

***Base molecolare delle malattie  
mieloproliferative croniche e  
sviluppo di nuove terapie***

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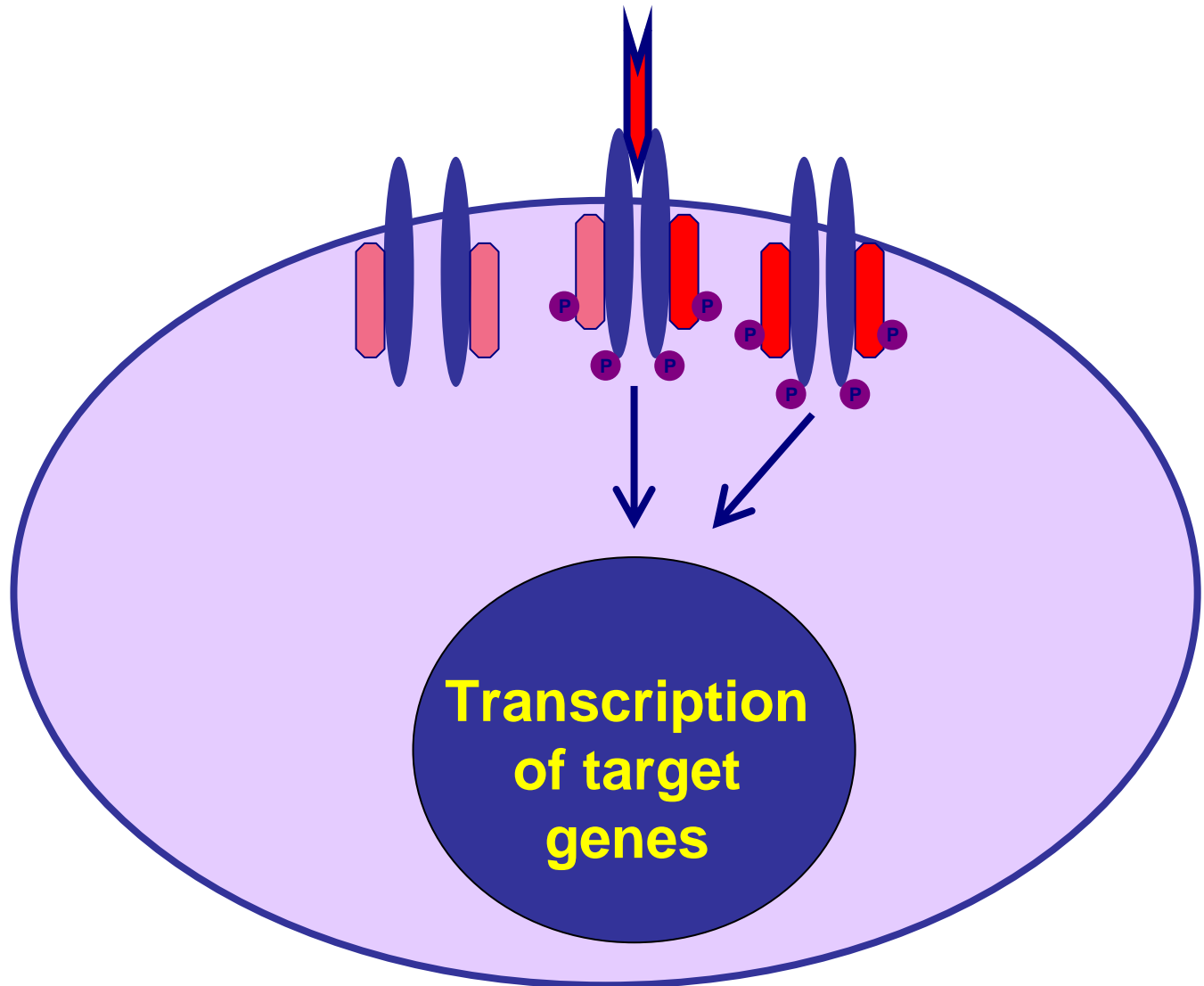
***Università di Pavia &***

