INTRODUCTION
Treating Slow-Growing Non-Hodgkin Lymphomas (NHL)

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The Leukemia & Lymphoma Society
DISCLOSURES
Treating Slow-Growing Non-Hodgkin Lymphomas (NHL)

Matthew S. McKinney, MD, has affiliations with Celgene, Epizyme, Kite/Gilead Sciences, Pharmacyclics, and Roche/Genentech (Consultant); Beigene, Celgene, Pharmacyclics, Novartis, and Roche/Genentech (Grant Support); Kite/Gilead Sciences (Speakers Bureau).

OBJECTIVES

- Slow-growing non-Hodgkin lymphomas (NHL)
- Treatment advances for slow-growing lymphomas
- Side-effects management
- Ways to effectively communicate with your healthcare team about quality-of-life issues
WHAT ARE SLOW GROWING (INDOLENT) LYMPHOMAS?

- Lymphomas are cancers that form from part of the blood/lymph system
- Now there are greater than 50 recognized lymphoma diagnoses as recognized by World Health Organization
- Indolent or slow growing or low-grade lymphomas are entities that generally are incurable but do not grow rapidly in the body

CURRENT LYMPHOMA CLASSIFICATION (WHO 2016)

<table>
<thead>
<tr>
<th>Maturation-related lymphomas</th>
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<tbody>
<tr>
<td>Small B-cell lymphoma</td>
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<tr>
<td>Diffuse large B-cell lymphoma</td>
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<tr>
<td>High-grade B-cell lymphoma</td>
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<tr>
<td>Burkitt lymphoma</td>
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<tr>
<td>Primary mediastinal large B-cell lymphoma</td>
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<td>Mantle cell lymphoma</td>
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<tr>
<td>Follicular lymphoma</td>
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<tr>
<td>Primary effusion large B-cell lymphoma</td>
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<tr>
<td>Primary extranodal natural killer cell lymphoma</td>
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<tr>
<th>Acquired immunodeficiency-related lymphomas</th>
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<tr>
<td>HIV-associated lymphoma</td>
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<tr>
<td>Post-transplant lymphoproliferative disorders (PTLD)</td>
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<tr>
<td>Plasmacytic lymphoma</td>
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<tr>
<td>Plasmablastic lymphoma</td>
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<tr>
<td>Primary effusion plasmablastic lymphoma</td>
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<tr>
<td>Primary effusion large B-cell lymphoma</td>
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<tr>
<td>Primary extranodal natural killer cell lymphoma</td>
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<table>
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<tr>
<th>Malignant T and NK reactivities</th>
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<tr>
<td>T-cell prolymphocytic leukemia</td>
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<tr>
<td>B-cell lymphoma</td>
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<tr>
<td>Chronic lymphoproliferative disorder of NK cells</td>
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<tr>
<td>Aggressive NK-cell leukemia</td>
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<tr>
<td>Systemic EBV-T-cell lymphoma of childhood</td>
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<tr>
<td>Hydrosa vacciniforme-like lymphoproliferative disorder*</td>
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<tr>
<td>Adult T-cell leukemiaymphoma</td>
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<tr>
<td>Extramedullary NK/T-cell lymphoma, nasal type</td>
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<tr>
<td>Enteropathy-associated T-cell lymphoma</td>
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<tr>
<td>Monomorphic epitheliod lymphoma intestinal T-cell lymphoma</td>
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<tr>
<td>Inflammatory T-cell lymphoma</td>
</tr>
<tr>
<td>Sezary syndrome</td>
</tr>
<tr>
<td>Primary cutaneous CD30^+ T-cell lymphoproliferative disorders</td>
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<tr>
<td>Primary cutaneous large cell lymphoma</td>
</tr>
<tr>
<td>Primary cutaneous CD8^+ aggressive epithelial lymphoma</td>
</tr>
<tr>
<td>Primary cutaneous CD8^+ T-cell lymphoma</td>
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<tr>
<td>Primary cutaneous CD4^+ small-medium T-cell lymphoproliferative disorder</td>
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<tr>
<td>Primary cutaneous T-cell lymphoma</td>
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<tr>
<td>Follicular T-cell lymphoma</td>
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<td>Follicular T-cell lymphoma</td>
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<td>Follicular T-cell lymphoma,</td>
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<td>Post-transplant lymphoproliferative disorder (PTLD)</td>
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<td>Primary effusion plasmablastic lymphoma</td>
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<tr>
<td>Primary effusion large B-cell lymphoma</td>
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<tr>
<td>Primary extranodal natural killer cell lymphoma</td>
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<tr>
<td>Breast implant-associated anaplastic large-cell lymphoma*</td>
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</tbody>
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**DISTRIBUTION OF LYMPHOMA SUBTYPES**

