Program will begin shortly!

Welcome & Introductions
Diagnosing and Treating Mantle Cell Lymphoma

Sonali M. Smith, MD
Associate Professor, Section of Hematology/Oncology
Director, Lymphoma Program
The University of Chicago
Chicago, IL

Agenda

• Criteria for diagnosing mantle cell lymphoma (MCL)
• What to consider when planning treatment
• Current treatment approaches and interventions
• What patients should know about clinical trials for MCL
• Communicating about quality of life issues with your healthcare team
What is lymphoma?

Lymphoma is a family of blood cancers derived from white blood cells called lymphocytes.

- **B-cells**
- **T-cells**
- **NK-cells**

- Lymphocytes normally fight viruses, bacteria, fungi, and foreign organisms.
- Lymphocytes travel in the lymphatic system.
- These cells can grow in lymph nodes (nodal sites) or outside the lymph nodes (extranodal sites).

Lymphatic system: where the cells of the immune system work and travel

- We have a lot of “lymphoid tissue” in our bodies.
- Lymph nodes are normal.
- Lymph nodes normally enlarge and become painful with infection.

Lymphoma often grows in lymphoid tissues:
- "nodal" = growing in a lymph node.
- "extranodal" = growing outside of a lymph node.

Tonsil
Lymph vessels
Thymus
Diaphragm
Spleen
Lymph nodes
MCL is an uncommon type of non-Hodgkin lymphoma

- Mantle cell (5-6%)
- Burkitt (2.5%)
- Follicular (25%)
- Small lymphocytic (7%)
- Other subtypes (9%)
- Diffuse large B cell (DLBCL) (30%)
- Lymphoplasmacytic (<2%)
- MALT-type marginal-zone B cell (7.5%)
- Nodal-type marginal-zone B cell (<2%)

Who gets MCL?

- Mean annual incidence 2-3/100,000 per year
- 3000 new cases in US, 4000 in European Union
- Male predominance of 3:1 to 4:1
- Median age at diagnosis is around 68 years

**Cause of MCL is unknown**
How do patients first come to medical attention?

- Lymph node enlargement
- Organ enlargement
  - Cause pain or pressure
- Low blood counts
  - If hemoglobin is low, patients can have fatigue
- “B” symptoms (fevers, night sweats, weight loss)
- No symptoms
  - Might be found during a colonoscopy
  - Abnormal blood tests

How is lymphoma diagnosed?:

**TISSUE IS THE ISSUE**

<table>
<thead>
<tr>
<th></th>
<th>PRO</th>
<th>CON</th>
</tr>
</thead>
</table>
| Fine needle aspirate | • Can distinguish lymphoma from other cancers
                    | • Quick, easy, office-based                                         | • Unable to give architectural detail
                    |                                                                     | • Insufficient for most prognostic tests                             |
| Core needle biopsy   | • Can be done in hard to reach places (stomach, spinal cord)       | • Unable to give architectural detail
                    |                                                                     | • Insufficient for most prognostic tests                             |
| Incisional or excisional biopsy | • Gold standard
                         | • Allows architectural evaluation
                         | • Allows tests for prognosis
                         | • Can be used for research                                         | • May be more invasive
                         |                                                                     | • May require surgery and anesthesia                                 |
Cells can travel in the blood

Key diagnostic tests

- Lymph node biopsy
- Immunohistochemical stains and flow cytometry tests
  - CD20+, CD19+, CD5+, FMC7+, CD23-, Cyclin D1+ cells
- Chromosomal evaluation
  - FISH positive for t(11;14)(q13;q32)
**Cyclin D1-negative MCL**

- Rare cases of MCL (<5%)
  - Typical pathology of MCL
  - Same gene expression profile of MCL
  - Lacks t(11;14)(q13;q32)
  - Appear to over-express cyclin D2/D3
- SOX11 found to be expressed in MCL and also in cyclin D1⁻ MCL

