Quality of Life in Patients with Chronic Myeloid Leukemia

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Quality of Life (QoL) will be crucial in the next research CML agenda

Some key reasons...

While TKIs are “targeted therapies”, they do impact on patients’ QoL

Better management of intolerance:
The use of “Common Toxicity Criteria” (CTC) is not appropriate to define intolerance to therapy in CML. “Focusing on QoL might be more appropriate for the definition of intolerance”. (Pinilla-ibarz, Cortes, Mauro, Cancer, 2010)

Availability of more than one therapeutic option and need to identify additional treatment outcomes based on which making more informed decisions.
Targeted therapies have now reached outstanding efficacy and will all have similar clinical outcomes. In such a scenario, QoL will be of particular value in evaluating overall treatment effectiveness (Efficace et al, Crit Rev Oncol Hematol, 2011).

(Marin D, ASH Educational Book, 2012).
Who should measure symptoms or QoL?

Information: Pressure, Temperature, Blood test

Instrument: Blood pressure cuff, Thermometer, Syringe

Symptoms:
- Nausea
- Pain
- Fatigue

Ask the Patient!

QoL Instruments:
- Structured Questionnaires
- Valid
- Reliable (reproducible)

The Patient is the only source of data
# EORTC QLQ-CML24

Patients sometimes report that they have the following symptoms or problems. Please indicate the extent to which you have experienced these symptoms or problems during the past week. Please answer by circling the number that best applies to you.

## During the past week:

<table>
<thead>
<tr>
<th>Question</th>
<th>Not at All</th>
<th>A Little</th>
<th>Quite a Bit</th>
<th>Very Much</th>
</tr>
</thead>
<tbody>
<tr>
<td>31. Have you had abdominal pains or cramps?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>32. Have you had a dry mouth?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>33. Have you been concerned about changes in your weight?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>34. Have you had skin problems (e.g. color changes, itchy, dry or flaking skin)?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>35. Have you had headaches?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>36. Have you had aches or pains in your muscles or joints?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>37. Have you had hair loss?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>38. Have you sweated excessively?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>39. Have you had acid indigestion or heartburn?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>40. Have you felt drowsy?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>41. Have you experienced any swelling in certain parts of your body (e.g. ankles, legs or around your eyes)?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>42. Have you had to urinate frequently?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
</tbody>
</table>
What do we know about TKIs therapy and Quality of Life in CML patients?


- Systematic review
- All studies including a PRO in CML patients treated with TKI
- 1990-October 2012

RESULTS:

- 8 studies
- 4 studies on Imatinib therapy only
- 4 studies on TKIs other than imatinib
How is Quality of Life of CML patients treated with long-term **Imatinib** and in CCyR compared to the general population?

**PHYSICAL HEALTH**
- Physical functioning (PF)
- Role limitations due to physical health problems
- Bodily pain
- General health perceptions

**MENTAL HEALTH**
- Vitality
- Social Functioning
- Role limitations due to emotional problems
- Mental health

*Analyses Adjusted by: Age, Gender, Education, Living arrangements, Geographical region*

To what extent patients can perform daily activities

**PHYSICAL HEALTH** by age categories

Patient-Reported Symptoms
Chronic Symptoms in CML Patients treated with TKI (i.e. Imatinib)

Duration of treatment: 5 years (median)

Which is the symptom affecting the most Quality of Life

Main Symptoms related to Imatinib therapy

- Abdominal Discomfort
- Nausea
- Fatigue
- Musculoskeletal Pain
- Diarrhea
- Edema
- Headache
- Skin Problems
- Muscular Cramps
- Nausea
- Diarrhea

PHYSICAL HEALTH by Fatigue Severity

<table>
<thead>
<tr>
<th>SF-36 Scale</th>
<th>Δ=Low-Medium vs. Low Fatigue</th>
<th>Δ=Medium-High vs. Low Fatigue</th>
<th>Δ=High Fatigue vs. Low Fatigue</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical Functioning</td>
<td>-10.70</td>
<td>-20.65</td>
<td>-40.40</td>
</tr>
<tr>
<td>Role Physical</td>
<td>-16.49</td>
<td>-43.12</td>
<td>-70.44</td>
</tr>
<tr>
<td>Bodily Pain</td>
<td>-12.85</td>
<td>-22.24</td>
<td>-45.78</td>
</tr>
<tr>
<td>General Health</td>
<td>-11.18</td>
<td>-25.53</td>
<td>-38.29</td>
</tr>
</tbody>
</table>