Indolent lymphomas:
- Follicular lymphoma
- Marginal zone or MALT lymphoma
- Lymphoplasmacytic lymphoma/Waldenström macroglobulinemia
- CLL/SLL

**QUESTIONS TO ASK AT DIAGNOSIS?**

- Is the biopsy sample adequate to make the diagnosis?
- What is stage?
  - Mostly important for limiting treatment, less for prognosis
- What markers indicate the patient’s prognosis?
  - Different than same question having to do with staging
- What is the best observation or treatment plan?
SPECIAL CHALLENGES OF LIVING WITH SLOW GROWING LYMPHOMAS

- Most indolent lymphomas are incurable, and patients deal with chronically
- Indolent lymphomas can cause serous health problems
- Therapies for lymphoma can have significant side effects
- It is important to address social, family, mental and financial stressors brought on by the challenges of dealing with a slow growing lymphoma
- Patients deserve a personalized “30 year plan”

LYMPHOMA TREATMENT OPTIONS/MODALITIES

- Chemotherapy
- Radiation
- Immunotherapies (antibodies, radioimmunotherapy, checkpoint inhibitors, bispecific antibodies)
- Small molecule inhibitors
- Stem cell transplant (autologous = self, allogeneic = donor infusion)
- Cell therapy (chimeric antigen receptor modified T cells = CAR T cells)
LOW GRADE/INDOLENT LYMPHOMA PRINCIPLES OF TREATMENT

- Early stage (usually stage I) lymphomas may be amenable to curative radiation treatment
- Otherwise treatment should only be administered for symptoms and using GELF or similar criteria (iwCLL18, IWWM etc.)

STAGE I-II DISEASE

- 100 pts w/stage I/II FL Radiation +/- chemotherapy
- Freedom from Tx Failure (FFTF)
  - 46% 10 years
  - 39% 15 years
- Overall survival:
  - 10 year 75%
  - 15 year 62%
  - 57% deaths from lymphoma
- No difference in outcomes +/- chemotherapy

**WATCH AND WAIT STRATEGIES FOR LOW GRADE (INDOLENT) LYMPHOMAS**

<table>
<thead>
<tr>
<th></th>
<th>Watch and Wait</th>
<th>ProMACE-MOPP + XRT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients</td>
<td>41</td>
<td>43</td>
</tr>
<tr>
<td>Alive off therapy</td>
<td>5/16 (31%)</td>
<td>25/43 (58%)</td>
</tr>
<tr>
<td>Alive without disease</td>
<td>5/41 (12%)</td>
<td>22/43 (51%)</td>
</tr>
<tr>
<td>Alive, continuously free of disease</td>
<td>0/41 (0%)</td>
<td>22/43 (51%)</td>
</tr>
<tr>
<td>Alive</td>
<td>34/41 (83%)</td>
<td>36/43 (84%)</td>
</tr>
</tbody>
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**TREATMENT PROGRAMS FOR INDOLENT LYMPHOMAS (ADVANCED DISEASE)**