**3 “clinicopathologic” types of MCL**

- Classic MCL
- Blastoid
- Indolent MCL

These are treated similarly and management is based on age and general health of the patient. May not always need immediate treatment.
**MCL is a heterogeneous disease: the MIPI**

4 key factors:
- Age
- Performance status
- LDH
- White blood cell count

**What is Ki-67?**

- A marker of “proliferation”
- The higher the Ki-67, the more aggressive the lymphoma
- Currently, Ki-67 is a prognostic factor
- In the future, Ki-67 may be helpful in choosing treatment

---

### Biologic MIPI: adding Ki-67 to the MIPI

**Time to treatment failure**

- <10, median = 56
- 10-30, median = 64
- >30, median = 19

**Overall survival**

- <10, median = 82
- 10-30, median not reached
- >30, median = 40

---

**IMPORTANT:** Prognostic scales are not meant to be applied to an individual. They are helpful in predicting outcomes for a GROUP of individuals.

---

### Staging: how much disease is present?

- **Standard tests:**
  - CT scans of neck, chest, abdomen, pelvis
  - Bone marrow biopsy
  - Blood tests for complete blood count, chemistries, LDH, beta2 microglobulin

- **Other tests that may be useful:**
  - PET scan
  - Spinal tap (lumbar puncture)
  - Colonoscopy and EGD
Some notes on diagnosis, staging and prognosis

• Most patients with MCL are over age 60 years
• Most patients have advanced stage
  – B symptoms: < 50% cases
  – 90% extranodal involvement: BM, blood, liver, GI
  – Generalized adenopathy: 70-90%
  – CNS involvement at relapse: 4-22% (↑ with blastoid)
• Survival is improving
• All of the prognostic tools we have discussed apply to GROUPS of patients and are difficult to accurately apply to an INDIVIDUAL

TREATMENT
Types of treatment for MCL

- Systemic treatments
  - Chemotherapy
  - Monoclonal antibodies
  - Biologic agents
- Surgery—only used to make the diagnosis and is never the main treatment
- Radiation—occasionally used to treat a specific area but is never used alone

Basic approach to newly diagnosed MCL

Mantle cell lymphoma

“Fit”
- R-HyperCVAD
- NORDIC regimen
- RICE/R-DHAP
- RCHOP/R-DHAP
- +/- autoHCT

“Unfit”
- RCHOP
- purine analogs
- bendamustine

Indolent MCL

Palliative steroids
AGGRESSIVE TREATMENT

R-HyperCVAD

• Intensive treatment regimen developed at MD Anderson Cancer Center
  – “CVAD” is cyclophosphamide, vincristine, doxorubin, dexamethasone (Treatment A)
  – “Hyper” is methotrexate and cytarabine (Treatment B)
• Excellent responses but...still not a cure
• Up to 6-10% of patients do not survive all 8 rounds of treatment
• If all 8 rounds are given, there is no role for consolidative autologous stem cell transplant
**R-HyperCVAD / MTX / Ara-C in first-line MCL phase II, long-term results**

MDACC, 99 patients, 6-8 cycles, no ASCT if in CR after 6 cycles

<table>
<thead>
<tr>
<th>Age group</th>
<th>n</th>
<th>CR %</th>
<th>PR %</th>
<th>8-year TTF %</th>
<th>8-year OS %</th>
</tr>
</thead>
<tbody>
<tr>
<td>All ages</td>
<td>97</td>
<td>87</td>
<td>11</td>
<td>43%</td>
<td>56%</td>
</tr>
<tr>
<td>≤ 65 yrs</td>
<td>66</td>
<td>88</td>
<td>9</td>
<td>46%</td>
<td>68%</td>
</tr>
<tr>
<td>&gt; 65 yrs</td>
<td>31</td>
<td>84</td>
<td>16</td>
<td>16%</td>
<td>33%</td>
</tr>
</tbody>
</table>

If intensive chemotherapy has high response rates, but doesn’t last—What about consolidation?