***Fondazione IRCCS Policlinico***

***San Matteo, Pavia***

# *Jak2 in signal transduction of homodimeric type I cytokine receptors*

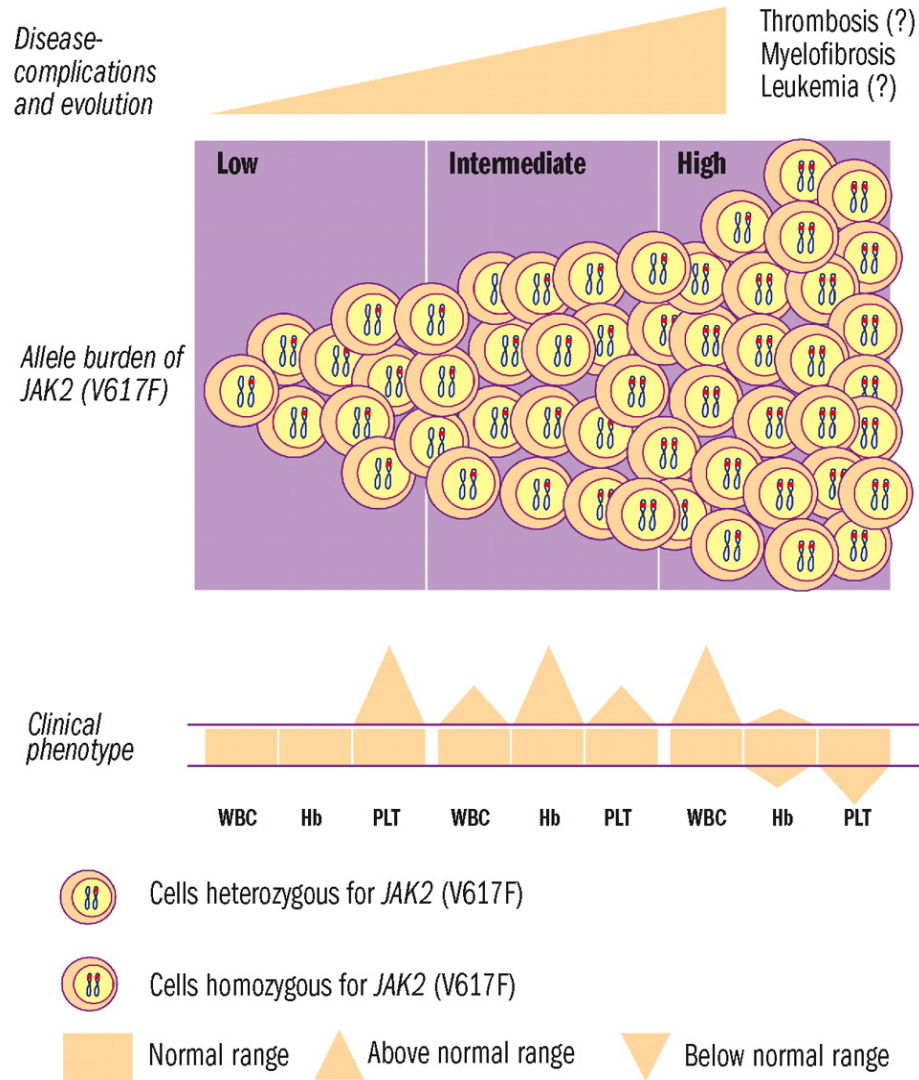
***EPO R***  
***G-CSF R***  
***TPO R***