- Goal of treatment is to decrease symptoms and improve patient survival; patients doing well do not need treatment
- Several regimens exist for follicular lymphoma others
- Bendamustine based regimens give longest response in most patients
- We may be moving toward chemotherapy free approaches
- Relapsed disease may also be treated with only novel agents
GELF CRITERIA

- Single node > 7 cm
- More than nodal sites > 3 cm
- Systemic symptom(s)
- Compression syndrome or serous effusion
- Cytopenia
- Lymphocyte count > 50,000/µL

CD20—MONOCLONAL ANTIBODY IMMUNOTHERAPY
**RITUXIMAB VS WATCHFUL WAITING IN ASYMPTOMATIC FL: IS TREATMENT NEEDED?**

Randomized phase III study

- **Patients with asymptomatic stage II, III, IV FL with low tumor burden** (N = 463)
  - Rituximab 375 mg/m² wkly for 4 wks (n = 192)
  - Rituximab 375 mg/m² every 2 mos for 2 yrs (n = 187)
  - Watchful waiting with regular clinic visits (n = 184)

- Stratified by age, grade, stage, and institution
- Mo 3: CT scan*
- Mo 7: CT scan if clinical CR*
- Mo 13: CT scan if clinical CR*
- Mo 25: Continue d follow up

*If CT shows CR, bone marrow biopsied for restaging.

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**RITUXIMAB VS WATCHFUL WAITING IN ASYMPTOMATIC FL: SURVIVAL**

- **PFS**
  - HR: 0.23 (95% CI: 0.16-0.32; log-rank P < .0001)
  - Maintenance rituximab
  - Watch and wait

- **OS**
  - HR: 0.73 (95% CI: 0.34-1.54; log-rank P = .40)

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STIL NHL 1-2003: BR VS R-CHOP IN NEWLY DIAGNOSED FL

Randomized, open-label phase III noninferiority trial

Treatment-naive patients with MCL or indolent CD20-positive lymphoma, including FL (N = 549)

- Primary endpoint: noninferiority of BR vs R-CHOP for PFS (decrease < 10% at 3 yrs)
- Secondary endpoints: response rate, time to next treatment, EFS, OS, safety

BR: bendamustine 90 mg/m$^2$ on Days 1-2; rituximab 375 mg/m$^2$ on Day 1; 4-wk cycles for 6 cycles max.
R-CHOP: cyclophosphamide 750 mg/m$^2$ on Day 1; doxorubicin 50 mg/m$^2$ on Day 1; vincristine 1.4 mg/m$^2$ on Day 1; prednisone 100 mg on Days 1-5; rituximab 375 mg/m$^2$ on Day 1; 3-wk cycles for 6 cycles max.
No maintenance or consolidation treatment given.

Median follow up: 45 mos

* n = 261 assessed. † n = 253 assessed.

STIL NHL 1-2003: PFS IN FL

No OS difference between treatment arms (for both, median OS: NR)

Median, Mos (IQR)
- BR NR (22.1-NR)
- R-CHOP 40.9 (35.2-NR)

HR: 0.61 (95% CI: 0.42-0.87; P = .0072)

**OBINUTUZUMAB BASED CHEMOIMMUNOTHERAPY FOR FL: PHASE III GALLIUM STUDY**

*International, open-label, randomized Phase III study*

**Induction**
- **G-chemo**
  - G 1000mg IV on D1, D8, D15 of C1 and D1 of C2-8 (q3w) or C2-6 (q6w) plus CHOP, CVP, or bendamustine

**Maintenance**
- **CR or PR at EOI visit**
- **G**
  - G 1000mg IV q2mo for 2 years or until PD
- **R**
  - R 375mg/m² IV q2mo for 2 years or until PD

**Primary endpoint**
- PFS (INV-assessed in FL)

**Secondary and other endpoints**
- PFS (IRC-assessed)*
- OS, EFS, DFS, DoR, TTNT
- CR/ORR at EOI (+/- FDG-PET)
- Safety

*FL and MZL pts were randomized separately; stratification factors: chemotherapy, FUR (FL) or PI (MZL) risk group, geographic region; *CHO* 3×c × 4 cycles; CVP 3×c × 4 cycles; bendamustine 3×c × 4 cycles; choice by site (FL) or by PI (MZL); *Pts with SD at EOI were followed for PD for up to 2 years; +Confirmaatory endpoint.

