chimeric Antigen Receptor (CAR) T-Cell Therapy (BCEL-D).
[o] Tisagenlecleucel is not FDA-approved for relapsed/refractory primary mediastinal large B-cell lymphoma.
[p] It is unclear if tafasitamab will have a negative impact on the efficacy of subsequent anti-CD19 CAR T-cell therapy.
[q] Selinexor is FDA approved only for DLBCL and transformed DLBCL arising from FL

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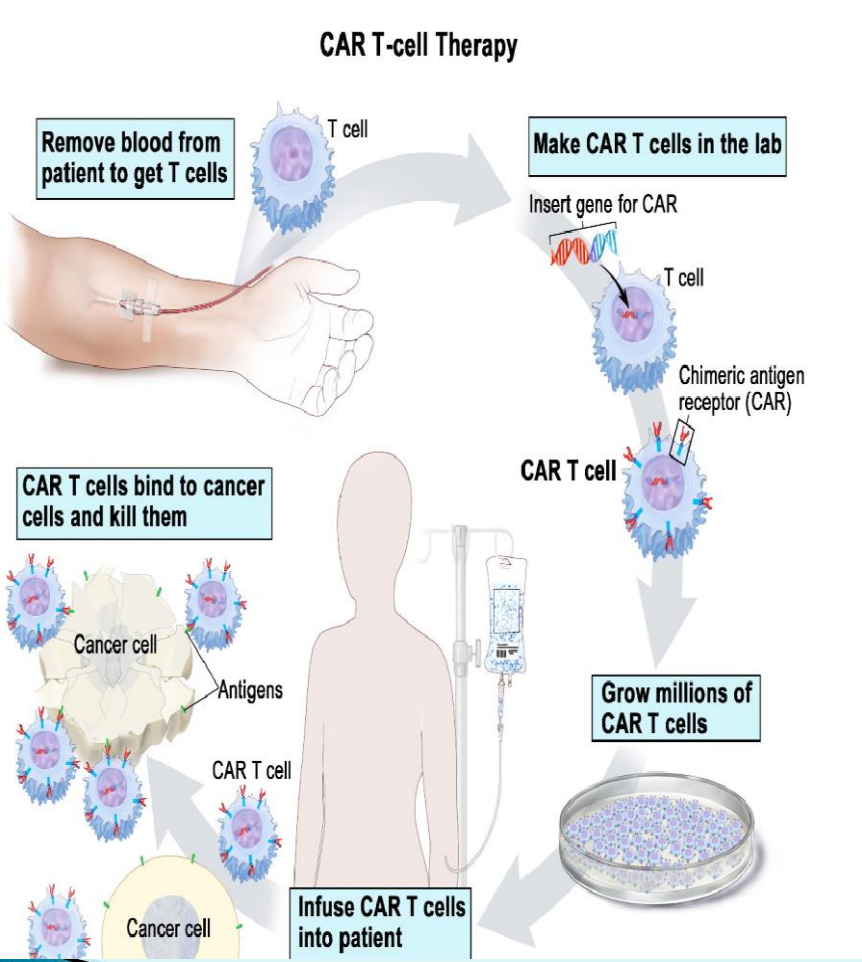
CAR-T Therapy for DLBCL



- Previously treatment options for patients with relapsed/refractory disease was limited
- CAR-T has changed the treatment landscape in this subset of patients.
- Majority of previously incurable patients can now be cured with this technique.
- Newer CAR-T products are in the pipeline with increased efficacy and decreased toxicity

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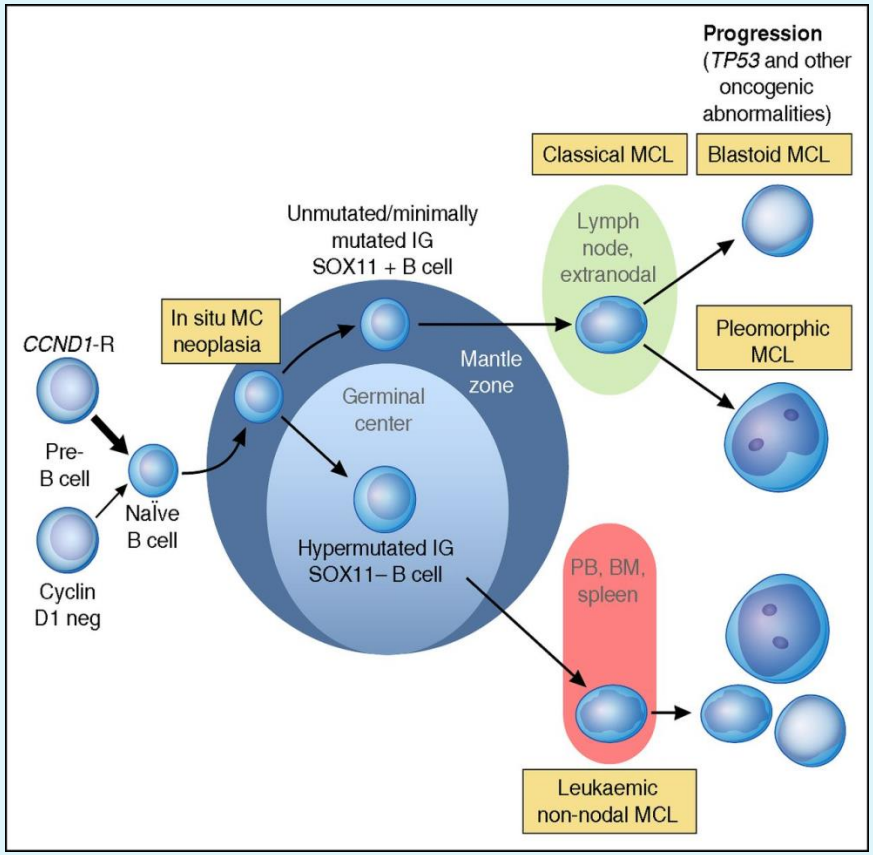
Pushing the boundaries

- Newer FDA approved drugs like Polatuzumab, tafacitamab and selinexor have further expanded the treatment options
- Many more drugs are in the pipeline
- Clinical trials

MANTLE CELL LYMPHOMA (MCL)

Mantle cell Lymphoma

- 5% to 10% of all NHL
- ≈ 0.5/100,000 per yr
- Advanced age at presentation
  - Median age: 65–70 yrs
- Male predominance
  - Male:female ratio 2–3:1



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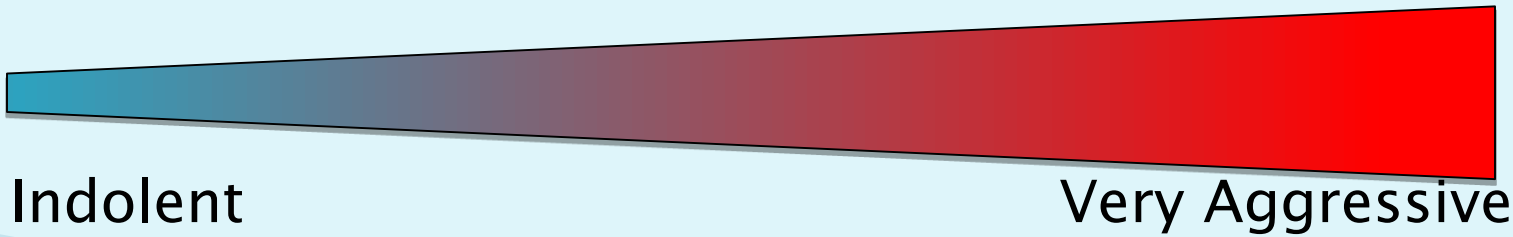
Clinical Presentation