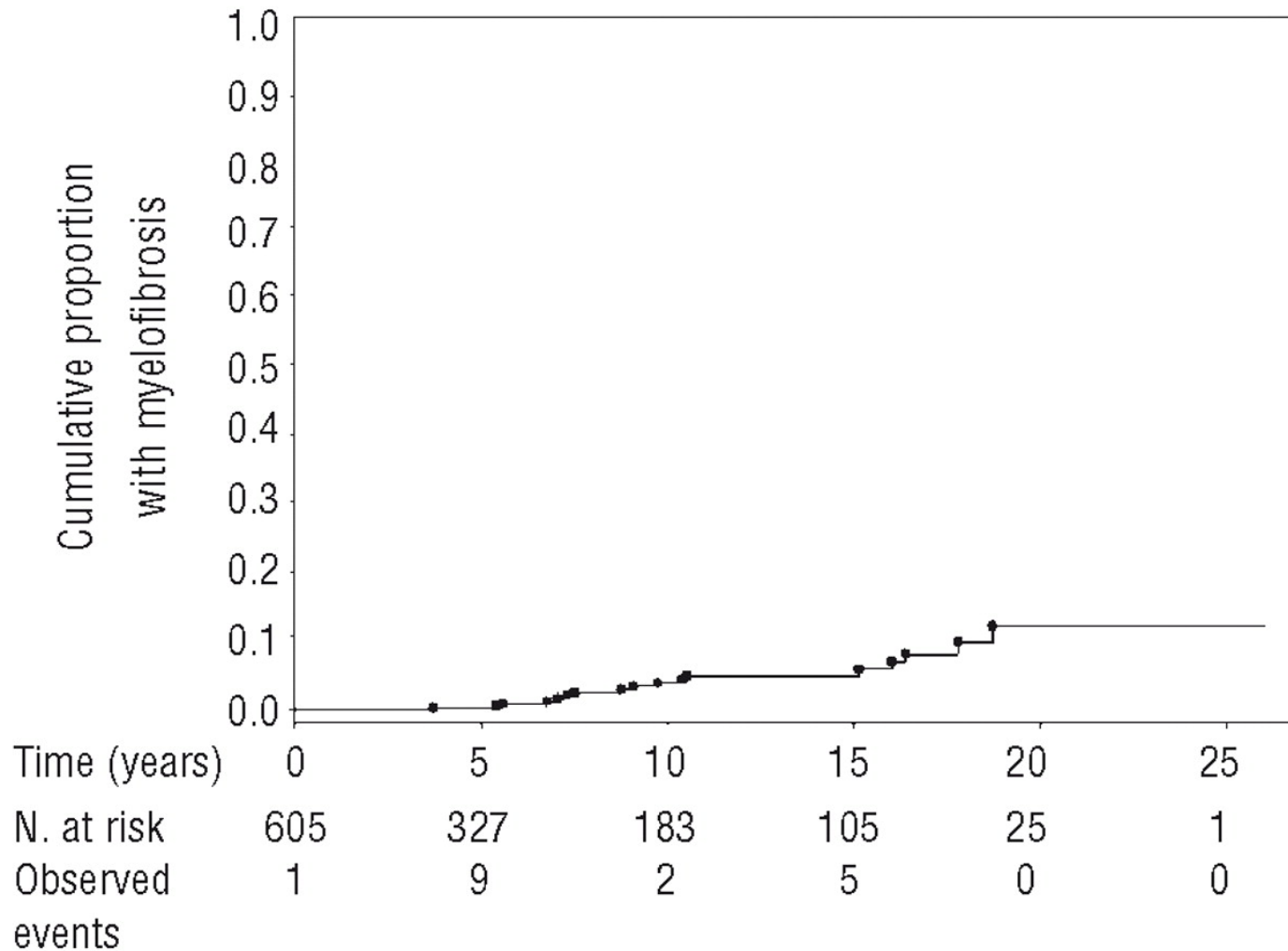
# *Molecular basis of Philadelphia-negative myeloproliferative neoplasms*

<b>Polycythemia vera:</b>	<b>~95% <i>JAK2</i> (V617F)</b> <b>~2-3% <i>JAK2</i> exon 12</b>
<b>Essential thrombocythemia:</b>	<b>50-60% <i>JAK2</i> (V617F)</b> <b>~5% <i>MPL</i> exon 10</b>
<b>Primary myelofibrosis</b>	<b>50-60% <i>JAK2</i> (V617F)</b> <b>5-10% <i>MPL</i> exon 10</b>