- Induction chemotherapy
  - R-CHOP
  - R-DHAP
  - Abbreviated R-HyperCVAD
  - Bendamustine-rituximab?

- Consolidative autologous stem cell transplant (autoSCT)
  - AutoSCT is based on the concept that high doses of chemotherapy can overcome resistant cancer cells.
  - Then, the patient’s OWN stem cells rescue the bone marrow from the effects of the chemotherapy.
Choice of induction chemotherapy may make a difference

**Remission duration**

<table>
<thead>
<tr>
<th>ARM</th>
<th>36</th>
<th>48</th>
<th>60</th>
</tr>
</thead>
<tbody>
<tr>
<td>R-DHAP</td>
<td>81%</td>
<td>76%</td>
<td>74%</td>
</tr>
<tr>
<td>R-CHOP</td>
<td>67%</td>
<td>53%</td>
<td>44%</td>
</tr>
</tbody>
</table>

**Median follow-up = 50**
- R-DHAP, median not reached
- R-CHOP, median = 55

p < 0.0001

Overall survival: p=0.0485 in favor of R-DHAP arm

The most important factor may be minimal residual disease (MRD)

<table>
<thead>
<tr>
<th>Variable</th>
<th>HR</th>
<th>95% CI</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular response</td>
<td>2.4</td>
<td>(1.4-3.9)</td>
<td>0.001</td>
</tr>
<tr>
<td>MIPI score</td>
<td>1.7</td>
<td>(1.2-2.5)</td>
<td>0.008</td>
</tr>
<tr>
<td>Treatment arm</td>
<td>0.6</td>
<td>(0.3-1.1)</td>
<td>0.1</td>
</tr>
<tr>
<td>CR</td>
<td>0.9</td>
<td>(0.5-1.6)</td>
<td>0.68</td>
</tr>
</tbody>
</table>
LESS AGGRESSIVE TREATMENT

R-CHOP alone: high response rate but not long-lasting

1) German LGL (n=122)
   - R-CHOP x 6
   - CHOP x 6
   - CR/PR
   - IFN maint
   - ASCT
   - R-CHOP: ORR 94%, CR 34%, med TTF 21m

2) Cornell (n=36 MCL)
   - R-CHOP x 6
   - Bortezomib D1, D4 x 6
   - R-CHOP: ORR 91%, CR 72%, med PFS 23m

3) ECOG1499 (n=56)
   - R-CHOP x 4
   - Y90-ibritumumab tiuxetan
   - R-CHOP: ORR 82%, CR 55%, med TTF 34m

What about adding maintenance rituximab?

- R-FO (n=265)
- R-CHOP (n=267)

CR/PR

- IFN maint 3MIU/week (n=131)
- Maint rituximab q8 weeks (n=143)

Are there risks to maintenance rituximab?

- Low blood counts
- Prolonged B-cell depletion
- Low immunoglobulins
- Increased infections
- Viral reactivations (shingles, hepatitis, JC virus)
- Inability to respond to vaccines
- Resistance to future treatments

What about resistance?

• “Intrinsic resistance”
  – Not everyone responds to rituximab the first time

• “Acquired resistance”
  – Disease progressing within 6 months is called “rituximab refractory”
  – Disease progression while receiving rituximab is by definition “rituximab refractory”

• Mechanisms are unknown

A “new” chemotherapy: bendamustine

Available in Germany, 1971-1992
Unique in vitro anti-tumor profile

**Is BR better than R-CHOP?**

Untreated pts with indolent MCL (n = 546)

- Primary endpoint: To prove a noninferiority of BR vs R-CHOP in EFS (defined as a difference of less than 10% in EFS after 3 years)

**All patients required treatment**

BR x 6 cycles
- 260 pts

R-CHOP x 6 cycles
- 253 pts

---

**Comparison BR versus R-CHOP (StiL Trial)**

**Progression-free survival**

PFS: mantle cell (n=93)