- Advanced disease
  - 70% stage IV
  - 30% localized
- B symptoms ≈ 50% (fever, night sweats, weight loss)
- Involved sites
- Lymph nodes (70% to 90% generalized)
  - Spleen
  - Waldeyer's ring (palatine/lingual tonsil)
  - Bone marrow (60% to 80%)
  - Blood (up to 50%)
  - Extranodal
    - Gastrointestinal
    - CNS (4% to 20% in relapsed disease, especially blastoid)

Clinical Presentation

- Aggressive course
  - Historically, low rates of CR with standard therapy
  - Survival in some patients can be compromised
  - Some patients can be long-term survivors

- Indolent course
  - Variable clinical course
  - May be observed without treatment for quite some time



Treatment of MCL

First-line Treatment Options

Aggressive Chemotherapy
R-DHAP (or oxaliplatin)
R-CHOP/R-DHAP
NORDIC (maxi-CHOP/R+HD cytarabine)
HyperCVAD + Rituximab

Maintenance
HDT + ASCT → Rituximab maint for 3 yrs

Less Aggressive Chemotherapy
Bendamustine +Rituximab
VR-CAP
R-CHOP
Lenalidomide + Rituximab

Maintenance
After R-CHOP: Rituximab maint until PD

Second-line Treatment Options

Ibrutinib
Acalabrutinib
Zanubrutinib
Lenalidomide + R
Venetoclax

Brexicabtagene Autoleucel
Bortezomib ± R
Alternative chemoimmunotherapy
(particularly if durable initial response)

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B cell receptor signaling pathway

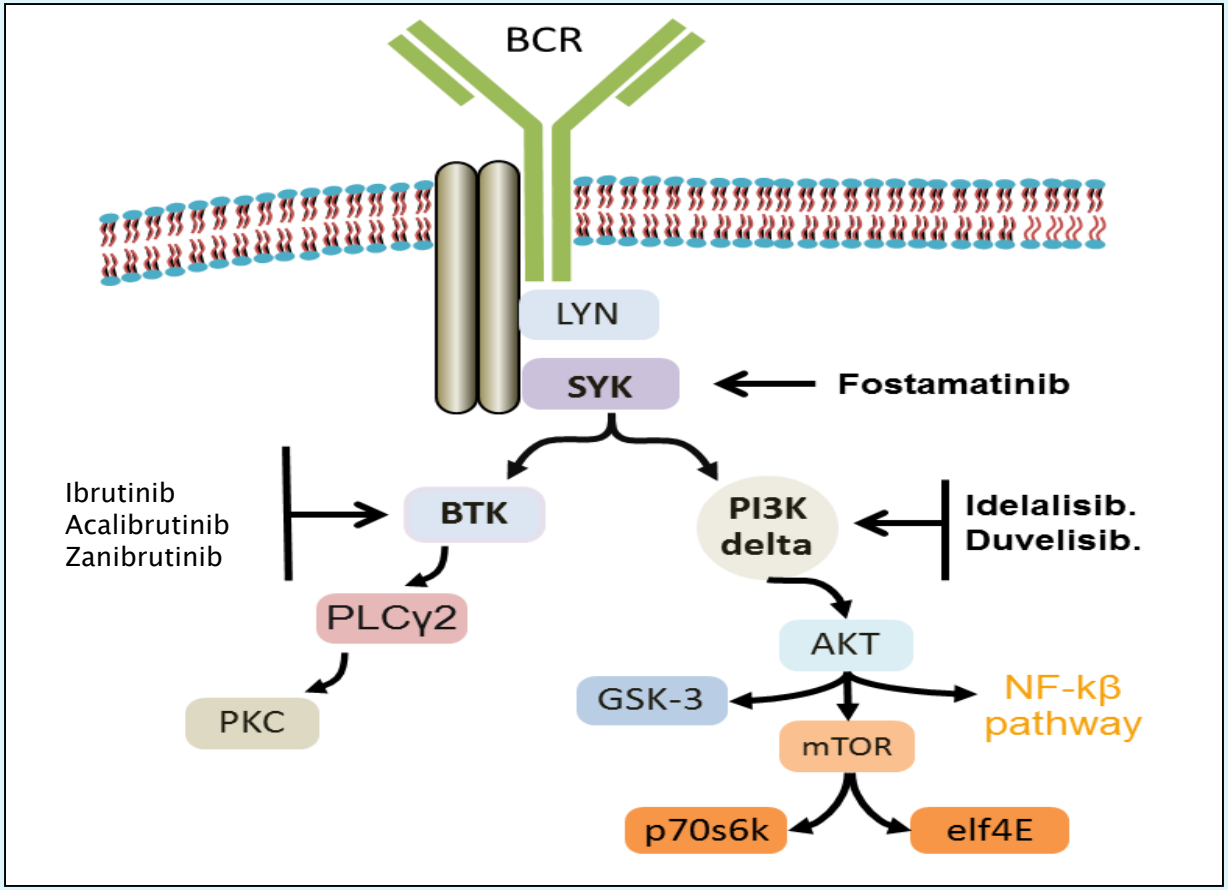

Figure 1. BCR signaling pathway and site of inhibition by new targeting agents in B-cell NHL. *BCR, B-cell antigen receptor; BTK, Bruton's tyrosine kinase; GSK-3, glycogen synthase kinase 3; mTOR, mammalian target of rapamycin; NF-kβ, nuclear factor kappa-light-chain-enhancer of activated B cells; PI3K, phosphatidylinositide 3-kinases; PKC, protein kinase C; PLC, phospholipase C; Syk, spleen tyrosine kinase.*

(Adapted with modification from Davis et al. *Nature 2010;463:88-92)*

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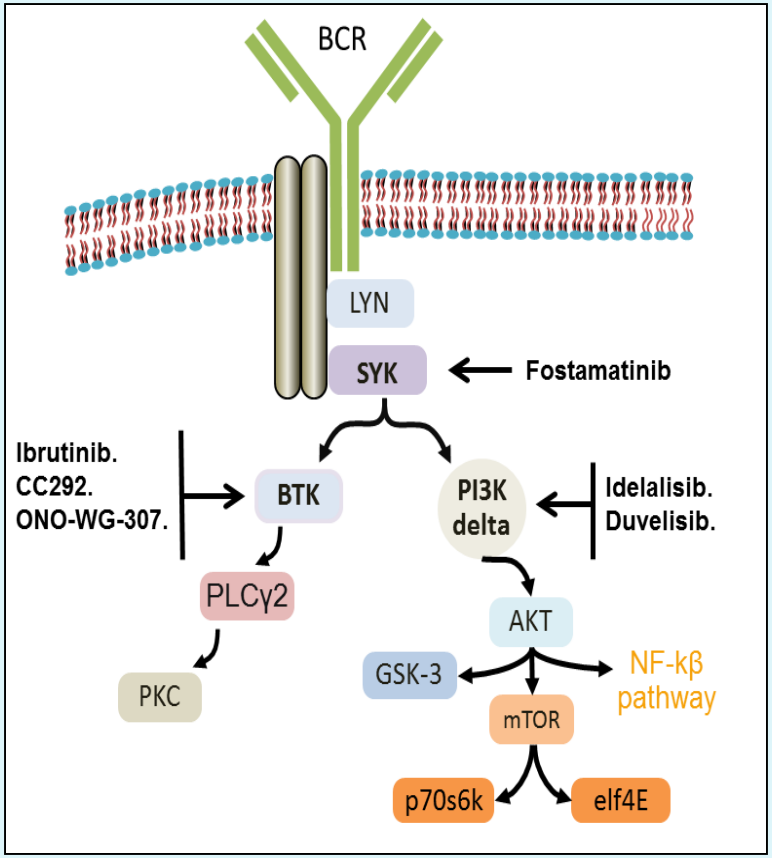
B- Cell Receptor (BCR) pathway



- Signals originating from BCR engages downstream pathways and promotes development, expansion and survival of normal B cells
- These same pathways are used by malignant B cells to drive proliferation, growth and survival in an uncontrolled manner.
- Blocking these signals with new medications (small molecule tyrosine kinase inhibitors)- have changed the treatment landscape of B – Cell NHL.