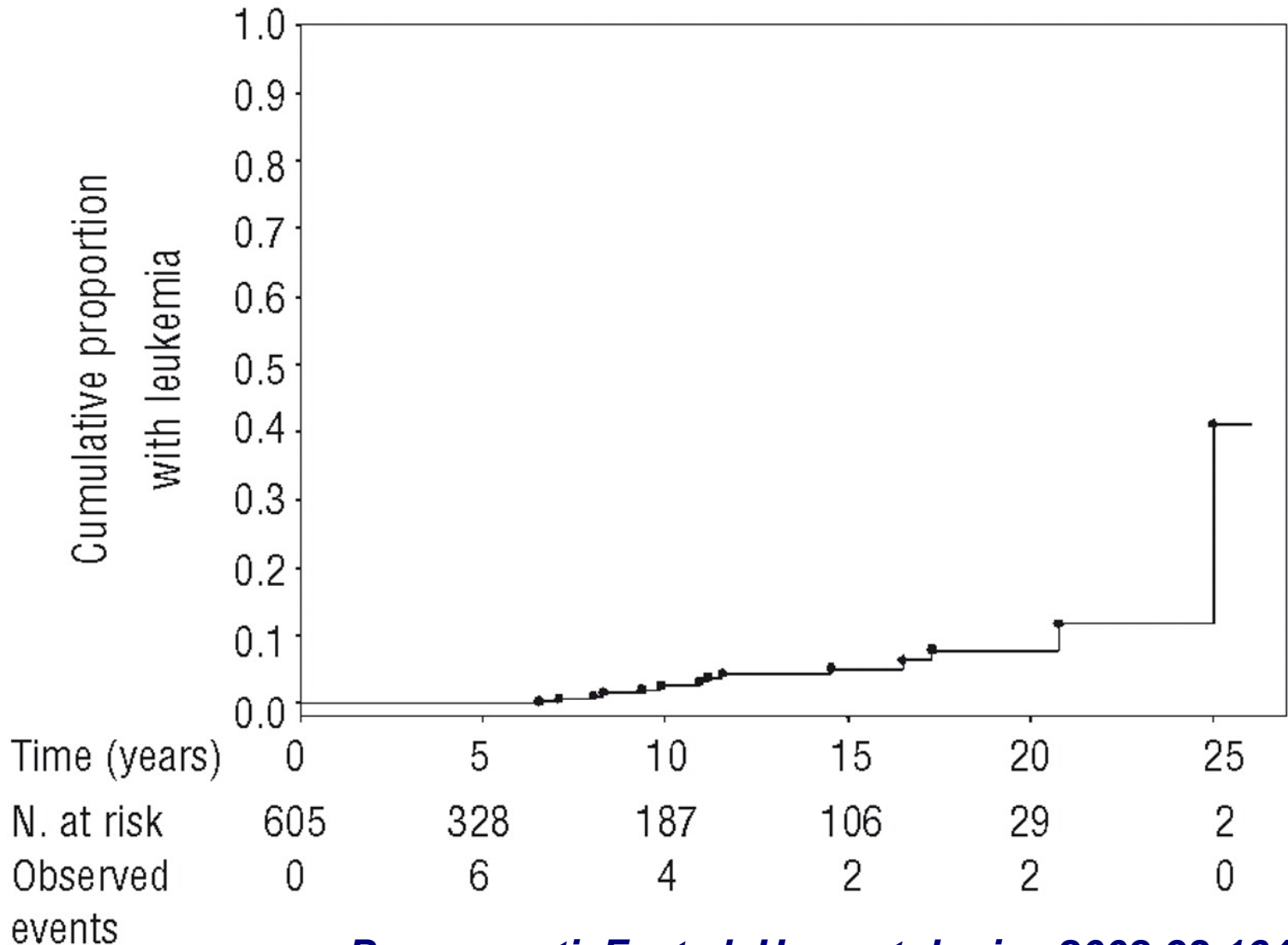
# Schematic representation of JAK2 (V617F) allele burden and its relationship with clinical phenotype, and disease progression