- Median (months): B-R 35.4 vs CHOP-R 22.1
- HR: 0.50 (95% CI 0.29 - 0.81)
- p = 0.0061

---


**Bendamustine plus rituximab vs. R-CHOP: less toxicity**

![Graph showing comparison between BR and R-CHOP for hair loss, infection, and low blood counts]

*All grades; †Grade 3/4


---

**VcR-CVAD with Maintenance R (ECOG 1405): trying to reduce toxicity**

- 75 patients (40-76 years) with MCL
- 44 patients on MR arm, others consolidated with ASCT
- CR = 68%, PR = 27%
- 3 year PFS 67% (95% CI 52-85)

### Agents in the relapsed setting now being tested in initial treatment

<table>
<thead>
<tr>
<th>Agent</th>
<th>Class</th>
<th>ORR</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bortezomib</td>
<td>Proteosome inhibitor</td>
<td>30-50%</td>
<td>Med PFS 6-12m</td>
</tr>
<tr>
<td>Lenalidomide</td>
<td>Immunomodulatory agent</td>
<td>28%</td>
<td>Med DR 16+m</td>
</tr>
<tr>
<td>Temsirolimus</td>
<td>mTOR inhibitors</td>
<td>25-50%</td>
<td>Med PFS 3-6m+</td>
</tr>
<tr>
<td>Ibrutinib</td>
<td>BCR-signaling inhibitor</td>
<td>68%</td>
<td>Med PFS 13.9m</td>
</tr>
<tr>
<td>GS1101</td>
<td>PI3Kδ inhibitor</td>
<td>48%</td>
<td>NR</td>
</tr>
</tbody>
</table>

---

**LYM-3002: Replace vincristine with bortezomib**

- Recruitment at 128 centers in 28 countries (Europe, Asia, North America, South America) between 26 May, 2008 and 05 December, 2011

**Treatment-naïve MCL either ineligible for or refusing transplant**

- **R-CHOP**
  - Rituximab 375 mg/m² IV d 1
  - Cyclophosphamide 750 mg/m² IV d 1
  - Doxorubicin 50 mg/m² IV d 1
  - Prednisone 100 mg/m² PO d 1–5
  - **Vincristine 1.4 mg/m² (max. 2 mg) IV d 1**

- **VR-CAP**
  - Rituximab 375 mg/m² IV d 1
  - Cyclophosphamide 750 mg/m² IV d 1
  - Doxorubicin 50 mg/m² IV d 1
  - Prednisone 100 mg/m² PO d 1–5
  - Bortezomib 1.3 mg/m² IV d 1, 4, 8, 11

**Central laboratory confirmation of MCL diagnosis**

Concordance: 97%
Superior PFS by IRC with VR-CAP vs R-CHOP: 59% improvement

- Median follow-up 40 months; 298 (61%) PFS events
- 59% improvement with VR-CAP vs R-CHOP (hypothesized: 40% improvement)
- Median PFS by investigator was 16.1 vs 30.7 months with R-CHOP vs VR-CAP; 307 (63%) events; HR 0.51, p<0.001; 96% improvement with VR-CAP

Presented by: Franco Cavalli, MD

Peripheral neuropathy

<table>
<thead>
<tr>
<th></th>
<th>R-CHOP N=242</th>
<th>VR-CAP N=240</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peripheral neuropathy*, %</td>
<td>29</td>
<td>30</td>
</tr>
<tr>
<td>Grade ≥3 peripheral neuropathy, %</td>
<td>4.1</td>
<td>7.5</td>
</tr>
<tr>
<td>Treatment discontinuations, %</td>
<td>&lt;1</td>
<td>2</td>
</tr>
<tr>
<td>Median time to onset, days (range)</td>
<td>52 (2–158)</td>
<td>83 (8–256)</td>
</tr>
<tr>
<td>Events improved/resolved, %</td>
<td>79</td>
<td>90</td>
</tr>
<tr>
<td>Events resolved, %</td>
<td>75</td>
<td>81</td>
</tr>
<tr>
<td>Median time to improvement/resolution, months (95% CI)</td>
<td>4.8 (2.8, 6.4)</td>
<td>1.5 (0.9, 2.0)</td>
</tr>
<tr>
<td>Median time to resolution, months (95% CI)</td>
<td>5.5 (3.9, 8.1)</td>
<td>3.0 (1.6, 4.7)</td>
</tr>
</tbody>
</table>