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**PROGRESSION FREE SURVIVAL WITH OBINUTUZUMAB VERSUS RITUXIMAB WITH CHEMOTHERAPY IN FL**

**Median follow-up: 34.5 months**

- **R-chemo, n=601**
  - Pts with event, n (%) = 125 (20.8)
  - 3-yr PFS, % (95% CI) = 77.9 (73.8, 81.4)
  - HR (95% CI), p-value* = 0.71 (0.54, 0.93), p=0.0138

- **G-chemo, n=601**
  - Pts with event, n (%) = 93 (15.5)
  - 3-yr PFS, % (95% CI) = 81.9 (77.9, 85.2)

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*Stratified analysis; stratification factors: chemotherapy regimen, FUR risk group, geographic region
### DIFFERENCES IN OBINUTUZUMAB VERSUS RITUXIMAB-CHEMOTHERAPY TOXICITIES

<table>
<thead>
<tr>
<th>% (n)</th>
<th>R-chemo (n=597)</th>
<th>G-chemo (n=595)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any AE</td>
<td>98.3% (587)</td>
<td>99.5% (592)</td>
</tr>
<tr>
<td>Grade 3+ AEs (≥5% in either arm)</td>
<td>67.8% (405)</td>
<td>74.6% (444)</td>
</tr>
<tr>
<td>Neutropenia</td>
<td>37.9% (226)</td>
<td>43.9% (261)</td>
</tr>
<tr>
<td>Leucopenia</td>
<td>8.4% (50)</td>
<td>8.6% (51)</td>
</tr>
<tr>
<td>Febrile neutropenia</td>
<td>4.9% (29)</td>
<td>6.9% (41)</td>
</tr>
<tr>
<td>IRRs*</td>
<td>3.7% (22)</td>
<td>6.7% (40)</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>2.7% (16)</td>
<td>6.1% (36)</td>
</tr>
</tbody>
</table>

Grade ≥3 AEs of special interest by category (selected)

| Infections | 15.6% (93) | 20.0% (119) |
| IRRs² | 6.7% (40) | 12.4% (74) |
| Second neoplasms | 2.7% (16) | 4.7% (28) |
| SAEs | 39.9% (238) | 46.1% (274) |
| AEs causing treatment discontinuation | 14.2% (85) | 16.3% (97) |
| Grade 5 (fatal) AEs | 3.4% (20) | 4.0% (24)²² |

Median (range) change from baseline in IgG levels at end of induction, g/ml

-1.46 (-16.4 - 9.1)¹¹ | -1.50 (-22.3 - 6.5)¹¹

*As MedDRA preferred term: ¹All events in MedDRA System Organ Class ‘Infections and infestations’; ²Any AE occurring during or within 28d of infusion of G or R and considered drug-related. ¹Standardized MedDRA query for malignant or unspecified tumors starting ≥2 mo after treatment start; Ig levels were measured during screening, at ED1 and end of maintenance and during follow-up; ²Includes patient who died after clinical cut-off date from AE starting before cut-off date; ¹¹n=472; ¹²²n=482

### CHEMOTHERAPY FREE APPROACH IN FOLLICULAR LYMPHOMA (FL)

**RELEVANCE Trial**

Ongoing Phase 3 Trial—Lenalidomide + Ruxitumab²²

- CO²⁺ FL (grade 1, 2, 3a)
- Stage II to IV
- No prior systemic therapy
- Target accrual N = 1031

- R-chemo: Investigator’s choice of R-CHOP, R-CVP, or BR
- Primary endpoint: CR/Cru rate at 120 wk, PFS
- Secondary endpoint: EFS, TTI, OS, MRD using PCR, and HRQoL
- In a single-center trial, patients with untreated FL who received the combination of ruxitumab + lenalidomide had an ORR of 98% and a CR rate of 87%²²