Figure 1. BCR signaling pathway and site of inhibition by new targeting agents in B-cell NHL. *BCR, B-cell antigen receptor; BTK, Bruton's tyrosine kinase; GSK-3, glycogen synthase kinase 3; mTOR, mammalian target of rapamycin; NF-kβ, nuclear factor kappa-light-chain-enhancer of activated B cells; PI3K, phosphatidylinositide 3-kinases; PKC, protein kinase C; PLC, phospholipase C; Syk, spleen tyrosine kinase.*

(Adapted with modification from Davis et al. *Nature 2010;463:88-92)*

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Treatment of relapsed refractory Mantle cell lymphoma

- Understanding of B cell receptor pathway has paved way for many new treatment options.
- **BTK pathway inhibitors**- Ibrutinib, acalibrutinib, zanibrutinib
- **BCL2 inhibitor** – venetoclax
- Most of them are oral- making it convenient for use.
- Generally well tolerated, minimal toxicity.
- Overall Response rate 70-80% for most of these drugs

BURKITTS LYMPHOMA

Burkitts Lymphoma

- Highly aggressive B cell lymphoma
- Characterized by alteration (translocation and dysregulation) in gene called c-myc on chromosome 8.
- Three distinct forms endemic (African), sporadic (non-endemic) and immune deficiency associated.
- Despite epidemiological and genetic differences, they have similar clinical features and histopathological findings.

Burkitt Lymphoma (BL)

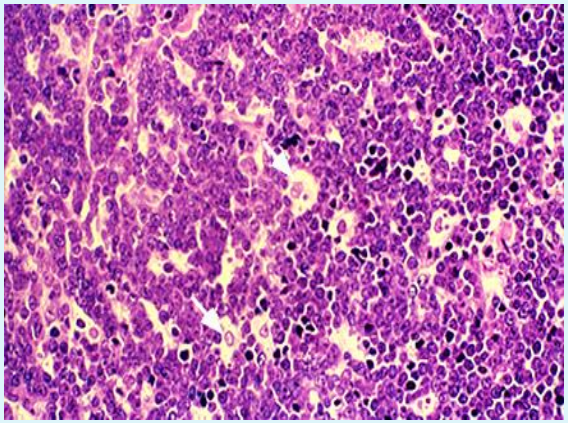
- Fastest growing tumor (doubling time in hours)
- In US- Mainly sporadic type and related immunodeficiency (HIV and following organ transplant)
- Accounts for <1% of all NHL.
- Despite novel anti HIV treatment- incidence of Burkitt Lymphoma has not significantly decreased

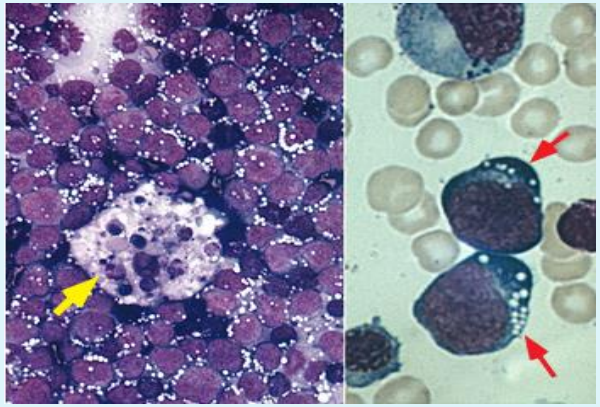
Burkitt Lymphoma- Clinical Symptoms

- Rapidly growing tumor masses.
- B symptoms- weight loss, fever, excessive sweating.
- Usually involves bone marrow and other extranodal sites.
- Tumor lysis syndrome (Abnormal electrolytes and kidney injury)

Diagnosis

- Biopsy and genetic testing of tumor cells.
- Lab work to monitor for tumor lysis syndrome





Treatment of Burkitt Lymphoma

- Bone marrow biopsy is recommended for all patients.
- Lumbar puncture and treatment of CNS is recommended for all patients.
- If unknown HIV testing should be performed.
- Young patients should be offered fertility preservation (Limited option given the need for rapid treatment)
- Hydration and monitoring and correction of electrolytes and kidney function is of high importance.
- High cure rates (>90%)

Treatment of BL

- Intensive multiagent chemotherapy is recommended along with CNS prophylaxis.
- Regimen such as CHOP is not recommended- resulted in high rate of relapse.
- Commonly used regimens
  - **EPOCH + Rituximab**
  - **Hyper CVAD + Rituximab**
  - CODOX plus IVAC with rituximab
  - CALGB 9251 regimen + Rituximab

Outcomes with use of Intensive chemotherapy

Treatment Outcomes: Dose-Intensive Regimens

Investigators	Regimen	EFS (%)	CR (%)	OS (%)
Moleti[a]	CODOX-M/IVAC (NCI/Magrath protocols)	80	91	83
NCI[b]	DA-EPOCH+R	93	100	100
M.D. Anderson[c]	R-HyperCVAD	80	87	65

a. Moleti ML, et al. *Leuk Lymphoma*. 2007;48:551-559.
b. Dunleavy K, et al. *J Clin Oncol (Meeting Abstracts)*. 2007;25:Abstract 8035.
c. Fayad L, et al. *Clin Lymphoma Myeloma*. 2007;8Supp2:S57-S62.

Hodgkins Lymphoma

HODGKINS LYMPHOMA

Dr Thomas Hodgkins
Described HL in 1832

Lymphoid malignancy whose hallmark is the Reed-Sternberg Cell

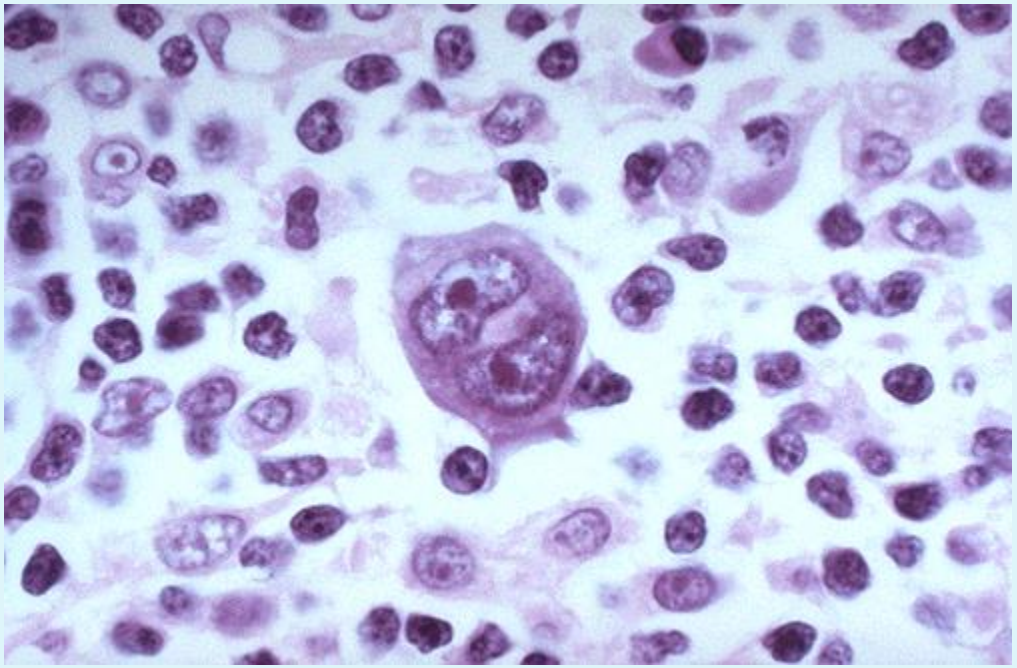
Clinical behavior ranges from being indolent to rapidly progressive