No difference in OS to date
Lenalidomide/rituximab in frontline MCL: R2 regimen

Treatment-naïve MCL
Low tumor burden or defers transplant

Induction
Lenalidomide 20mg/d D1-21 q28d x 12 cycles
Rituximab weekly x 4, then every 8 weeks

Maintenance
Lenalidomide 15mg/d D1-21 q28d x 12 cycles
Rituximab every 8 weeks

Ruan et al., ASH 2013, ASH 2014.

R2 in MCL: Progression-Free Survival

Abstract #247
WHEN MCL COMES BACK
(also called recurrent or relapsed disease)

Approved agents for relapsed MCL

**Chemotherapeutic agents**
- Bendamustine
- Cytarabine
- Purine analogs

**Biologic agents/pathway inhibitors**
- Bortezomib
- Lenalidomide
- Ibrutinib

**Monoclonal antibodies**
- Rituximab
- Radioimmunotherapy

**mTOR inhibitors**
- (Temsirolimus)
New agents on the horizon...

<table>
<thead>
<tr>
<th>Mechanism</th>
<th>Agents</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bcl-2 inhibition</td>
<td>ABT-199, Navitoclax</td>
</tr>
<tr>
<td>BTK inhibition</td>
<td>GDC-0834, CGI-560, CGI-1746, HM-71224, CC-292, ONO-4059, CNX-774, andLFM-A13</td>
</tr>
<tr>
<td>CD20 inhibition</td>
<td>Obinotuzimab</td>
</tr>
<tr>
<td>HDAC inhibition</td>
<td>Vorinostat</td>
</tr>
<tr>
<td>IMIDs</td>
<td>Pomalidomide</td>
</tr>
<tr>
<td>JAK2 inhibition</td>
<td>SB1518</td>
</tr>
<tr>
<td>mTOR inhibition</td>
<td>Everolimus</td>
</tr>
<tr>
<td>NFkB inhibition</td>
<td>Carfilzomib</td>
</tr>
<tr>
<td>PI3K inhibition</td>
<td>Idelalisib</td>
</tr>
<tr>
<td>PKC inhibition</td>
<td>Enzastaurin</td>
</tr>
<tr>
<td>Ras/Raf inhibition</td>
<td>Sorafenib</td>
</tr>
<tr>
<td>SYK inhibition</td>
<td>Fostamatinib</td>
</tr>
</tbody>
</table>

Bortezomib is the first drug FDA-approved for relapsed MCL

- Primary objective
  - Formal comparison of TTP with historical controls
    - *Could not be accomplished due to lack of comparable historical controls*
- 2° objectives

<table>
<thead>
<tr>
<th>Response*, n (%)</th>
<th>DR, months (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ORR</td>
<td>48 (31)</td>
</tr>
<tr>
<td>CR/CRu</td>
<td>12 (8)</td>
</tr>
</tbody>
</table>

*Response rates were determined according to the International Workshop Response Criteria (IWRC) based on independent radiologic review of CT scans.

