An Overview of Practical Points of Lymphoma Management for the GPO

Dr Tara Baetz
BC Cancer Victoria

Conflicts of Interest

- Advisory Board/Honorarium: Gilead, Abbvie, Astra Zeneca, Roche, Bristol Myers Squibb, Beigene, Pfizer, Merck, Incyte

- Research Support: Bristol Myers Squibb

This is how I treat – lots of treatment variation and things are changing almost monthly - treatment direction for specific patients please utilize provincial lymphoma conference

Objectives

1)Describe a **recommended patient monitoring schedule**, including the timing of lab investigations and imaging for patients with indolent lymphoma on systemic and post-systemic therapy using follicular lymphoma as an example;

2) Review **clinical and lab findings suggesting possible disease progression** and findings suggesting histologic transformation;

3) Apply a **patient monitoring schedule,** including the timing of lab investigations and imaging, for patients with aggressive lymphoma on systemic therapy and post-systemic therapy, as applicable, using diffuse large B cell lymphoma as an example; and

4) Identify **clinical findings and lab results** suggestive of aggressive lymphoma relapse.

Approach to Lymph node Biopsy

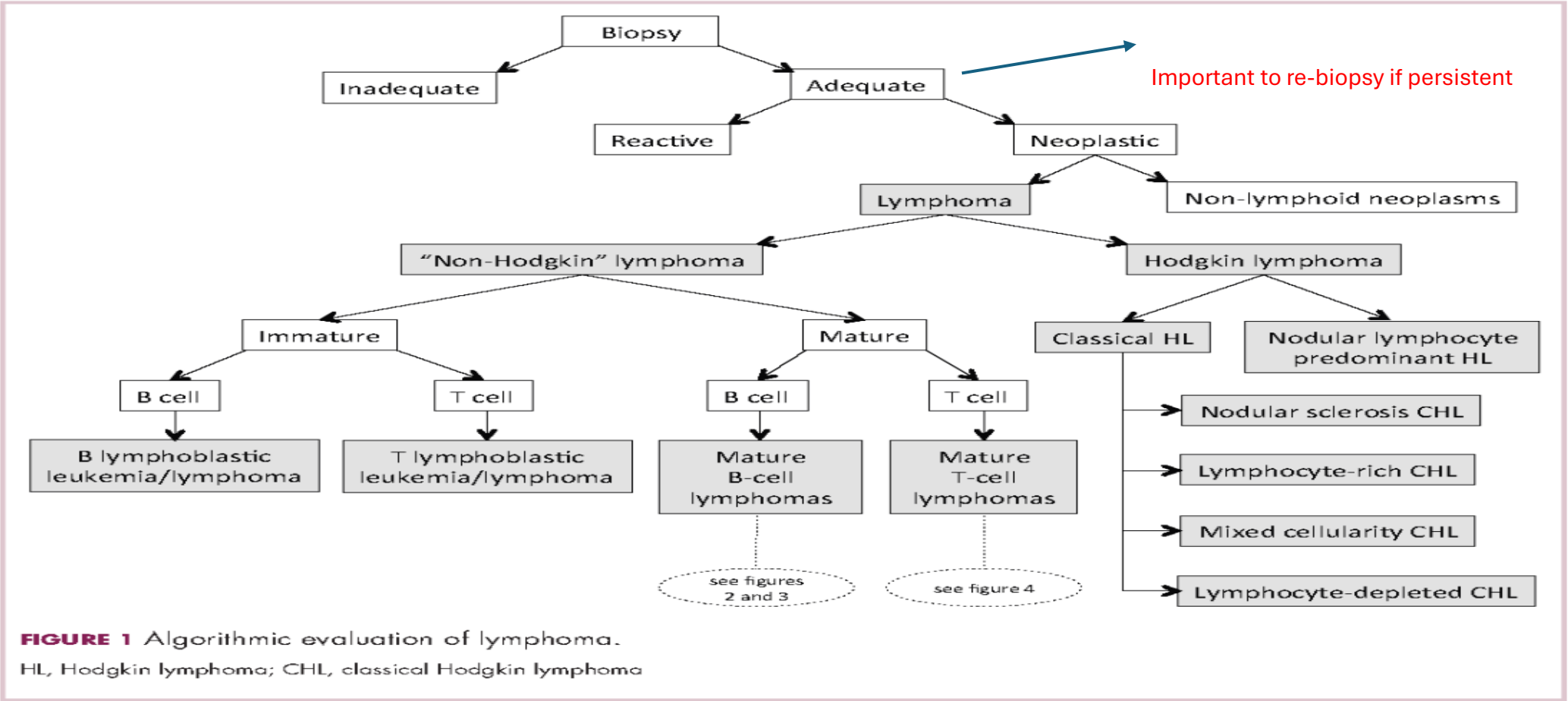

FIGURE 1 Algorithmic evaluation of lymphoma.

HL, Hodgkin lymphoma; CHL, classical Hodgkin lymphoma

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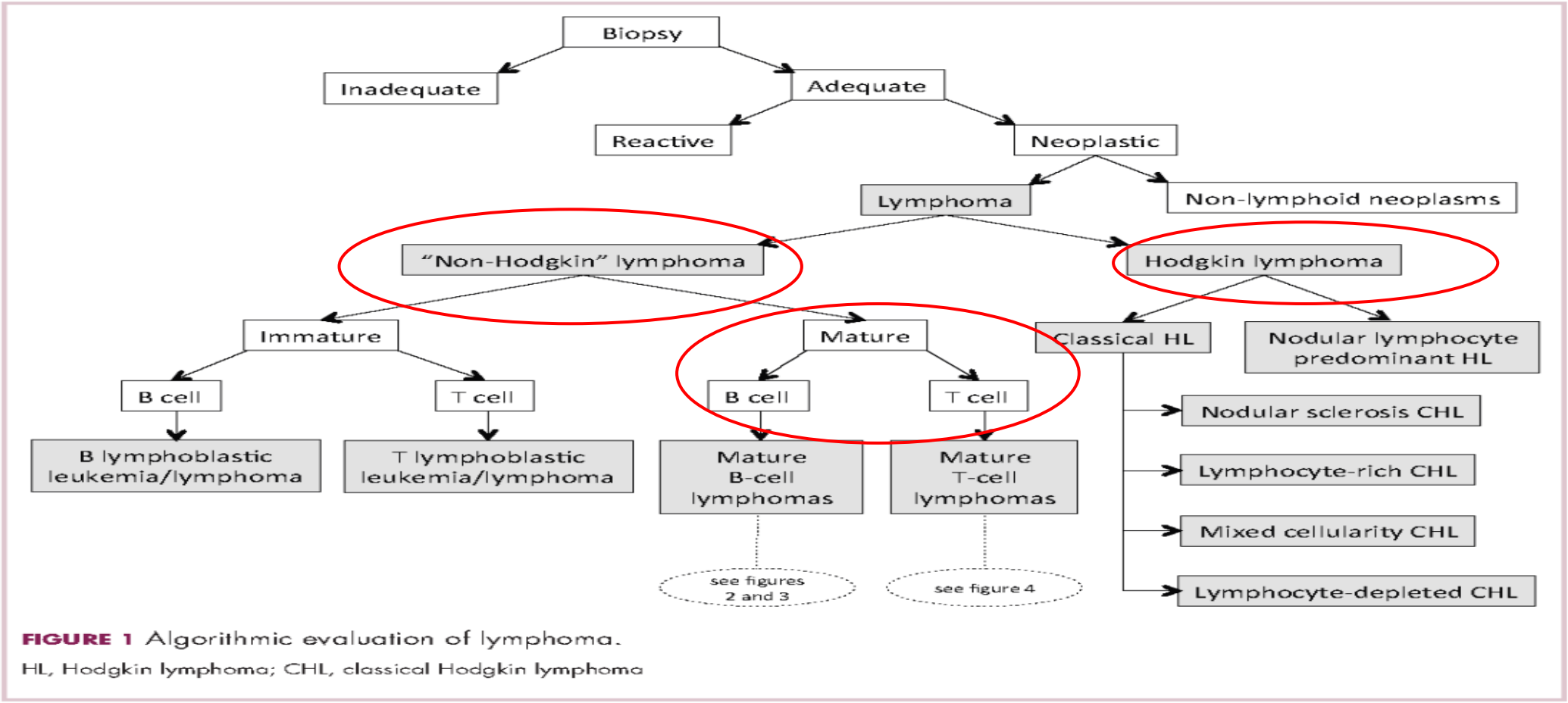