Curable in majority of cases

WHO CLASSIFICATION

- Classical Hodgkin lymphoma
  - Nodular sclerosis
  - Mixed cellularity
  - Lymphocyte-rich
  - Lymphocyte-depleted
- Nodular lymphocyte predominant Hodgkin's lymphoma

REED-STERNBERG CELL



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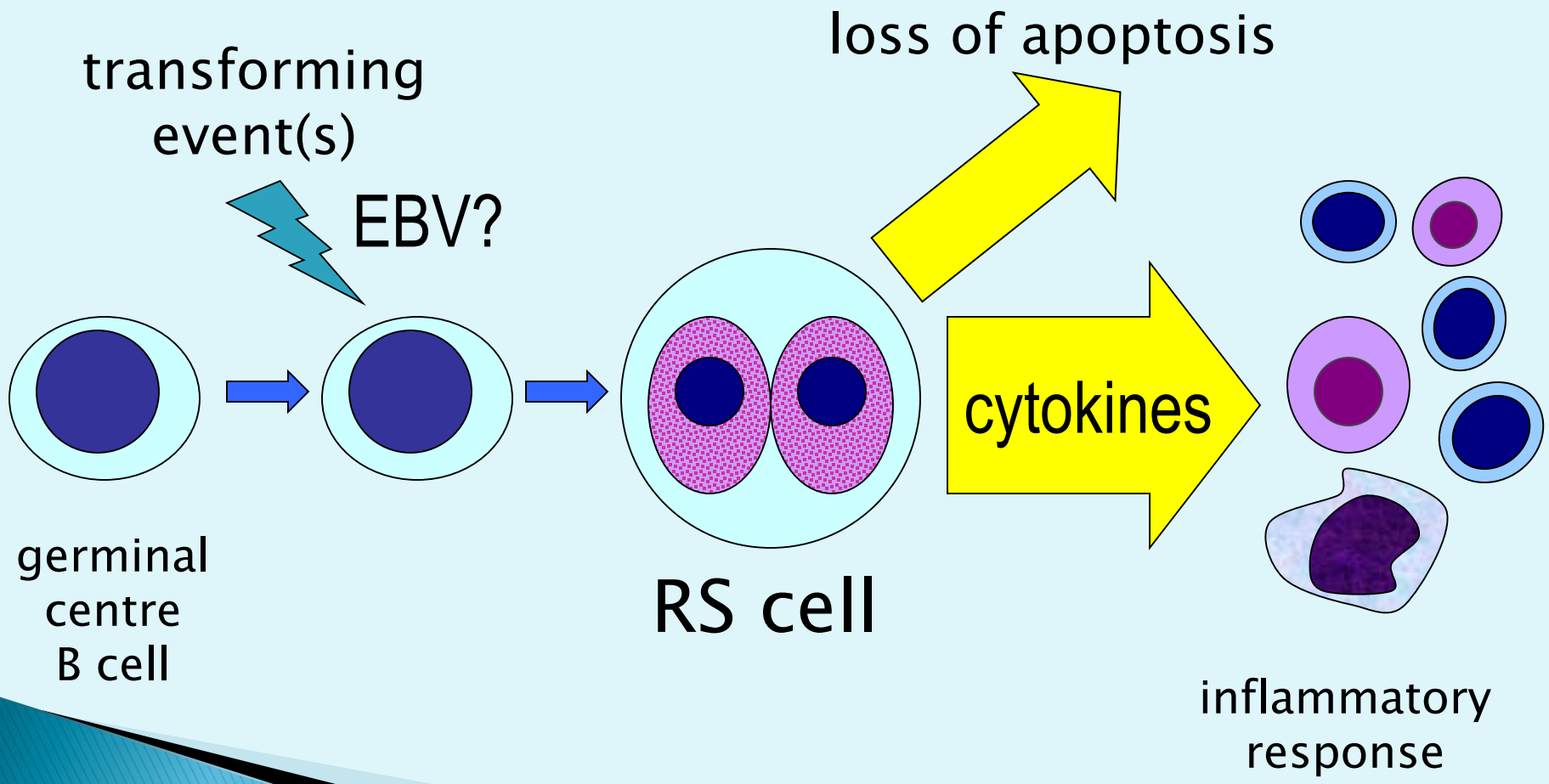
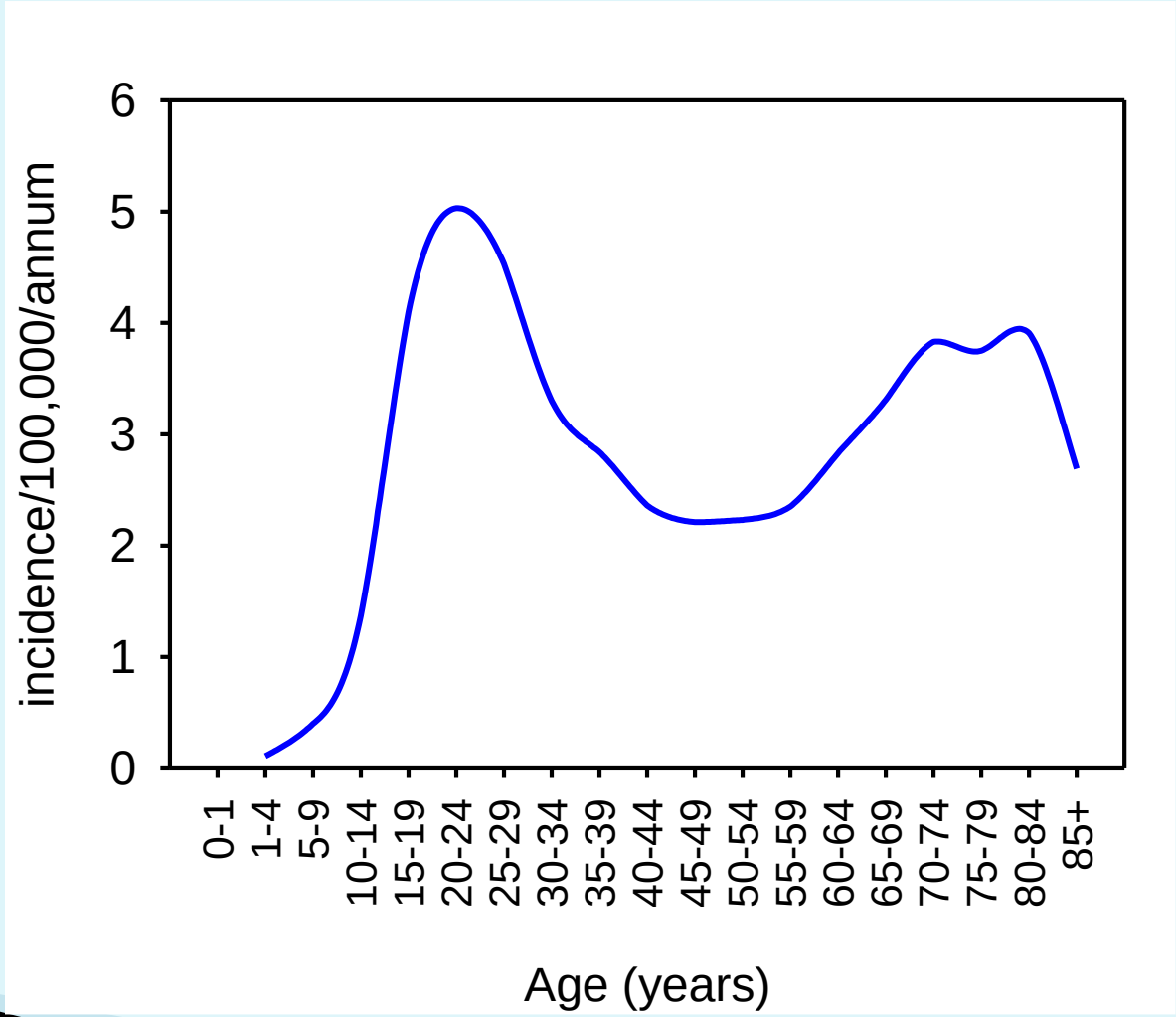
Pathogenesis