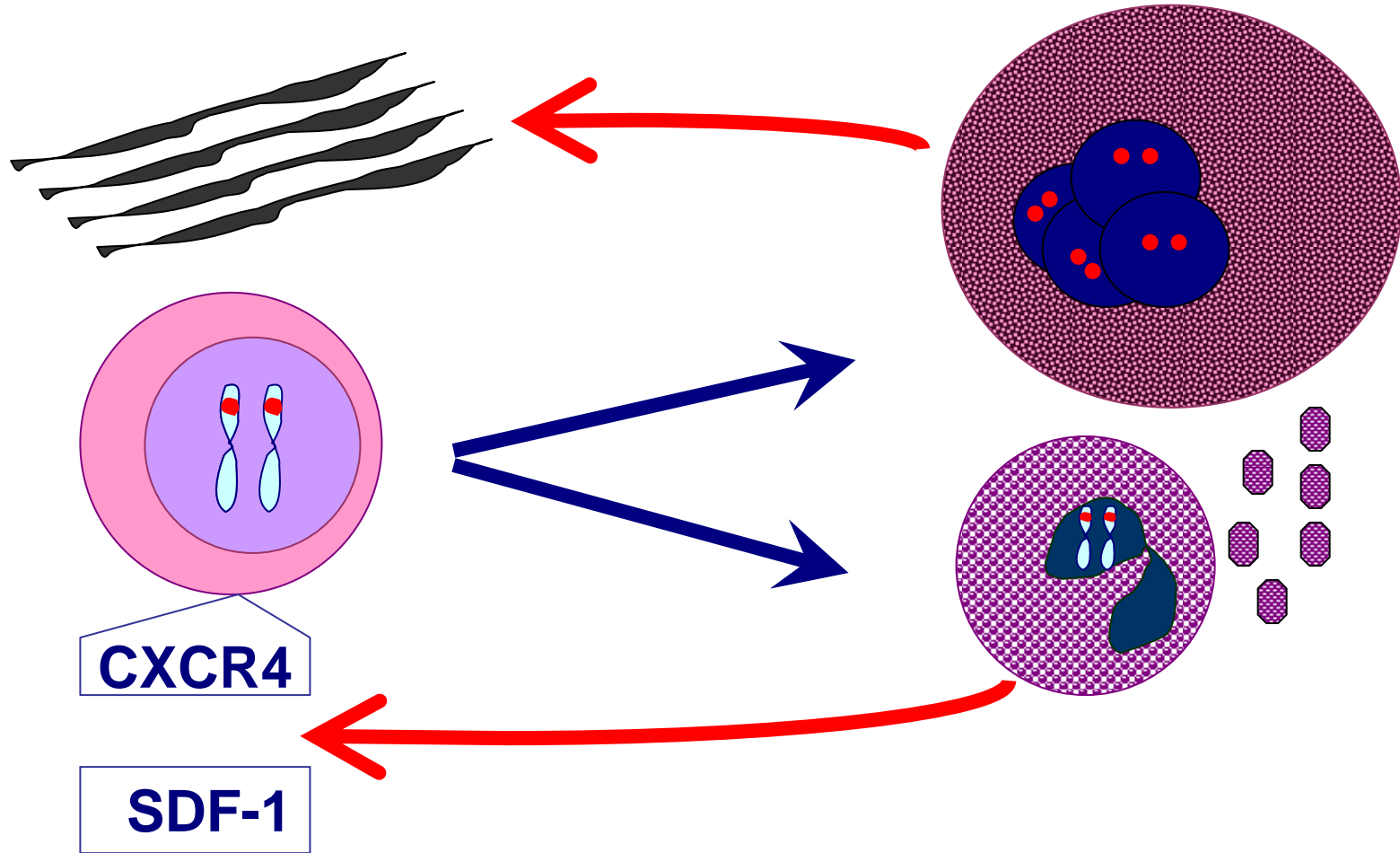
# ***Risk of myelofibrosis in 605 patients with essential thrombocythemia***