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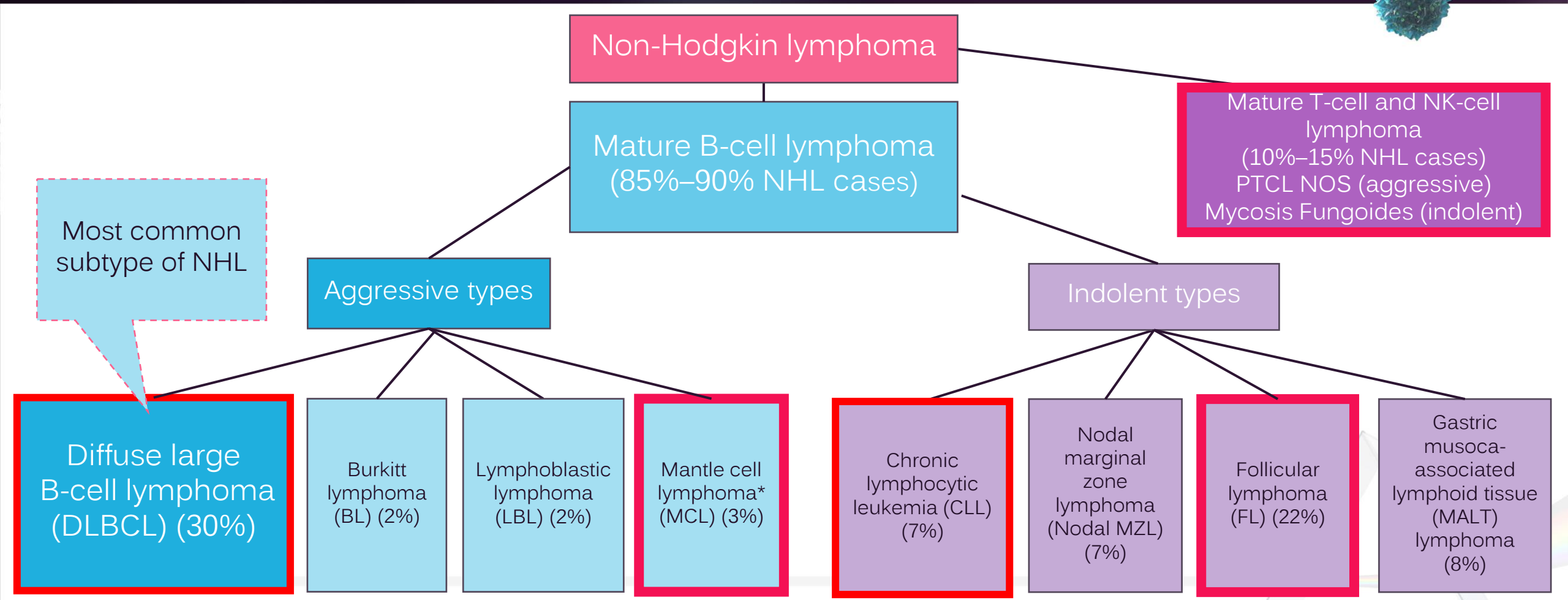
Subtypes of non-Hodgkin lymphoma (NHL)



*Has features of both indolent and aggressive NHL
NK, natural killer

NHL subtypes. Available at https://www.lls.org/lymphoma/non-hodgkin-lymphoma/nhl-subtypes. Accessed November 29, 2023.