One-third of patients respond, and if the response is a complete remission, the response will last approximately 15 months
Immunomodulatory agents: seed vs. soil

Anti-cancer drug

Cancer cell

FDC

T-cell

T-cell

Lenalidomide has many effects on lymphoma and the microenvironment

Lenalidomide

↓ Angiogenesis

↓ VEGF, ↓ IL-6

↓ Osteoclastogenesis

↓ Survival factors

↓ TNF α, IL-1, IL-6

(Pro-inflammatory Cytokines)

↑ p21 Expression

(Tumor suppressor gene)

↑ T-cell Co-stimulation

↑ T-cell clonal proliferation

↑ Th1 Cytokines

(IFN-γ, IL-2)

Augments NK Cells function/number

Cytotoxicity against tumor cells

Lenalidomide in relapsed MCL: MCL-001 (EMERGE trial)

N=134 MCL pts who relapsed, progressed or were refractory to bortezomib

Lenalidomide 25mg D1-21 q28d CT q2 cycles

PD or toxicity

Primary endpoint: ORR and DOR
Secondary endpoints: PFS, OS

EMERGE Study

- Lenalidomide in MCL patients relapsed refractory to Bortezomib
- 134 patients with median 4 prior therapies
- ORR - 28% (CR - 7.5%)  
- Median DOR 16.6 months
- Median OS 19 months

Side effects of lenalidomide

- Neutropenia, thrombocytopenia
- Most common grade 3 toxicities: fatigue, diarrhea, pneumonia
- Rare grade 4 toxicities

<table>
<thead>
<tr>
<th>Any Grade</th>
<th>Grade 3</th>
<th>Grade 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>AE</td>
<td>%</td>
<td>%</td>
</tr>
<tr>
<td>Hematologic</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neutropenia</td>
<td>66</td>
<td>9</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>48</td>
<td>6</td>
</tr>
<tr>
<td>Anemia</td>
<td>41</td>
<td>11</td>
</tr>
<tr>
<td>Leukopenia</td>
<td>20</td>
<td>10</td>
</tr>
<tr>
<td>Nonhematologic</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fatigue</td>
<td>45</td>
<td>34</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>42</td>
<td>9</td>
</tr>
<tr>
<td>Nausea</td>
<td>48</td>
<td>30</td>
</tr>
<tr>
<td>Cough</td>
<td>39</td>
<td>24</td>
</tr>
<tr>
<td>Pyrexia*</td>
<td>81</td>
<td>23</td>
</tr>
<tr>
<td>Rash</td>
<td>30</td>
<td>22</td>
</tr>
<tr>
<td>Dyspnea*</td>
<td>24</td>
<td>18</td>
</tr>
<tr>
<td>Pruritus</td>
<td>23</td>
<td>17</td>
</tr>
<tr>
<td>Constipation</td>
<td>21</td>
<td>16</td>
</tr>
<tr>
<td>Urticarial rash</td>
<td>21</td>
<td>16</td>
</tr>
<tr>
<td>Hypertension</td>
<td>89</td>
<td>7</td>
</tr>
<tr>
<td>Pulmonary</td>
<td>28</td>
<td>22</td>
</tr>
<tr>
<td>Arthralgia*</td>
<td>19</td>
<td>14</td>
</tr>
<tr>
<td>Decreased appetite</td>
<td>18</td>
<td>14</td>
</tr>
<tr>
<td>Back pain</td>
<td>18</td>
<td>13</td>
</tr>
<tr>
<td>Hypokalemia</td>
<td>17</td>
<td>12</td>
</tr>
<tr>
<td>Mucosal ulcers</td>
<td>17</td>
<td>12</td>
</tr>
<tr>
<td>Upper respiratory tract infection</td>
<td>17</td>
<td>12</td>
</tr>
<tr>
<td>Decreased weight</td>
<td>17</td>
<td>12</td>
</tr>
<tr>
<td>Vomiting</td>
<td>14</td>
<td>10</td>
</tr>
</tbody>
</table>

Abbreviations: AE, adverse event; MCL, mantle-cell lymphoma.
*Denotes two grade 3 events per AE.
†Two grade 4 pneumonia events.

What are signaling pathways and why do we care?