MENTAL HEALTH by Fatigue Severity

**Graph:**
- **Vitality**
- **Social Functioning**
- **Role Emotional**
- **Mental Health**

**Table: SF-36 Scale**

<table>
<thead>
<tr>
<th>SF-36 Scale</th>
<th>Δ-Low-Medium vs. Low Fatigue</th>
<th>Δ-Medium-High vs. Low Fatigue</th>
<th>Δ-High Fatigue vs. Low Fatigue</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vitality</td>
<td>-13.82</td>
<td>-23.93</td>
<td>-43.93</td>
</tr>
<tr>
<td>Social Functioning</td>
<td>-8.06</td>
<td>-17.33</td>
<td>-40.11</td>
</tr>
<tr>
<td>Role Emotional</td>
<td>-14.11</td>
<td>-32.99</td>
<td>-62.88</td>
</tr>
<tr>
<td>Mental Health</td>
<td>-8.35</td>
<td>-16.2</td>
<td>-33.47</td>
</tr>
</tbody>
</table>

Fatigue and its relationships with other symptoms in CML Patients

Legend:
- Not at all
- Mild
- Moderate/severe

Can we use current physician-reported toxicity criteria to define “intolerance” in CML patients?

Can we use CTC criteria to define “intolerance” in CML patients?


Common Terminology Criteria for Adverse Events v3.0 (CTCAE)

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>Short Name</th>
<th>Grade</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ulcer, GI</td>
<td>Ulcer, GI – Select</td>
<td>Asymptomatic; radiographic or endoscopic findings only</td>
<td>Symptomatic; altered GI function (e.g., altered dietary habits, oral supplements); IV fluids indicated &lt;24 hrs</td>
<td>Symptomatic and severely altered GI function (e.g., inadequate oral caloric or fluid intake); IV fluids, tube feedings, or TPN indicated ≥24 hrs</td>
<td>Life-threatening consequences</td>
<td>Death</td>
<td></td>
</tr>
<tr>
<td>Anus</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>Cecum</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Colon</td>
<td></td>
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<tr>
<td>Duodenum</td>
<td></td>
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<tr>
<td>Esophagus</td>
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<td></td>
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</tr>
<tr>
<td>Ileum</td>
<td></td>
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<tr>
<td>Jejunum</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Rectum</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Small bowel NOS</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Stoma</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stomach</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>ALSO CONSIDER: Hemorrhage, GI – Select.</td>
<td></td>
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<td></td>
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<td></td>
</tr>
<tr>
<td>Vomiting</td>
<td>Vomiting</td>
<td>1 episode in 24 hrs</td>
<td>2 – 5 episodes in 24 hrs; IV fluids indicated &lt;24 hrs</td>
<td>≥6 episodes in 24 hrs; IV fluids, or TPN indicated ≥24 hrs</td>
<td>Life-threatening consequences</td>
<td>Death</td>
<td></td>
</tr>
<tr>
<td>ALSO CONSIDER: Dehydration.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gastrointestinal – Other (Specify, ___)</td>
<td>GI – Other (Specify)</td>
<td>Mild</td>
<td>Moderate</td>
<td>Severe</td>
<td>Life-threatening; disabling</td>
<td>Death</td>
<td></td>
</tr>
</tbody>
</table>

Mild severity
How accurate are Hematologists in estimating Symptom severity of their patients?  
(N=422 patient-physician comparisons)

Conclusions

- Very few evidence-based data exist on the impact of Targeted therapies on CML Patient’s Quality of Life. Urgent efforts needed...

- Younger patients (18-59 years) - treated with imatinib - are those whose Quality of Life is mostly impaired compared to their peers in the general population.

- Quality of Life of older patients (>60 years) is basically comparable to that of their peers in the general population.

- Fatigue is the most important aspect compromising Patients daily life.

- Physicians tend to underestimate symptom severity of their Patients
Thanks all for your attention!