Basic Subtypes - >70% Lymphoma

Aggressive Lymphoma : Classical Hodgkin Lymphoma,
Diffuse Large B cell Lymphoma,
Peripheral T cell Lymphoma

Indolent Lymphoma : CLL/SLL,
Follicular Lymphoma,
Mycosis Fungoides*

Aggressive Lymphoma

- Typically grows quickly
- Can be cured with aggressive treatment
- Need to treat even if asymptomatic
- If stays in remission for ~3 years usually does not reoccur
- Goal of treatment is CR
- Typically very PET avid

Indolent Lymphoma

- Typically grows **slowly – may not need treatment for many years**
- Treat if **symptomatic** * (B Symptoms, pancytopenia, renal dysfunction)
- **Goal of treatment is not cure but symptom control and time off treatment**
- CR is nice but not necessary
- Patients may die with but not of this
- **High prevalence of patients as many are on surveillance**
- Uptake on PET not as consistent

Polling Question? : What are the B symptoms?

A: Fever >39 degrees, Mild Night Sweats, Weight loss > 5%

B: Fever > 38 degrees, Drenching Night Sweats, Weight loss >10%

C: Fever >39 degrees, Drenching Night Sweats, Rash, Weight loss > 10%

D: Fever > 40 degrees, Drenching Night Sweats, Rash, Weight loss > 15%,

Transformation

- Low grade lymphomas **can transform** to more Aggressive Lymphoma (DLBCL – ABC subtype most common)

- Typically present with B symptoms, elevated LDH, very elevated SUV (>15 SUV) on PET scan in one region

Polling Question: What do you think the risk of a Follicular Lymphoma Transforming per year?

- 20%
- 10%
- 7%
- 2%
- <1%

Special Subtypes – that aren't like others

LP (lymphocyte predominant) Hodgkin Lymphoma – acts more like Follicular Lymphoma than Classical HL – CD 20+, often can relapse many years later – can be very indolent and you don't treat like classical HL

Mantle Cell Lymphoma – classified as indolent lymphoma but can act very aggressively, have multiple extra-nodal sites of disease (CNS, GI), goal of treatment is CR if possible