SIMILAR OUTCOMES WITH CHEMO-FREE APPROACH IN FL

Progression-free Survival

Overall Survival

Hazard ratio for progression or death, 1.10 (95% CI, 0.83–1.43)
P = 0.48

Hazard ratio for death, 1.16 (95% CI, 0.72–1.86)

ADVANCED FOLLICULAR LYMPHOMA APPROACH

- I recommend observation for patients not symptomatic from their lymphoma
- If treatment is needed options range from chemo-free approach to aggressive regimens such as obinutuzumab-bendamustine
- Each patient’s treatment must be individualized based on preferences and underlying health
- Most patients need multiple specific treatment regimens over many years
- CD20 antibody maintenance can be offered but is an individualized decision—it improves progression free time but not overall survival
**SIMILAR OUTCOMES WITH CHEMO-FREE APPROACH IN FL**

<table>
<thead>
<tr>
<th>Stage III</th>
<th>Minimal disease</th>
<th>Low burden asymptomatic</th>
<th>High burden progressive disease</th>
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<tbody>
<tr>
<td>&lt;60 years</td>
<td>rituximab or watch and wait</td>
<td>obinutuzumab + bendamustine</td>
<td>+/- rituximab maintenance</td>
</tr>
<tr>
<td>60-70 years</td>
<td>rituximab or watch and wait</td>
<td>rituximab + bendamustine</td>
<td></td>
</tr>
<tr>
<td>&gt;70 or comorbidities</td>
<td>rituximab or watch and wait</td>
<td>rituximab +/- CVP/CHOP</td>
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**APPROACH TO RELAPSED FOLLICULAR LYMPHOMA**

- Most patients will undergo multiple therapies for follicular lymphoma
- Treatment approach should be individualized but we generally look toward novel agents (e.g. lenalidomide/rituximab)
- Multiple new therapies recently approved so we are moving away from chemotherapy and stem cell transplant.
IMPORTANT RECENT FDA APPROVALS FOR NEW LYMPHOMA DRUGS

• Follicular lymphoma
  • Obinutuzumab frontline treatment
  • Lenalidomide with rituximab
  • Duvelisib
  • Tazemetostat
  • Umbralisib
  • Axicabtagene ciloleucel

• Waldenstrom macroglobulinemia
  • Ibrutinib with rituximab (the only FDA approved therapy in Waldenstrom’s)
  • Zanubrutinib indication filed with FDA

• Marginal zone lymphoma
  • Ibrutinib
  • Lenalidomide with rituximab
  • Umbralisib

PI-3 KINASE INHIBITORS FOR FL

• Phosphatidylinositol-3-kinase delta (PI3Kδ) inhibitor

• 57% response rate, 1.9 months to response, durability 12.5 months

• Phase II protocol
  • 125 patients
  • Refractory/relapsed within 6 months of rituximab/alkylator

Gopal, et. al. NEJM (2014)
**CONSIDERATIONS FOR PI3K INHIBITOR SELECTION**

- All 3 FDA-approved PI3K inhibitors have shown similar efficacy in the setting of relapsed/refractory FL
- Different toxicity profiles may factor into choice of PI3K inhibitor, particularly in patients with comorbidities
  - Hepatic toxicity and immune-related colitis are the most clinically concerning with idelalisib and duvelisib, hyperglycemia and hypertension with copanlisib
- Route of administration is another difference among PI3K inhibitors
  - Idelalisib and duvelisib are taken orally, copanlisib is administered by IV
- Choice of therapy should be individualized

