Meet a Young Investigator
Young Patients with WM

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2017 IWMF Educational Forum
• Relevant conflicts of interest/financial relationship(s)
  • None
Learning Objectives

• Meet a young investigator…

• Review the clinical presentation and outcomes of young patients with WM
IWWM - 2014

• 2014 International Workshop on WM – London, UK
  • Young Investigator Award - Clinical Features and Survival Outcome of Young Patients with WM
Mayo Clinic – Rochester, MN
Young Waldenstrom

- Dr. Jan G. Waldenstrom, 1944
WM – Epidemiology

Estimated new cases in 2017

- B-cell lymphoma
  - Non-Hodgkin lymphoma
    - Lymphoplasmacytic lymphoma
      - Waldenstrom macroglobulinemia

- Estimated incidence: 3.5 to 5.5 cases per million-person year
- Almost twice as common in males as females
Young Patients with WM

- Median age at diagnosis: ~ 70 years
  - ~ 25% younger than 60 years
  - ~ 10% younger than 50 years

6,200 WM patients (NCDB database)

NCDB database – unpublished data
Paludo, J. Blood 2016 128:1810
Young Patients with WM

• Most of young WM patients are healthy
  • Moderate to severe comorbidities in the general population:
    • 18% at 50 years; 37% at 70 years

• Long life expectancy
  • At 50 years old: +32 years

Human Mortality Database. University of California, Berkeley (USA) [www.mortality.org](http://www.mortality.org)
Young Patients with WM

- More than 90% of young WM (≤ 50 years) will succumb from WM-related complications.

Surviving

Median: 11 years of life lost
Young Patients with WM

- Mayo Clinic experience – 1960 to 2013
- 140 young WM patients (≤ 50 years) compared to 140 older WM patients (≥ 65 years)

<table>
<thead>
<tr>
<th>Parameter at WM diagnosis*</th>
<th>Cases (n=140)</th>
<th>Control(n=140)*</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at diagnosis, years</td>
<td>45 (30-50)</td>
<td>73 (65-85)</td>
<td></td>
</tr>
<tr>
<td>Hemoglobin, g/dL</td>
<td>10.2 (5.4-15.7)</td>
<td>10.4 (4.8-15.3)</td>
<td>0.23</td>
</tr>
<tr>
<td>Platelets, x10⁹/L</td>
<td>222 (59-543)</td>
<td>225 (21-634)</td>
<td>0.58</td>
</tr>
<tr>
<td>B2 microglobulin, mcg/mL</td>
<td>2.5 (0.7-9.3)</td>
<td>3.5 (1-17)</td>
<td>0.02</td>
</tr>
<tr>
<td>IgM, mg/dL</td>
<td>4,466 (24-14,400)</td>
<td>2,820 (19-13,900)</td>
<td>0.0002</td>
</tr>
<tr>
<td>BM involvement, % (range)</td>
<td>45 (5-90)</td>
<td>30 (5-95)</td>
<td>0.59</td>
</tr>
<tr>
<td>Splenomegaly, n (%)</td>
<td>22 (31)</td>
<td>10 (12)</td>
<td>0.004</td>
</tr>
<tr>
<td>Lymphadenopathy, n (%)</td>
<td>29 (39)</td>
<td>19 (22)</td>
<td>0.03</td>
</tr>
<tr>
<td>Hyperviscosity symptoms, n (%)</td>
<td>23 (46)</td>
<td>2 (7)</td>
<td>0.0003</td>
</tr>
<tr>
<td>Family history**, n (%)</td>
<td>16 (13)</td>
<td>7 (7)</td>
<td>0.19</td>
</tr>
</tbody>
</table>

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Young Patients with WM

<table>
<thead>
<tr>
<th></th>
<th>Young WM</th>
<th>Older WM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smoldering WM</td>
<td>30 pts (21%)</td>
<td>30 pts (21%)</td>
</tr>
<tr>
<td>Time from diagnosis to first treatment (SWM)</td>
<td>median 2.4 years</td>
<td>median 2 years</td>
</tr>
</tbody>
</table>

• Young WM:
  • More aggressive variant vs. late presentation (better organ reserve)?
University of Miami
Young Patients with WM

- Median disease specific survival from first treatment
  - Young cohort: 15.6 years; 10-years 77%
  - Older cohort: 11 years; 10-years 51%

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Young Patients with WM

- NCDB database: Overall survival from WM diagnosis
  - Young cohort: median NR, 10-years 75%
  - Older cohort: 8.1 years; 10-years 40%

NCDB database – unpublished data
Young Patients with WM

- Survival changes over time

**Median DSS, years**

<table>
<thead>
<tr>
<th>Group</th>
<th>Younger Cohort</th>
<th>Older Cohort</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1</td>
<td>13 y (95% CI: 5-23; 10-y OS 81%)</td>
<td>5.2 y (95% CI: 4-9; 10-y OS 0%)</td>
</tr>
<tr>
<td>Group 2</td>
<td>16 y (95% CI: 14-22; 10-y OS 80%)</td>
<td>9.6 y (95% CI: 5-13; 10-y OS 43%)</td>
</tr>
<tr>
<td>Group 3</td>
<td>15 y (95% CI: 10-NR; 10-y OS 71%)</td>
<td>12 y (95% CI: 8-NR; 10-y OS 62%)</td>
</tr>
</tbody>
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  • No survival improvement in young WM patients (≤ 50 years) diagnosed before 2000 compared to after 2000
    • Nelson, et al: Median NR vs. 204 months; p=0.53
    • Castillo, et al: Median NR vs NR

Young Patients with WM

- Survival changes of young patients with WM

Rio Grande do Sul - Brazil
Porto Alegre, RS - Brazil
**Young Patients with WM**

- How should we treat young/fit patients with WM??

<table>
<thead>
<tr>
<th>Disease control</th>
<th>vs</th>
<th>Deep responses</th>
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<tbody>
<tr>
<td>Lower toxicity</td>
<td>Continuous treatment</td>
<td>Long periods off any treatment</td>
</tr>
<tr>
<td>Convenient administration</td>
<td>Cumulative cost</td>
<td>Higher up-front toxicity</td>
</tr>
<tr>
<td></td>
<td>Long term side effects?</td>
<td>Limited treatment duration</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Long term side effects</td>
</tr>
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- Tailor treatment to patient characteristics and preferences
Research goals/interests in WM

- Treatment strategies
- Minimal residual disease?
- Depth of response
Summary

• Young patients with WM are more likely to be diagnosed at a more advanced stage of their disease.

• Although survival rates have improved in WM patients as a whole over the last several decades, no significant improvement in survival of the younger WM population was seen.

• The optimal treatment strategy for young patients with WM is yet to be defined.
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