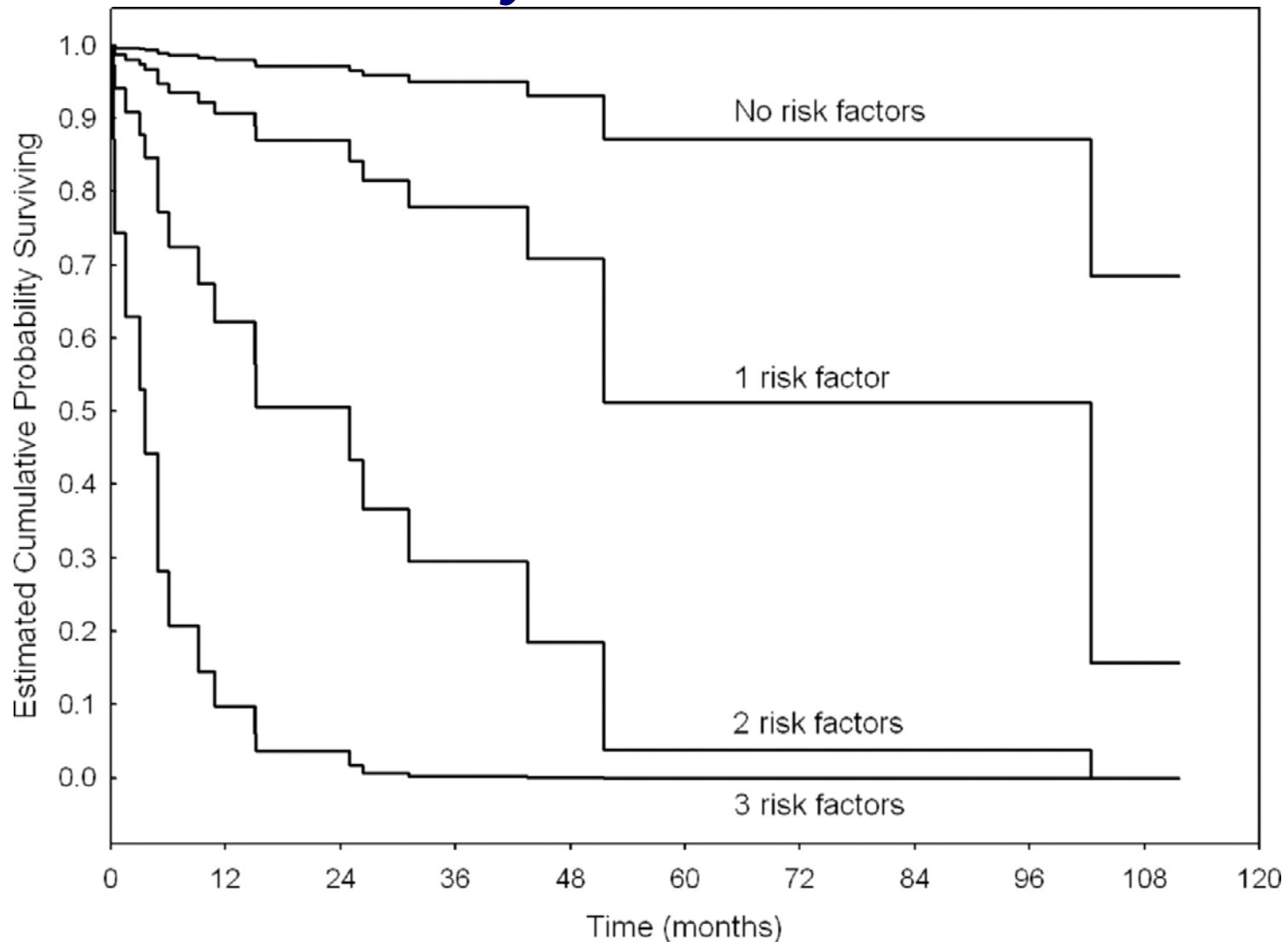
# ***Risk of leukemia in 605 patients with essential thrombocythemia***



# *Progression to myelofibrosis: abnormal stem cell trafficking and megakaryocyte activation*



# ***A dynamic prognostic model to predict survival in post-polycythemia vera myelofibrosis***



# ***Current treatment of chronic myeloproliferative neoplasms***

- **Low dose aspirin**
- **Phlebotomy (PV)**
- **Cytoreductive therapy (hydroxyurea)**
- **Anagrelide**
- **Interferon alfa**

## ***Kinase inhibitors***

**Lestaurtinib (CEP701, for activated FLT3 in AML)**

**Erlotinib (for mutated EGFR)**

**ITF2357 (histone deacetylase inhibitor)**

**TG101348 (selective inhibitor of JAK2)**

**INCB018424 (inhibitor of JAK1 and JAK2)**