Diffuse Large B cell Lymphoma

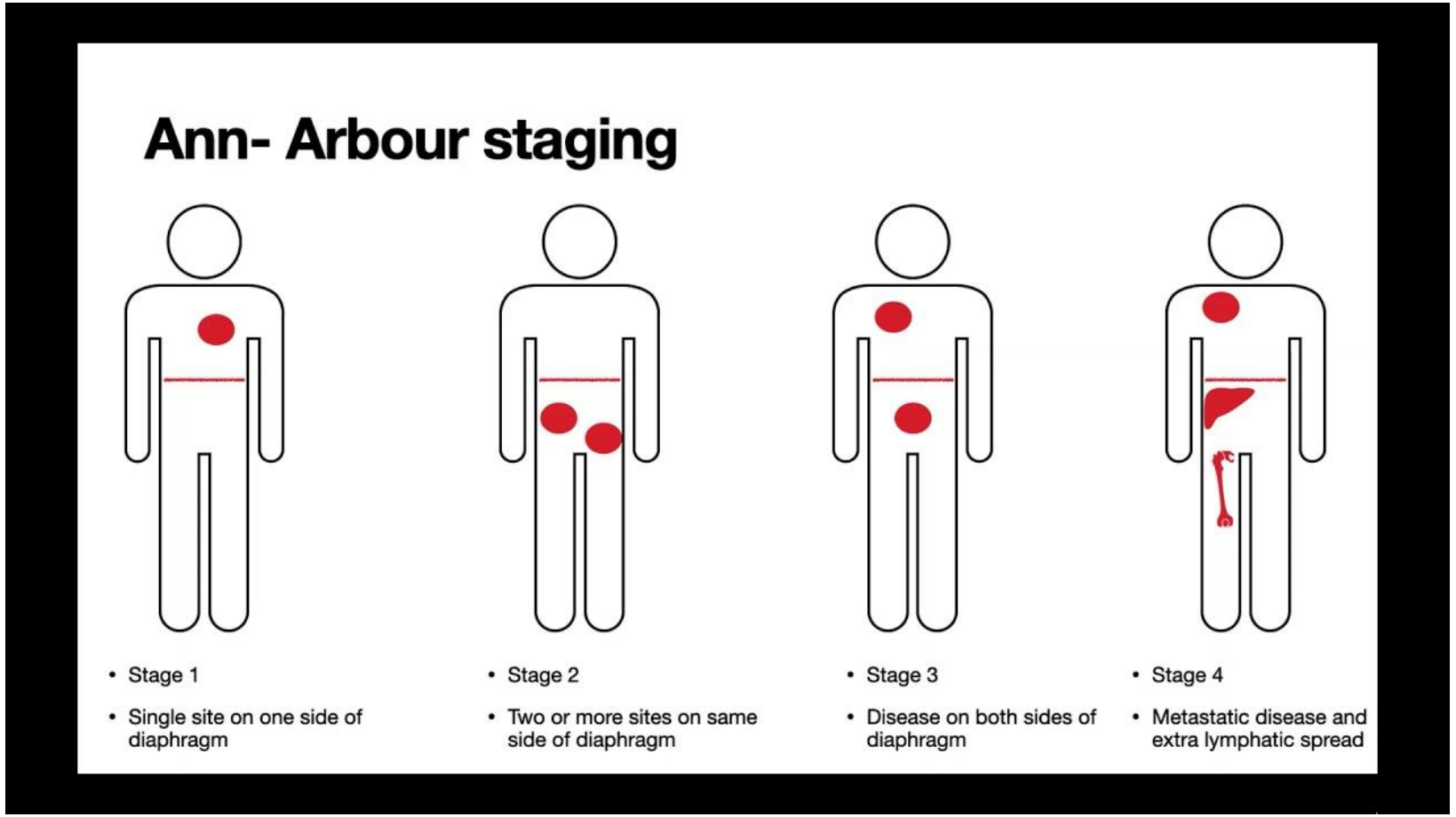
Molecular Subtypes

- **GCB (Germinal Centre) –** usually better outcome except for small subgroups of **double / triple hit (FISH positive MYC + BCL2 /BCL6)** and **Darkzone Signature** which do not respond well to RCHOP

- **ABC (Activated B cell) –** higher risk, often transformed lymphoma, not as responsive to RCHOP

- we also do Ann Arbour Staging and IPI risk factor to determine risk level

Staging



CNS staging (testicular, adrenal, kidney, CNS symptoms)
Look for EN disease
Biopsy if unsure – may have two malignancies
Check Hep B/C HIV status

I always ask if **TB exposure, prior radiation exposure, family history lymphoma,** autoimmune

Diffuse Large Cell Treatment – 1st Line

- RCHOP x 3 followed by IFRT OR RCHOP x 6 for stage I/2 A
- B symptoms or advanced stage - RCHOP x 6

- For double hit (?Darkzone) DA REPOCH x 6

- *For ABC - Polatuzumab R CHP is an option (not yet available)

- Some patients need CNS penetrating chemo(MTX) but we are moving away from this and only use in very small patient population

How I treat - DLBCL

- Try to give the **highest dose** that you feel patient can tolerate and then dose reduce if needed with subsequent cycles
- Adjust for **elevated bilirubin, renal dysfunction**
- Baseline **echo** and watch for cardiac dysfunction -Watch for **hyperglycemia –** may need insulin support if borderline diabetic
- **Baseline Hep B/C and HIV serology**
- Can start with **prednisone to debulk before chemo start**