**PRECISION MEDICINE HAS ARRIVED FOR FOLLICULAR LYMPHOMA--TAZEMETOSTAT**

- 25-30% of follicular lymphomas have mutation in gain of function mutations in **EZH2** (most often codon Y646)
- Tazemetostat is a selective EZH2 inhibitor that reduces **EZH2** mutant related H3K27me3
- Tazemetostat approved 6/18/2020 for FL after 2 or more lines of therapy in EZH2-mutated FL
- Side effect profile favorable relative to lenalidomide, PI-3 kinase inhibitors

<table>
<thead>
<tr>
<th></th>
<th>EZH2 mutated lymphoma</th>
<th>EZH2 wild type</th>
</tr>
</thead>
<tbody>
<tr>
<td>Partial response %</td>
<td>57</td>
<td>34</td>
</tr>
<tr>
<td>Complete response %</td>
<td>12</td>
<td>4</td>
</tr>
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</table>
UPDATE(S) ON UPCOMING NEW THERAPIES

- Novel approaches can be classified into 3 types:
  - New applications of existing therapies (e.g. stem cell transplantation in certain subgroups or new combinations)
  - Molecularly targeted agents
    - Specifically pairing characteristics of patient’s tumor to a drug
    - May be guided by new laboratory studies
    - Targeted “Smartbomb” delivery of chemotherapy agents in tumor cells
  - Immunotherapy
    - Immune “checkpoint” blockade
    - Modified activated T cell therapies
    - T cell engaging bi-specific antibodies (BiTEs)

CTL019 IS DESIGNED TO HUNT AND DESTROY CD19-POSITIVE B-CELL CANCERS IN PATIENTS

Figure courtesy of Novartis
CAR T CELL TREATMENT IN LYMPHOMAS

- B cell lymphoma can be treated with CAR T cells directed against the CD19 protein (among others)
- Response rates high in studied patients with lymphoma where other therapies have failed
- Therapy is complicated, expensive and requires inpatient hospitalization for side effect monitoring
- Numerous trials are now evaluating CAR T cells for other lymphoma types
  - Recent approvals for mantle cell lymphoma, follicular lymphoma

ZUMA-5: PHASE II TRIAL OF AXICABTAGENE CILOLEUCEL (AXI-CEL) IN HIGH-RISK R/R INDOLENT NHL

- Lymphodepleting Conditioning Regimen
  - Leukapheresis
  - Cyclophosphamide + Fludarabine on Days -5 to -3
  - Axicabtagene Ciloleucel IV on Day 0

- Patients with high risk*: indolent FL or MZL after ≥ 2 prior lines of CIT; ECOG PS 0/1; no CNS involvement or transformed disease (planned N = 160; n = 96 for efficacy analysis!)

- Manageable toxicity profile with axi-CEL; early onset of AEs, generally reversible
  - 1 grade 4, no grade 5 neurologic events; events ongoing in 4 patients at data cutoff
  - 1 grade 5 CRS event; no ongoing CRS at data cutoff

- Median PFS, Mos (95% CI)
  - FL (n = 80)
    - Median 23.5 mos (22.8-NE)
  - MZL (n = 16)
    - Median 11.6 mos (6.0-12.0)

- Patients followed up to 15 yrs for safety

*High risk: with POD24, relapse post ASCT, or PD within 6 mos of second-line CIT or beyond.
†n = 80 with FL and ≥ 9 mos of follow-up; n = 16 with MZL and ≥ 1 mo of follow-up. Axi-CEL: CD19-directed CAR T-cell therapy.
MARGINAL ZONE LYMPHOMA

- 3 types:
  - Extranodal (MALT) lymphomas
    - Mucosa associated lymphatic tissue
  - Nodal MZL
  - Splenic MZL
- Association with chronic antigenic stimulation by infection or autoantigens in lymph tissues
- 70% are mucosal associated lymphoid tissue (MALT) lymphomas
- Gastric MALT lymphoma in 30% of cases