BiModal Age Distribution of Hodgkins Lymphoma



Presentation

SIGNS & SYMPTOMS	% OF PATIENTS
Lymphadenopathy	90
Mediastinal mass	60
"B" symptoms	30
Fever, weight loss, night sweats	
Hepatosplenomegaly	25

- Most commonly involved lymph nodes are the cervical and supraclavicular in 75%
- Bone marrow is involved in 5% of patients

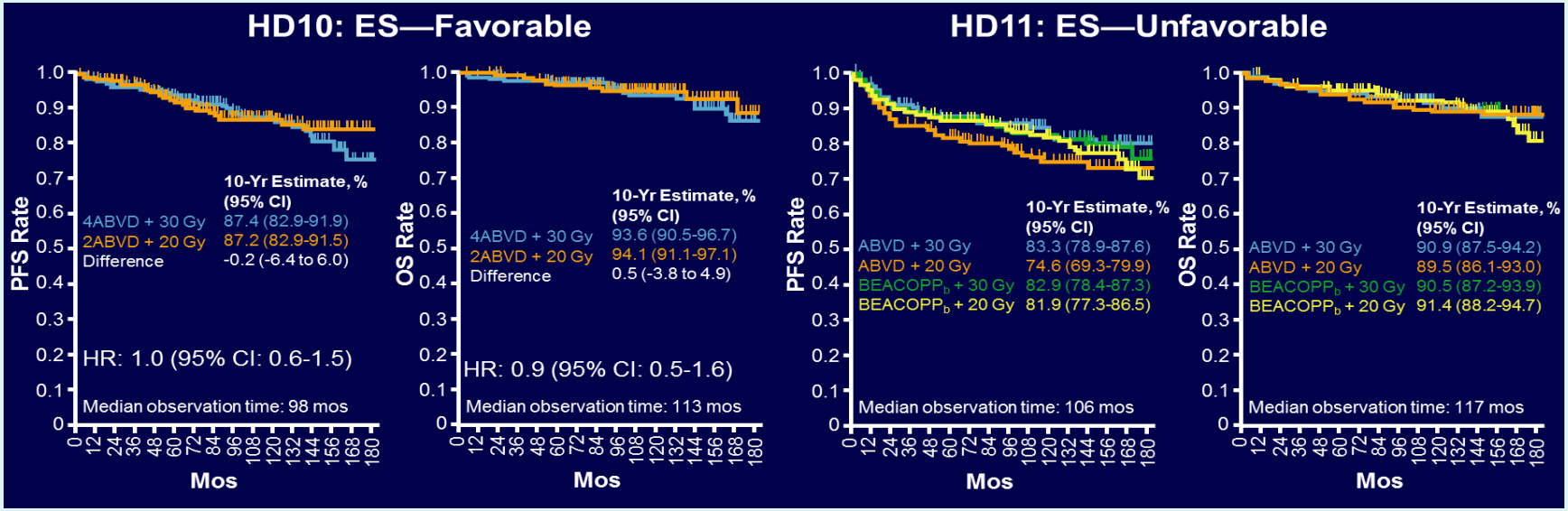
Clinically Relevant Stages

- Stage I/II: Limited Stage Disease
  - Favorable
  - Un-favorable
- Stage III/IV: Advanced Stage Disease
  - Risk stratified using IPS

Management of cHL

- Mainly younger patients
- Fertility preservation
- Toxicity of the regimen.
- Importance of PET CT in treatment.

Long Term Efficacy Data in GHSG Trials in Early Stage HL– 10 yr results



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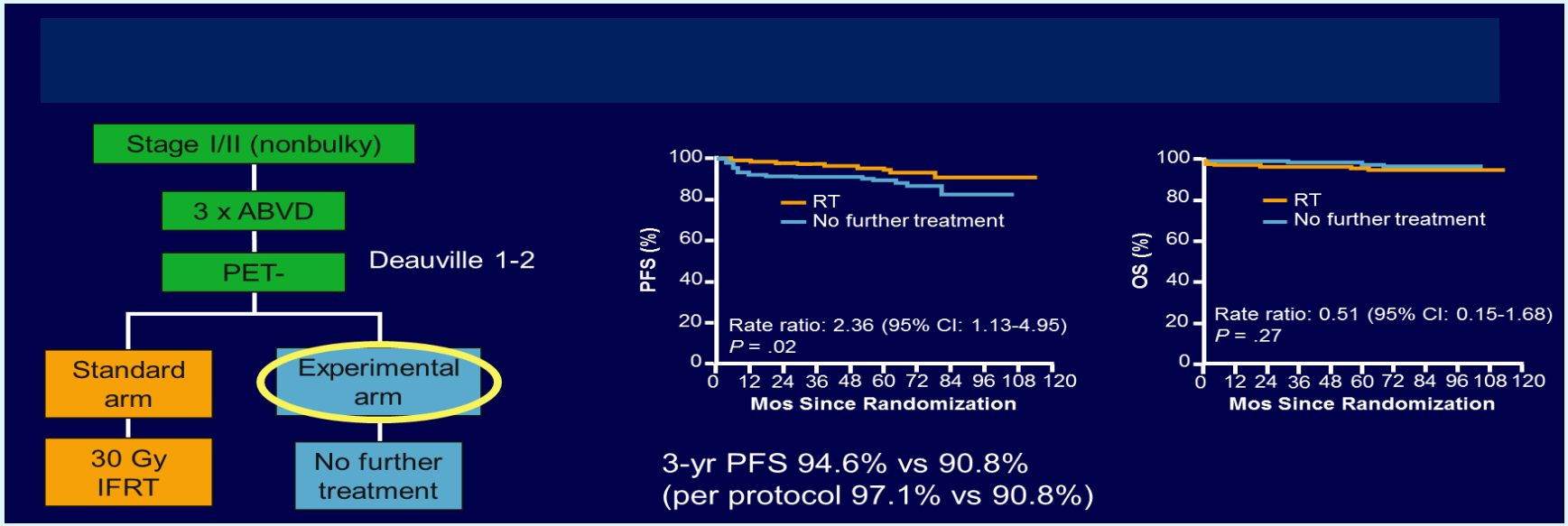
PET CT Adapted Approach in early HL

Given that most of the patients are young and generally the disease high cure rate.

Emphasis is on preventing long term toxicity.