- I put **everyone on filgrastim primary prophylaxis** (5-7 days mid treatment)
- For patients with history of HSV infections I use prophylaxis with Valtrex 500 mg /day
- **If history of TB then need to see ID** also if evidence of hep B prior infection or HIV
- I put everyone on **allopurinol 300 mg x 1** week starting day before treatment for TLS risk – rasburicase if inpatient

- Baseline PET , mid treatment CT and post treatment PET – if Deauville 1-3 I do not do anything further – if Deauville 4 then consider radiation to residual mass or surveillance PET and if Deauville 5 rebiopsy
- If FISH not back **start with RCHOP and then switch to DA REPOCH**

At Relapse

- Restage (PET)
- Repeat bloodwork, echo etc
- **Re biopsy** - core biopsy minimum
- Still considered **potentially curable**
- Lots of immune based treatments

Follicular Lymphoma

- First line treatment typically R Bendamustine x 6 cycles
- **If concern about transformation should biopsy** but treatment with RCHOP reasonable
- Typically, if in remission post treatment put on **Maintenance Rituximab** q 3 months x 2 years – no OS benefit but PFS improvement

- Can give single agent Rituximab x 4 weekly doses for asymptomatic patients – delays progression
- For **rare stage I or II patient curative radiation may be an option** – consider long term toxicity
- If asymptomatic same surveillance schedule as post treatment **– Watchful Waiting**

How I treat FL

- Staging PET
- Bone marrow if cytopenic
- Check **SPEP as may have a monoclonal protein** to follow - if very high protein may hold rituximab with first cycle

- I **typically don't use single agent Rituximab** and wait until progression

- I **typically do not image regularly but if symptomatic or abnormal bloodwork** (cytopenia, increase Cr, increase LDH, elevated bili)
- If the patient is having a lot of issues with maintenance Rituximab then I would have **low threshold to stop**
- **Watch for recurrent infections** (can have low IGG and need replacement)

Extra things to be aware of

- **Lymphoma and autoimmune disorders are commonly seen together –** and treatments for autoimmune disorders can increase risk of lymphoma

- Patients are at **increased risk of second malignancies** (esp skin cancer, lung ca)
- Patients are at **increased risk DVT/PE**
- Patients are at **increased risk of infection** (vaccination important) – may need IGG

Symptoms to watch out on relapse

- New autoimmune disorder
- New skin cancer
- New **rash**/pruritis
- Significant Fatigue
- New DVT/PE

- These can be harbingers of disease progression …

- *new Bell's palsy or other neuro symptom worrisome!

CLL – 1st line

- First Line typically **Venetoclax Obinutuzumab** except if 17P deleted (Then we would do BTK continuous treatment)

- **Venetoclax + Ibrutinib time limited (15 months) available soon –** combination with Acalabrutinib will be soon available as well

Similar symptoms to watch for and monitor **– watch for Richter's transformation**

Watch for infection and second primary cancer risk

Cardiac risk, hypertension, headache, **bleeding risk for BTK** – hold for one week around procedures

Venetoclax can cause cytopenias – can support with some filgrastim but may need to dose reduce if infections/ unable to keep counts up

Watch for hemolysis and other autoimmune conditions

Hodgkin lymphoma - Classical

ABVD chemotherapy for stage I , II

BV (Brentuximab) AVD for stage III/ IV (unless a lot of peripheral neuropathy or concern baseline)

BV- AVD- BV for **elderly (>60+) patients better tolerated**

Pre and Mid (after 2 -3 cycles) treatment PET helpful to direct therapy

Coming soon hopefully – Nivo +AVD and BrECADD (AVD+brentuximab and etoposide) for advanced stage disease

Watch for **bleo lung toxicity (SOB, hypoxia, cough), neuropathy**

How I treat HL

- Baseline PFT, fertility discussion, baseline echo, baseline PET /CT
- Baseline bloodwork – for young women FSH/LH
- Allopurinol as TLS prophylaxis
- Consider PORT/PICC for access