- Cascade of events inside a cell
- Usually cause cancer cells to grow and stay alive
- Can be targeted
- Some cancer cells are “addicted” to certain pathways
Signaling pathways: tell cancer cells what to do

Target drug

Protein 1

Protein 2

Protein 3

New targets in MCL

idelalisib

ibrutinib

bortezomib

Everolimus temsirolimus

Ibrutinib in Bortezomib-naive or -exposed MCL: study design

Phase II: Rel/ref MCL; phase II study of bortezomib-naive and bortezomib-exposed patients with MCL

Ibrutinib 560 mg/d PO; continuous 28-day cycles until PD

Primary: ORR (every 2 cycles)
Secondary: DOR, PFS, OS, and safety


Ibrutinib in rel/ref MCL: response by subset

Single agent idelalisib in relapsed/refractory MCL

N=40 pts

ORR 40%
CR 5%
Median response duration 8m
Med PFS 3.7m


Finding new lymphoma treatments

• Bottom line is that new drugs being developed in lymphoma today are:
  – Smarter
  – More targeted
  – Make sense (rational)
• High throughput analysis of new drugs
• Faster processing by FDA

So...how do we get there?
NIH: type of trials

- Prevention
- Screening
- Diagnostic
- Treatment
- Quality of Life
- Compassionate use

Pre-clinical studies

- In vitro studies
- Animal studies
New drug clinical trials

Phase I
- Safety
  - 20-100 pts
  - 1st in humans
don't dose, schedule

Phase II
- Efficacy
  - 100-500 pts
  - How well does itwork?

Phase III
- Confirm
  - >1,000 pts
  - Compare withstandard of care &study safety

FDA review
Phase IV
- Safety in typicalpatients

Phase I
- In non-cancer studies performed in healthyvolunteers
- In drugs directed against cancer, typically given topatients with different types of cancer
- Establish safe dose and schedule
- Evaluate side effects
- Give preliminary information regarding if the drugworks
Phase II

The drug or treatment is given to a larger group of people to see if it is effective and to further evaluate its safety.

Phase III

- In cancer studies, typically no placebo except in certain circumstances
Phase IV

- After drug approved by FDA
- Collect additional information on side effects
- Identify any rare or long term toxicity

Oversight

- Studies may be conducted by pharmaceutical companies, single or group of investigators (including cooperative groups)
- Careful oversight to ensure ethical and safe conduct
- Institutional Review Board (IRB)
  - Evaluate protocol
  - Review consent form
  - Oversee ongoing conduct of trial
Clinical trials in a nutshell

Clinical trials are the future...

to more effective and less toxic treatments for lymphoma
• MCL is not a very common lymphoma but it is very unique
• Treatments are getting better and patients are surviving longer
• There are many new treatments available, and the only way to know how to use them is to participate in a clinical trial
• So far, none of the treatments is known to cure the disease or to be better than others for survival

This is a time of great hope!!

Thank you!
Question and Answer Session

Dr. Smith’s slides are available for download at www.LLS.org/programs

The Leukemia & Lymphoma Society (LLS) offers:

• Live, Online Chats that provide a friendly forum to share experiences with others. Living with NHL held on Monday and Wednesday nights from 7:30-10:00 pm ET. Caregiver Chat held on Monday nights from 8:00-10:00 pm ET. Young Adults Chat held on Tuesday nights from 8:30-10:30 pm ET.
  ➢ WEBSITE: www.LLS.org/chat

• What to Ask: For a list of suggested questions to ask about certain topics, download and print any of the following guides.
  ➢ WEBSITE: www.LLS.org/whattoask

• Free education materials: www.LLS.org/publications

• Past MCL programs: www.LLS.org/lymphomaeducation

• Information Resource Center: Speak one-on-one with an Information Specialist who can assist you through cancer treatment, financial, and social challenges.
  ➢ EMAIL: infocenter@LLS.org ❄ TOLL-FREE PHONE: (800) 955-4572