Response adapted therapy is preferred



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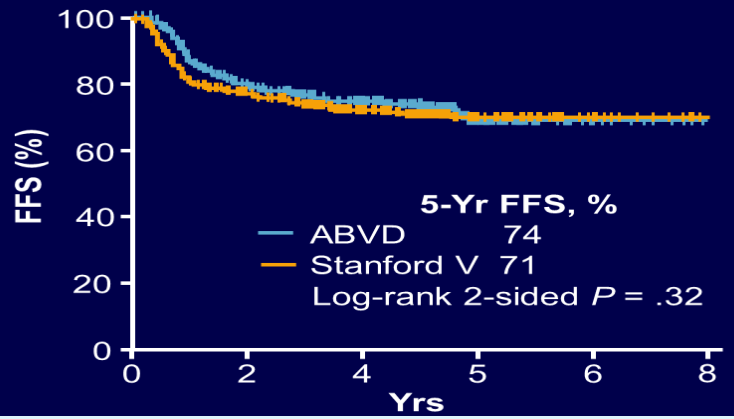
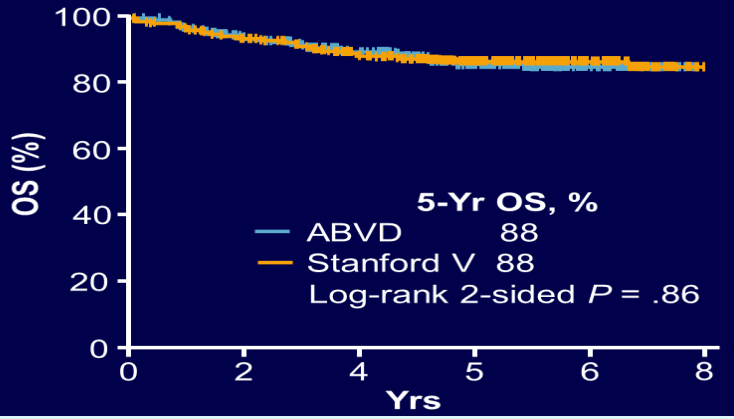
Management of Early Stage cHL

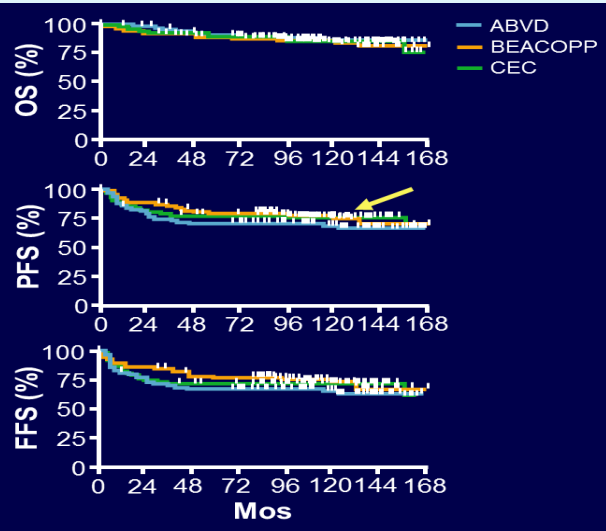
- Combination chemotherapy (ABVD) +/- Radiation treatment.
- Interim PET CT after 2-3 cycles to determine further management.
- Report symptoms such as cough or shortness of breath, neuropathy symptoms promptly to avoid long term complications.

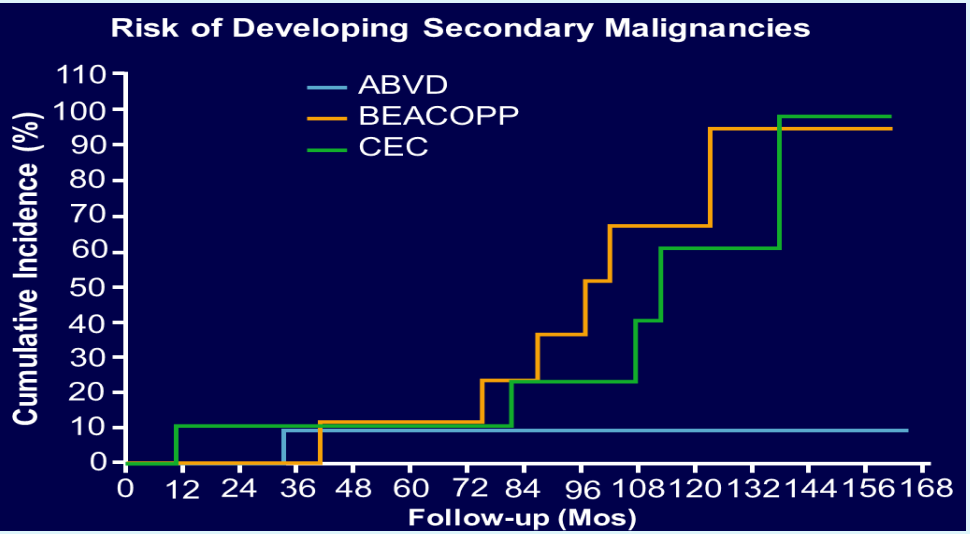
Management of Advance Stage cHL

- ABVD a standard therapy in North America based on balance of efficacy and toxicity









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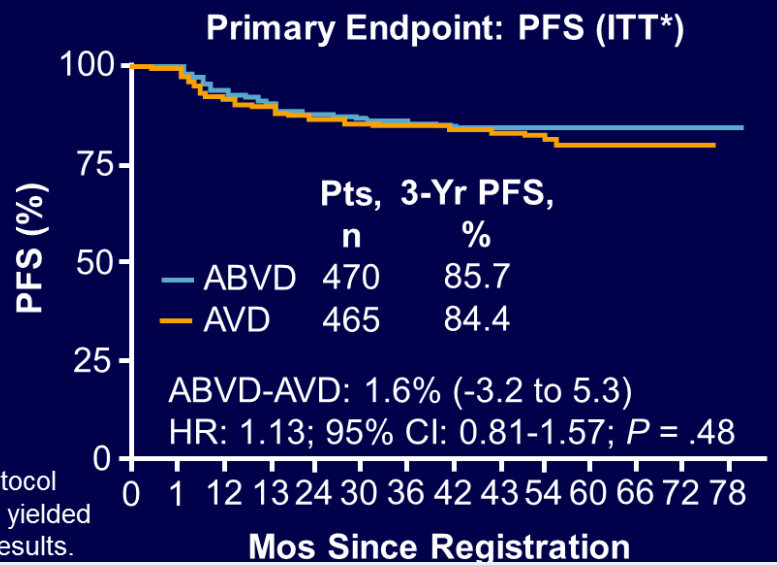
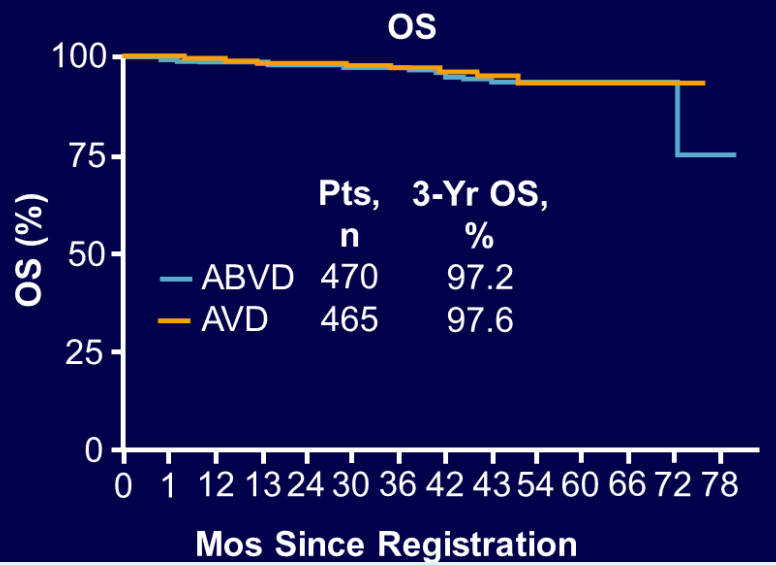
PET CT Based Approach in Treatment of Advanced Stage cHL

UK RATHL survival with ABVD vs AVD PET-2 Negative cHL

- Bleomycin can be omitted: AVD is noninferior to ABVD in all subgroups
  - Median follow-up: 41.2 mos (range: 2.0-79.7)





*Per protocol analysis yielded similar results.