PTCL NOS

- BV CHP chemotherapy x 6 cycles
- For transplant eligible patients will consider ASCT in first remission

- CHOP or CHOP+ Etoposide may be an option if BV not tolerated

- **Stage for stage T cell does half as well as B cell lymphoma!**

Mantle Cell – not like the others

- Changing quickly

*some can be indolent and watched

R Bendamustine followed by ASCT has been standard

Shifting to **BTK inhibitor with chemotherapy followed by BTK maintenance x 2** years (no ASCT) but this is still being finalized

CAR T available post chemo and BTK exposure

Watch for extra nodal involvement, CNS involvement, rapid progression of disease

Surveillance Aggressive Lymphoma

- Watch for disease progression (although very unlikely after 2 years and if PET negative)
- Toxicity of treatment – peripheral neuropathy, cardiac dysfunction (echo q 5 years if rads to heart) , bleo lung toxicity, hypothyroid, early menopause
- Radiation risk second malignancies (breast cancer screening – mammogram start age 40 or 10 years post rads)
- Continue regular screening (PAP, FIT)
- Counsel about lifestyle
- Ask patient to tell you if anything changes – new adenopathy /new symptoms

Lymphoma Surveillance Specifics

CBC, Cr, LDH, bili, AST and physical exam (LN, liver, spleen, look at exposed skin, cardiac)

Assess every 3-4 months x 2 years then every 6 months x 2 years then 1/year x 1 year then discharge to family doctor asking them to do this every year - can alternate with virtual visits but need physical exam at least once a year or if symptomatic

Echo if meets criteria (or if EF decrease during treatment – would refer to cardiology)

If fertility issues then endocrine/gyne – make sure you think about fertility preservation before treatment

If patient has an engaged **primary care provider can transition with clear instructions**

What if you think there is progression?

- Imaging (CT or PET)
- Biopsy for confirmation (May not be same malignancy) – usually interventional radiology
- If borderline abnormality then repeat imaging in short time frame (3 months) to ensure no change
- Change back to every 3 months assessment until you are sure this is not progression then go back to regular schedule

Surveillance Low grade lymphoma

- I typically follow for **5 years after treatment** with same surveillance schedule and then send to family doctor – if not family doctor I will keep for once /year assessment long term
- If never treated will typically follow for first 5 years and if very stable can consider discharge
- If abnormal monoclonal ptn would add SPEP to bloodwork
- If elevated bilirubin/LDH look for autoimmune hemolysis
- If recurrent bacterial infections then check IGG and if low may consider IGG replacement

- Consider derm for skin surveys yearly – **If you don't find a skin cancer you may not be looking hard enough!**

Fear of Cancer Recurrence

- **This can be very disabling**

Very high risk of anxiety and **depression after aggressive treatment completed** and in remission – referral to support but also normalize this time of processing the experience

Low grade lymphoma need to be told right away that this will likely not go away forever but is managed like other chronic conditions (like diabetes) – good opportunity to work on lifestyle changes (smoking cessation, stress decrease, exercise etc)

Management of fear of transformation and support if they are concerned that this is happening – **I have very permissive messaging that I am happy to see them and make sure this is not a concern rather then have them worry** – typically this does not result in a lot of extra visits and can decrease anxiety in patients

NP/GPO led clinic

- In Kingston we had NP/GPO led surveillance and survivorship clinic for lymphoma
- More than 400 patients managed with alternating in person and virtual clinics with a shared model
- Only 5% referred back to MRP with progression
- NP did surveillance and ordered biopsy or imaging if worrisome
- GPO /NP liked the ownership of patients and the break from pretreatment assessments

Something to consider in BC?

Questions!

Thank you so much for your interest in lymphoma!

Happy to have email or text anytime

Tara.Baetz@bccancer.bc.ca
613-530-0852 (cell)