Is there a possibility to cure APL without chemotherapy in the future?

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Curability of APL without Chemotherapy (or with minimal use of chemotherapy)

Long-lasting remissions have been reported

• ATRA ➔ Maintenance therapy (ATRA + MTX + 6MP) in anecdotal cases¹

• Liposomal ATRA monotherapy was curative in 10/26 patients with WBC <10,000 (MDACC)²

• Arsenic trioxide ± ATRA

<table>
<thead>
<tr>
<th></th>
<th>Iran(^1)</th>
<th>India(^2)</th>
<th>USA(^3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>197</td>
<td>72</td>
<td>82</td>
</tr>
<tr>
<td>CR rate</td>
<td>85</td>
<td>86</td>
<td>92</td>
</tr>
<tr>
<td>Median follow up</td>
<td>38 m</td>
<td>60 m</td>
<td>99 w</td>
</tr>
<tr>
<td>OS, 5-years</td>
<td>67</td>
<td>74</td>
<td>76</td>
</tr>
<tr>
<td>EFS, 5-years</td>
<td>NA</td>
<td>69</td>
<td>77</td>
</tr>
<tr>
<td>DFS, 5-years</td>
<td>64</td>
<td>80</td>
<td>NA</td>
</tr>
</tbody>
</table>

Is there a possibility to cure APL without chemotherapy in the future?

Yes
Is ATO-based better than chemo-based treatment for APL?

Standard approach
- CHT
- ATRA

Alternative approach
- ATRA
- ATO

Lack of published studies comparing these approaches

Ongoing randomized studies comparing both approaches
- British NCRI in all risk groups
Is ATO-based better than chemo-based treatment in a particular APL setting?

Standard approach

- CHT
- ATRA

Alternative approach

- ATRA
- ATO

Lack of published studies comparing these approaches

Ongoing randomized studies comparing both approaches

- GIMEMA-SAL-AMLSG in low- and intermediate-risk
### ATO-based vs. Chemo-based treatment

#### Potential scenarios

<table>
<thead>
<tr>
<th>Efficacy</th>
<th>Safety</th>
<th>Cost-effectiveness</th>
</tr>
</thead>
<tbody>
<tr>
<td>ATO &gt; chemo</td>
<td>ATO &gt; chemo</td>
<td>Highly probable ATO should be non cost-effective</td>
</tr>
<tr>
<td>ATO = chemo</td>
<td>ATO = chemo</td>
<td>ATO should be non cost-effective</td>
</tr>
<tr>
<td>ATO &lt; chemo</td>
<td>ATO = chemo</td>
<td></td>
</tr>
</tbody>
</table>
# Direct cost in euros of antileukemic drugs for a standard patient with APL

Patient: 1.8 m² (70 kg)

<table>
<thead>
<tr>
<th>Phase</th>
<th>ATRA</th>
<th>Idarubicin</th>
<th>ATO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Induction</td>
<td>655.20</td>
<td>1,390.62</td>
<td>13,399.05</td>
</tr>
<tr>
<td>Consol 1</td>
<td>280.80</td>
<td>582.12</td>
<td>9,570.75</td>
</tr>
<tr>
<td>Consol 2</td>
<td>280.80</td>
<td>568.80</td>
<td>9,570.75</td>
</tr>
<tr>
<td>Consol 3</td>
<td>280.80</td>
<td>349.27</td>
<td>9,570.75</td>
</tr>
<tr>
<td><strong>Total €</strong></td>
<td>1,497.60</td>
<td><strong>2,890.81</strong></td>
<td><strong>42,111.30</strong></td>
</tr>
</tbody>
</table>

Idarubicin: 16.17 € per mg; Mitoxantrone 6.32 € per mg; ATO: 36.46 € per mg; ATRA: 0.234 € per mg
Direct cost in euros of antileukemic drugs for a standard patient with APL

Patient: 1.8 m² (70 kg)

<table>
<thead>
<tr>
<th>Induction</th>
<th>Consol 1</th>
<th>Consol 2</th>
<th>Consol 3</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>ATRA</td>
<td>Idarubicin</td>
<td>ATO</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10000</td>
<td>20000</td>
<td>30000</td>
<td>40000</td>
<td>50000</td>
</tr>
</tbody>
</table>

Cost in Euros
Are these treatment options mutually exclusive?

- Standard approach: CHT, ATRA
- Alternative approach: ATRA, ATO

The “Third Way” approach: CHT, ATRA, ATO
The “third way” approach to cure APL

Three studies suggest an advantage of the **triple combination** of ATO, ATRA and chemotherapy:

• Shanghai study
• US intergroup study
• Australasian Leukaemia and Lymphoma Group study

PETHEMA/HOVON LPA2012 TRIAL

**CONSOLIDATION CHEMOTHERAPY**

2 cycles

**INDUCTION (AIDA)**

- Idarubicin
- Mitoxantrone
- Ara-C

**MAINTENANCE THERAPY**

- ATRA + 6MP + MTX

**Low risk**
- ATO
- ATRA

**High risk**
- ATO
- ATRA

**Idarubicin**
- Red

**Mitoxantrone**
- Blue

**Ara-C**
- Yellow
Curative Strategies in APL
Closing remarks

• A balanced administration of ATRA, chemotherapy, and ATO has emerged as a “third way” approach.

• Several strategies have been designed to obtain maximum efficacy and minimum toxicity of each component of this triple combination.