Identification of genetic markers as tools for risk stratification and treatment selection in very old acute myeloid leukemia patients

Patients with acute myeloid leukemia (AML), median age 76 (75-86 years)

**Induction chemotherapy**

<table>
<thead>
<tr>
<th></th>
<th>Overall</th>
<th>High-dose cytarabine and mitoxantrone (HAM)</th>
<th>Standard-dose cytarabine, daunorubicin and 6-thioguanine (TAD-9)</th>
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</thead>
<tbody>
<tr>
<td>Complete remission (CR)</td>
<td>44%</td>
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<tr>
<td>Median event-free survival (EFS)</td>
<td>1.7 months</td>
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<td>Median relapse-free survival (RFS)</td>
<td>12 months</td>
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<tr>
<td>Median overall survival (OS)</td>
<td>6 months</td>
<td>7.8 months</td>
<td>3.1 months p=0.09</td>
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<td>Three-year OS</td>
<td>21%</td>
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**Analysis of 64 genes recurrently mutated in AML**

- Identification of 622 driver mutations
- Median number of 4 mutated genes per patient (range, 1-10 mutations/patient)
- Most frequently mutated genes
  - TET2 42%  
  - DNMT3A 35%  
  - NPM1* 32%  
  - SRSF2 25%  
  - ASXL1 21%  
  - RUNX1 19%  
  - FLT3-ITD* 18%  
  - FLT3-TKD 12%  
  - IDH2 15%  
  - TP53 14%  
  - NRAS 17%  
  - IDH1 9%
- The number of mutated genes per patient was not associated with OS
- **Univariate analysis**
  - IDH1 was the only gene significantly associated with OS

  **IDH1 mutations were identified as the strongest genetic predictor of shorter survival**

*no significant impact on OS*

Prassek et al., Haematologica, 2018