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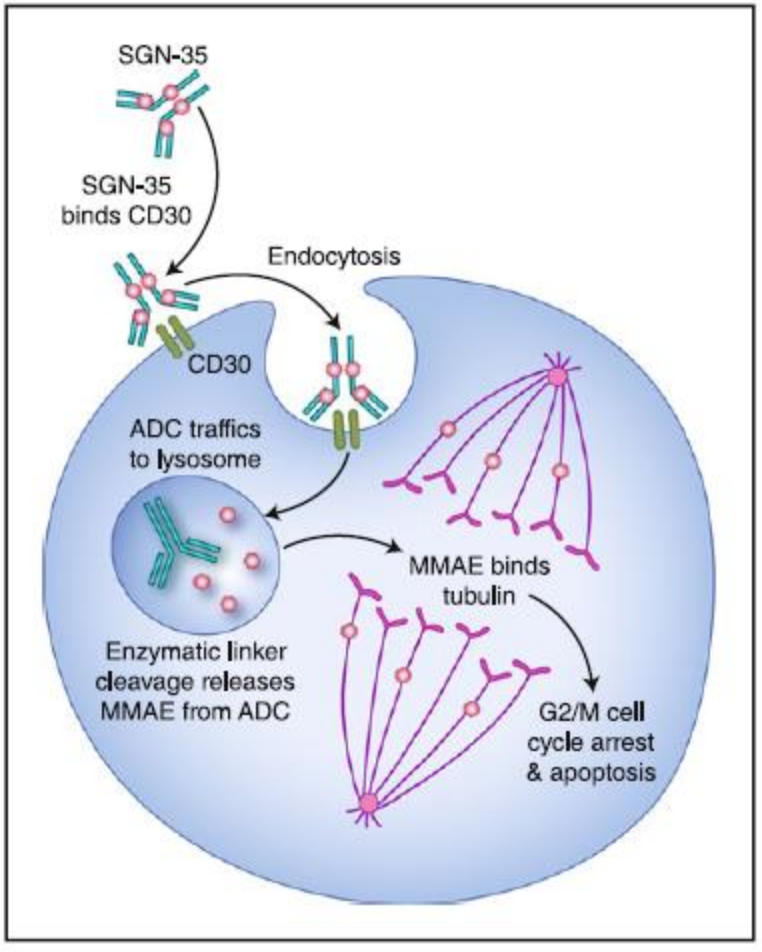
Conclusions: PET-Adapted Trials in Advanced-Stage HL

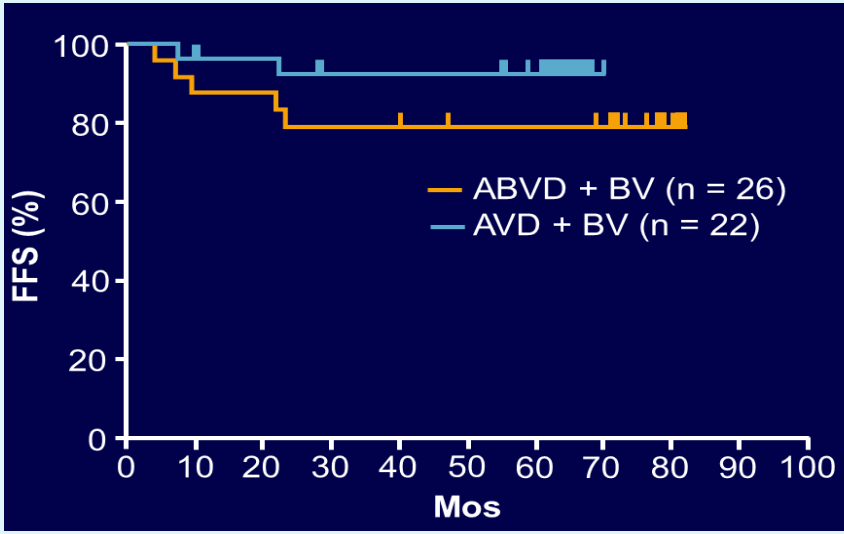
- Results of escalation/de-escalation strategies appear to be similar
- PET2 negative rate ~ 80% in most studies after ABVD x 2
- Bleomycin can be safely omitted with negative PET2
- Treatment failures seen even in PET2-negative pts
  - Not a perfect tool
  - Additional markers required
- Intensification of therapy to $BEACOPP_{escalated}$ with positive PET2 may improve outcome over historical results with ABVD
  - No control arm with continuing with ABVD
  - Increased toxicity issues

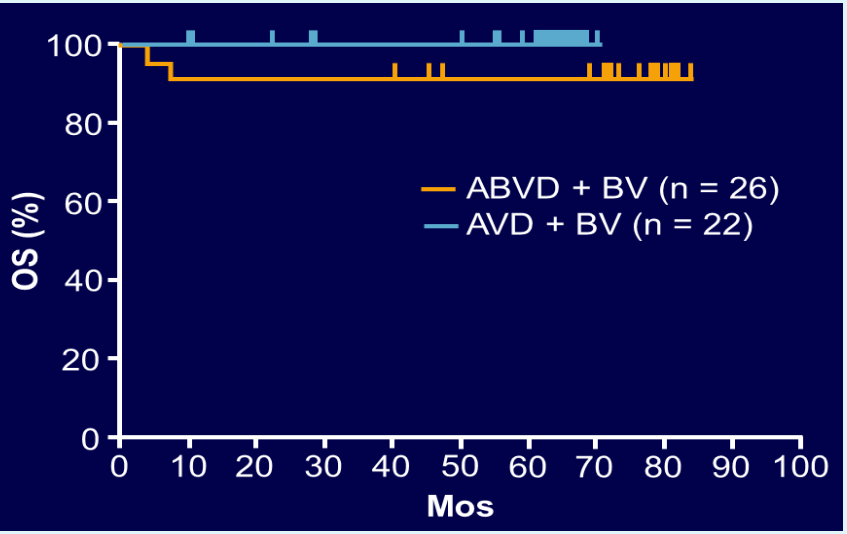
Novel Therapies: Brentuximab Vedotin (BV)

- Anti-CD30 antibody-drug conjugate
  - MMAE is a potent inhibitor of microtubule polymerization
- FDA approved in cHL for:
  - Pts who are not eligible for ASCT and who failed either ASCT or ≥ 2 regimens
  - Consolidation for pts with high risk of relapse/ progression after ASCT
  - Approval for frontline therapy (ECHELON-1 Study)



Addition of BV to AVD vs ABVD





Adult pts with newly diagnosed advanced cHL
(N = 1334)

→ **Brentuximab Vedotin + AVD** (n = 664)

→ **ABVD** (n = 670)

Treatment	2-Yr PFS, %	HR (95% CI)	Log-Rank *P* Value
BV + AVD	82.1	0.770 (0.603-0.982)	.035
ABVD	77.2		

Long term follow up

- Increased risk of secondary malignancies
- Cardiovascular risk factor
- Infertility and endocrine disorders.
- Neurological and psychiatric complications
- Follow up for relapse of disease

Management of relapse

- Repeat biopsy is a must to confirm disease relapse.