TREATMENT FOR MZL/MALT LYMPHOMAS

- Consideration for cure in early-stage disease (gastric MALT most common scenario)
- Treat infection if present followed by observation (H. pylori eradication and upper stomach endoscopy surveillance in gastric MALT)
- Radiation can be considered in early-stage disease if antibiotic treatment not successful
- Rituximab, chemotherapy used for extensive stage symptomatic lymphoma
- New agents approved for MZL include lenalidomide, ibrutinib, umbralisib after failure of chemo/immunotherapy
WALDENSTRÖM MACROGLOBULINEMIA/LYMFOPLASMACYTIC LYMPHOMA (WM/LPL)

- Waldenström macroglobulinemia (WM) is an indolent process where an underlying LPL or MZL secretes IgM protein
- IgM can cause blood hyperviscosity and that can cause seizures, bleeding, vision changes
- Most common WM/LPL symptoms are fatigue, anemia, neuropathy
- Treatment aimed at alleviating symptoms of WM/LPL
- Rituximab, chemotherapy, proteosome inhibitors and ibrutinib are most commonly used treatments

NEW AGENTS IN LYMPHOMA AND WHAT TO LOOK FOR NEXT

- Novel cell therapies and new agents are offering new options for patients across diseases
- Treatment of chemotherapy-refractory diffuse large B cell lymphoma example of progress in the field
- Upcoming advances to look for:
  - Better combination treatment for T cell lymphomas
  - CAR T cell approvals outside of DLBCL (?mantle cell or aggressive FL)
  - Chemotherapy free approaches
  - New molecules with activity
SUMMARY (1)

- There are many complex treatment programs for various lymphomas
- Hopefully we will continue to come up with new treatments and cure more patients

SIDE EFFECTS OF SLOW GROWING LYMPHOMA TREATMENTS

<table>
<thead>
<tr>
<th>Medication</th>
<th>administration</th>
<th>Most common side effects</th>
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<tbody>
<tr>
<td>rituximab</td>
<td>IV</td>
<td>infusion reactions, infections</td>
</tr>
<tr>
<td>bendamustine</td>
<td>IV</td>
<td>low blood counts, infections, rash, fatigue, nausea</td>
</tr>
<tr>
<td>CHOP</td>
<td>IV and oral</td>
<td>alopecia, low blood counts, infections, heart toxicity, neuropathy, nausea</td>
</tr>
<tr>
<td>lenalidomide</td>
<td>oral</td>
<td>low blood counts, diarrhea, rash</td>
</tr>
<tr>
<td>tazemetostat</td>
<td>oral</td>
<td>nausea, low blood counts</td>
</tr>
<tr>
<td>idelalisib</td>
<td>oral</td>
<td>liver toxicity, low blood counts, infection, diarrhea, lung damage</td>
</tr>
<tr>
<td>duvelisib</td>
<td>oral</td>
<td>liver toxicity, low blood counts, infection, diarrhea, lung damage</td>
</tr>
<tr>
<td>copanlisib</td>
<td>IV</td>
<td>low blood counts, diarrhea, high blood sugar, high blood pressure</td>
</tr>
<tr>
<td>axicabtagene cileoleucel</td>
<td>hospitalization</td>
<td>low blood counts, cytokine release syndrome, neurotoxicity</td>
</tr>
<tr>
<td>ibrutinib</td>
<td>oral</td>
<td>bleeding, atrial fibrillation, rash, joint and muscle pain</td>
</tr>
<tr>
<td>radiation</td>
<td>daily treatments on gantry</td>
<td>skin burn, nausea, fatigue, organ damage, risk for secondary leukemia</td>
</tr>
</tbody>
</table>
TALKING WITH YOUR DOCTOR ABOUT SIDE EFFECTS OF TREATMENT

- Side effects, route of administration, schedule and cost are important factors to consider in selecting and dealing with lymphoma therapy.
- There are a wide range of toxicities/side effects across treatment options.
- There are a number of simple solutions to side effects (e.g. steroids for rash, caffeine for acalabrutinib headache, anti-diarrheals, etc.).
- Knowledge is power—know the potential side effects.
- Communication is key—make sure you share symptoms and concerns with your physician and how these affect you.

