Session 6
Genetics Revealing the Biology of Myeloid Neoplasms, Excluding Acute Leukemias

Session Chairs

Prof. Dr. med. Falko Fend
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Session 4: Genetic Testing in the Diagnosis of Myeloid Neoplasms (Excluding Acute Leukemias)
Chairs: Robert Hasserjian and Todd Kelley

Session 6: Genetics Revealing the Biology of Myeloid Neoplasms (Excluding Acute Leukemias)
Chairs: Falko Fend and Elizabeth Morgan

Session 3: Genetic Testing in Diagnosis of Acute Leukemias
Chairs: Daniel Arber and Marian Harris

Session 7: Genetics Revealing the Biology of Acute Leukemias
Chairs: Magdalena Czader and David Czuchlewski

Session 2: Genetic Testing in the Diagnosis of Lymphoid Neoplasms
Chairs: Miguel Piris and Rebecca King

Session 8: Genetics Revealing the Biology of Lymphoid Neoplasms
Chairs: Megan Lim and Nate Bailey
<table>
<thead>
<tr>
<th>WHO myeloid neoplasm and acute leukemia classification</th>
<th>Myelodysplastic/myeloproliferative neoplasms (MDS/MPN)</th>
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<tbody>
<tr>
<td>Myeloproliferative neoplasms (MPN)</td>
<td>Chronic myeloid leukemia (CML), <em>BCR-ABL</em>&lt;sup&gt;+&lt;/sup&gt;</td>
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<tr>
<td>Chronic myeloid leukemia (CML)</td>
<td>Atypical chronic myeloid leukemia (aCML), <em>BCR-ABL</em>&lt;sup&gt;−&lt;/sup&gt;</td>
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<td>Chronic neutrophilic leukemia (CNL)</td>
<td>Juvenile myelomonocytic leukemia (JMML)</td>
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<td>Polycythemia vera (PV)</td>
<td>MDS/MPN with ring sideroblasts and thrombocytosis (MDS/MPN-RS-T)</td>
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<td>Primary myelofibrosis (PMF)</td>
<td>MDS/MPN, unclassifiable</td>
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<td>PMF, prefibrotic/early stage</td>
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<td>PMF, overt fibrotic stage</td>
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<td>Essential thrombocytemia (ET)</td>
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<td>Chronic eosinophilic leukemia, not otherwise specified (NOS)</td>
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<td>MPN, unclassifiable</td>
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<td>Mastocytosis</td>
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<td>Myeloid/lymphoid neoplasms with eosinophilia and rearrangement of <em>PDGFRα, PDGFRβ, or FGFR1, or with PCM1-JAK2</em></td>
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<td>Myeloid/lymphoid neoplasms with <em>PDGFRα</em> rearrangement</td>
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<td>Myeloid/lymphoid neoplasms with <em>FGFR1</em> rearrangement</td>
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<td><em>Provisional entity: Myeloid/lymphoid neoplasms with PCM1-JAK2</em></td>
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<td>Blastic plasmacytoid dendritic cell neoplasm</td>
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Polycythemia Vera


High throughput genetic analysis has identified a large number of recurrent alterations in myeloid neoplasms with chronic evolution:
- diagnosis
- prognosis
- therapeutic decisions

**Challenges**
- genetic complexity
- many alterations are not disease-specific
- serial acquisition or loss of mutations
- co-mutation patterns
- pre-malignant states

Topics of Session 6: Genetics Revealing the Biology of Myeloid Neoplasms

• Chronic myeloid leukemia (CML):
  – Atypical genetic/phenotypic features of blast crisis (7 cases)
  – CML with other myeloproliferative or lymphoid neoplasm (4 cases)

• Ph-negative myeloproliferative neoplasms (MPN)
  – MPN with multiple or unusual/non-canonical driver mutations (7 cases)
  – MPN with atypical progression or transformation (3 cases)

• Myelodysplastic syndromes (MDS)
  – Atypical clinical presentation or disease association (3 cases)
  – Atypical mutations, e.g. 5q- with JAK2 or MPL mutations (7 cases)

• MDS/MPN and other myeloid neoplasms
  – Atypical mutations or associated mastocytosis (7 cases)

• Myeloid/lymphoid neoplasm with PDGFRA rearrangement (1 case)
Questions Arising from Session 6

- The role and clinical impact of (extensive) genetic testing in unusual presentations or disease progression in “chronic” myeloid neoplasms

- The interpretation of typical driver mutations in atypical clinical and morphologic settings: classification issues
  - **JAK2** or **MPL** in MDS
  - **SF3B1** in MPN
  - **NPM1** in chronic myeloid neoplasms (CMML, aCML)

- Recognition and classification of unusual types of disease progression

- Interpretation of non-canonical variants in typical driver genes
6 Oral Presentations

• *Genetics revealing unusual disease progression*
  – #68: Dr. Al-Ghamdi

• *Shared genetic origin*
  – #244: Dr. Mroz

• *Typical driver mutation in atypical setting*
  – #267: Dr. Liontos

• *Myeloproliferative neoplasm with alteration of morphology/presentation reflecting underlying genetics*
  – #207: Dr. Nam
  – #238: Dr. Boiocchi

• *Overlapping genetic and molecular features*
  – #159: Dr. Lewis
Summary of 33 Additional Submitted Cases