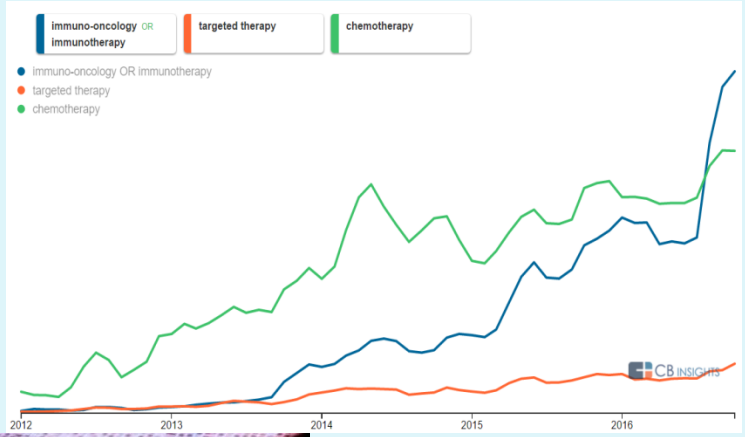
- Treatment strategy is based
- Eligibility for bone marrow transplant (Auto or unrelated)
- Functional response (based on PET/CT examination) to salvage chemotherapy
- Bulky disease
- Duration of remission
- Prior therapy, including chemotherapy, targeted chemotherapy, immunotherapy, HCT, and/or RT
- Comorbid illnesses that might limit treatment options

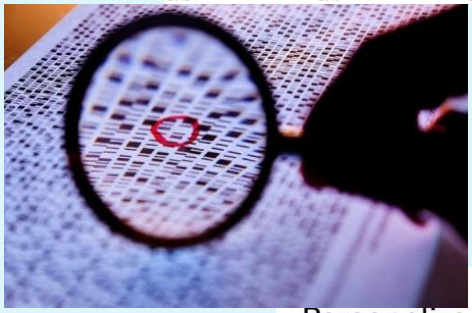
Treatment options

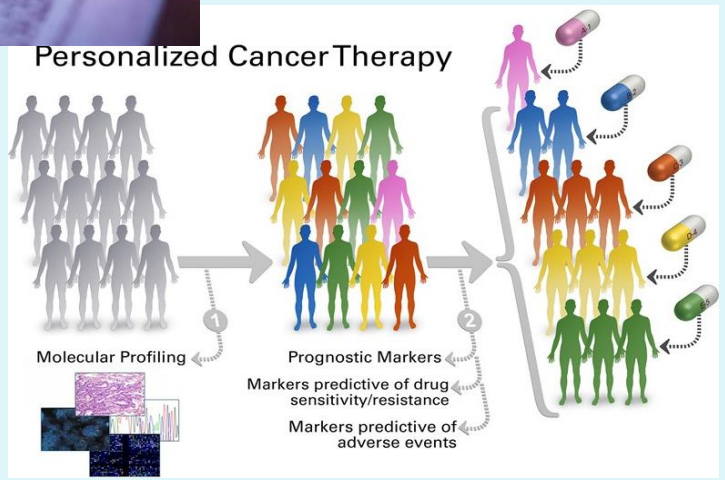
- Combination Chemotherapy
- Combination Chemotherapy with Immunotherapy
- Immunotherapy alone (BV and PD1 inhibitors)
- PD1 blockade (Pembrolimzumab and Nivolumab)
- Autologous and allogeneic hematopoietic cell transplantation

Future of cancer care is bright

- Advances in gene studies- better understanding of cancer.
- Identify genes that are responsible for tumor growth
- Targeting these genes to reverse tumor growth and possible cure is in the horizon.
- Ability to turn on tumor suppressor genes if they are down regulated.
- Chemotherapy given its toxicity will be slowly phased out with novel approach.







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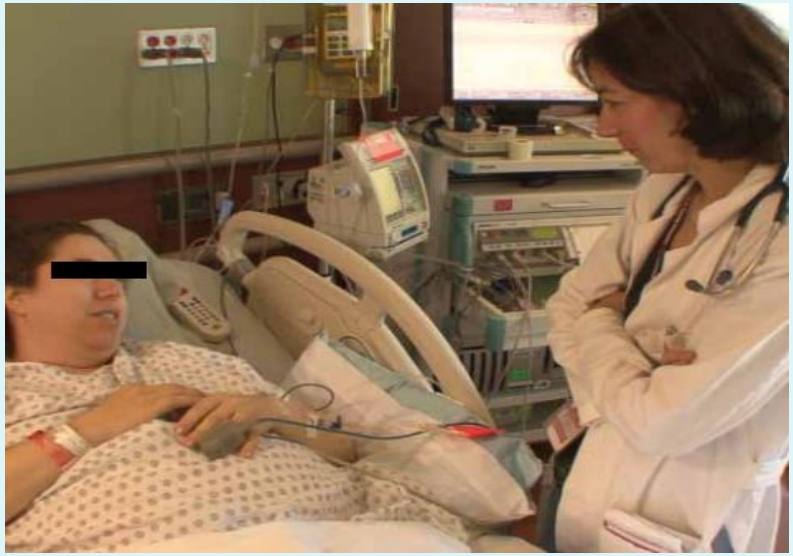
Bench to bedside
Patients who have enrolled into clinical trials



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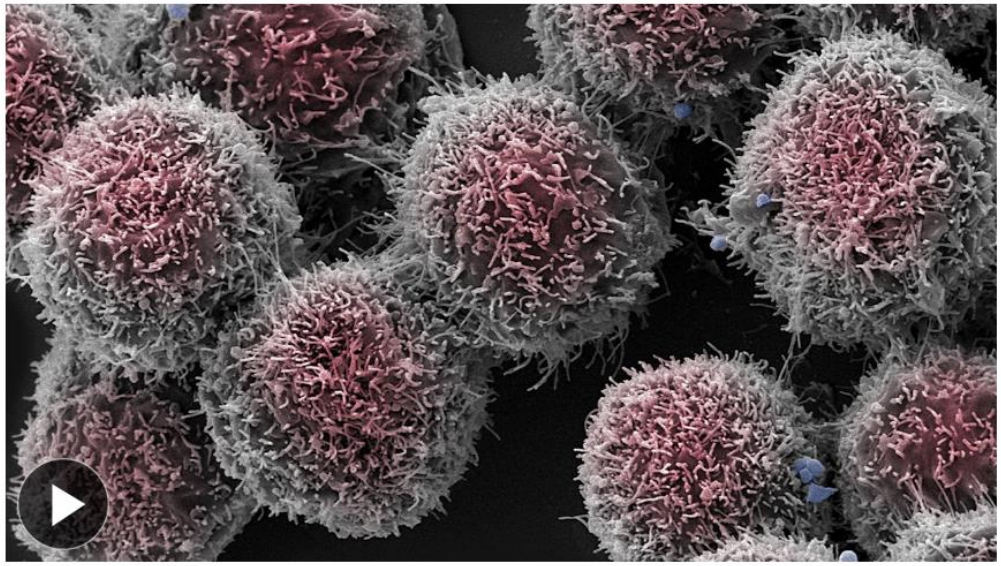

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- Acknowledgements
  - Leukemia Lymphoma Society

- Questions

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