HOW TO HELP FRIENDS/FAMILY DEAL WITH LYMPHOMA

- Caregivers are extremely important for lymphoma patients.
- Make sure patient is comfortable with your involvement.
- Respect patient’s views and wishes.
- Be another set of eyes/ears but not their doctor.
- Seek out resources as needed (LLS, Lymphoma Research Foundation, NCI PDQ, etc.).
SARS-CoV-2/COVID-19 IN SLOW GROWING LYMPHOMA PATIENTS—IMPORTANT CONSIDERATIONS

- Slow growing lymphoma patients appear to have worse outcomes with COVID-19 illness
- Systemic therapies likely reduce immunity to clearing infection and responding to vaccination (largely extrapolating data regarding rituximab and influenza vaccination).
- SARS-CoV-2 vaccination is very safe for slow growing lymphoma patients
- SARS-CoV-2 immunity in blood cancer patients is being actively studied (including by the LLS!)

HOW I ADVISE SLOW GROWING LYMPHOMA PATIENTS ON SARS-CoV-2 VACCINATION

- No restriction for treatment naïve patients
- For patients symptomatic from localized/contained disease consider low dose radiation with goal of control for 6-12 months and get vaccinated
- If patient is doing well on maintenance rituximab/obinutuzumab consider holding for 1-3 cycles and administering SARS-CoV-2 vaccine
- Consider holding oral agent for 3-4 months if patient in remission
- Advise against vaccination if recent chemotherapy/immune therapy; wait 4-6 months from last treatment
- Patients should know they may not fully respond to vaccination
SUMMARY AND WORDS OF ADVICE AND HOPE:

1. There is lots of hope for treatment/"cures" and for new therapies.
2. The devil is in the details; Don’t hesitate to seek out help from an expert.
3. We lack ways to prevent/detect lymphomas early (with rare exception) and rare for them to be inherited.
4. We are hopeful that we can cure these diseases in the future.

“Hope and fear cannot occupy the same space.
Invite one to stay”
– Maya Angelou

Q&A SESSION
Treating Slow-Growing Non-Hodgkin Lymphomas (NHL)

• Ask a question by phone:
  – Press star (*) then the number 1 on your keypad.

• Ask a question by web:
  – Click “Ask a question”
  – Type your question
  – Click “Submit”

Due to time constraints, we can only take one question per person. Once you’ve asked your question, the operator will transfer you back into the audience line.
HOW TO CONTACT US:
To contact an Information Specialist about disease, treatment and support information, resources and clinical trials:

Call: (800) 955-4572
Monday to Friday, 9 a.m. to 9 p.m. ET

Chat live online: www.LLS.org/InformationSpecialists
Monday to Friday, 10 a.m. to 7 p.m. ET

Email: infocenter@LLS.org
All email messages are answered within one business day.

CLINICAL TRIAL SUPPORT CENTER
Work one-on-one with an LLS Clinical Trial Nurse Navigator who will help you find clinical trials and personally assist you throughout the entire clinical-trial process.
www.LLS.org/Navigation

NUTRITION CONSULTATIONS
Our registered dietitian has expertise in oncology nutrition and provides free one-on-one consultations by phone or email.
www.LLS.org/Consult

LLS EDUCATION & SUPPORT RESOURCES

Online Chats
Online Chats are free live sessions, moderated by oncology social workers. To register for one of the chats below, or for more information, please visit www.LLS.org/Chat.

LLS Online Community
Community of blood cancer patients, survivors and caregivers supporting each other and giving trusted information and resources, please visit www.LLS.org/Community.

Patient Podcast
The Bloodline with LLS is here to remind you that after a diagnosis comes hope. To listen to an episode, please visit www.TheBloodline.org.
The Leukemia & Lymphoma Society (LLS) offers the following financial assistance programs to help individuals with blood cancer:

www.LLS.org/Finances

To order free materials: www.LLS.org/Booklets

THANK YOU