



# Diagnostic and Pre-treatment Work-up

**François Guilhot**



# **Chronic Myelogenous Leukemia**

**Diagnosis and pre-treatment work-up**

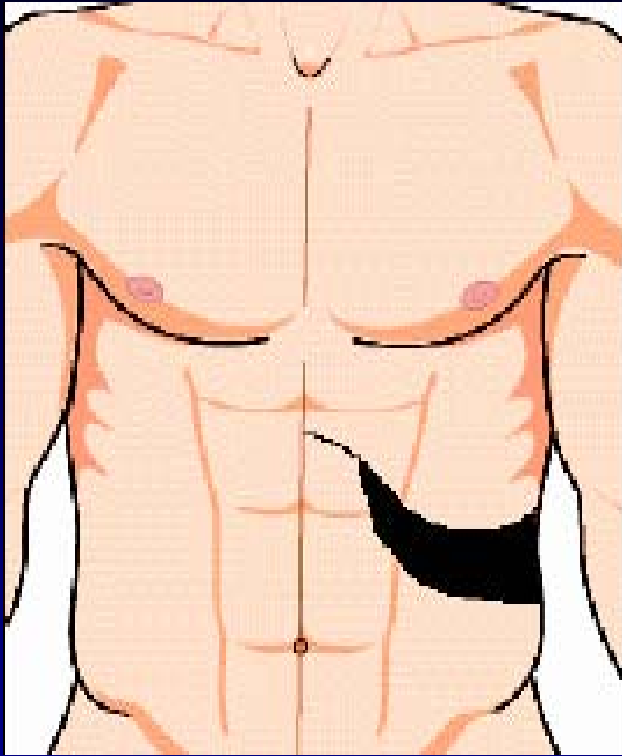
**Guidelines**

**Expert recommendations**

# 3 parts

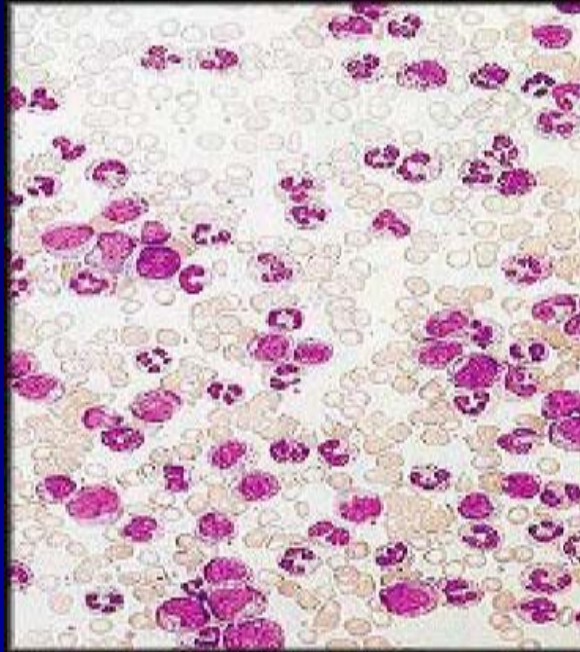
- **Diagnosis**
- **Pre therapeutic assessment**
- **Staging and prognosis**

# DIAGNOSIS

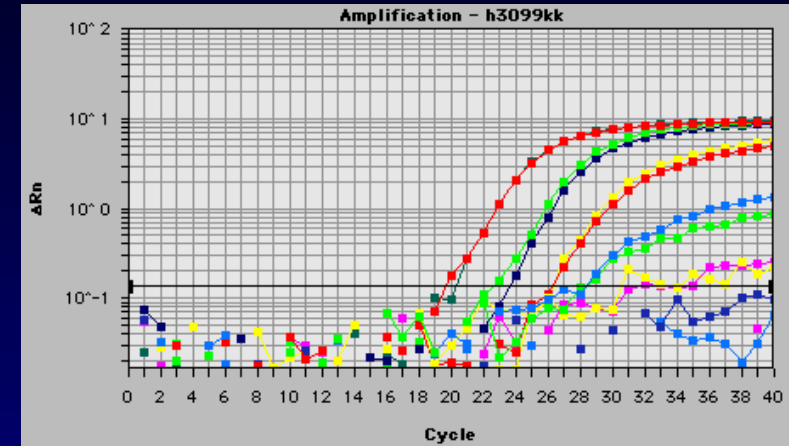


Spleen

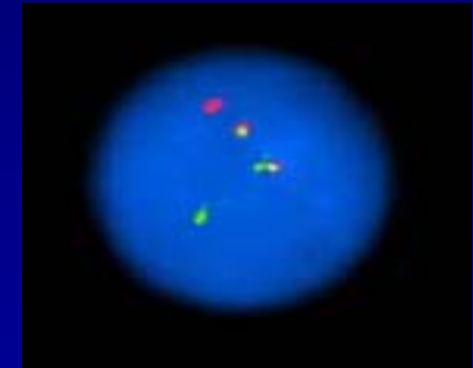
Quantitative reverse transcriptase  
polymerase chain reaction (RT-PCR)



Blood smear



FISH



Bcr-Abl rearrangement

# Cytogenetics - FISH

- **Bone marrow aspiration for cytogenetics**
- **FISH on peripheral blood**
  - **Dual probes for BCR and ABL genes**
  - **Detection of cytogenetically « silent » BCR-ABL rearrangements**
  - **Deletion in the derivative 9q+ (prognostic)**

# Cytogenetics

## Clonal evolution

second Ph chromosome

trisomy 8

isochromosome 17

trisomy 19



**Major route**

**-Y, +21, +17, -7**

# **Relationship between chromosome abnormalities and outcome**

**Lower cytogenetic response rate**

**Higher hematologic relapse rate (50% versus 9%)**

**Shorter overall survival (90% versus 75% at 2 years)**

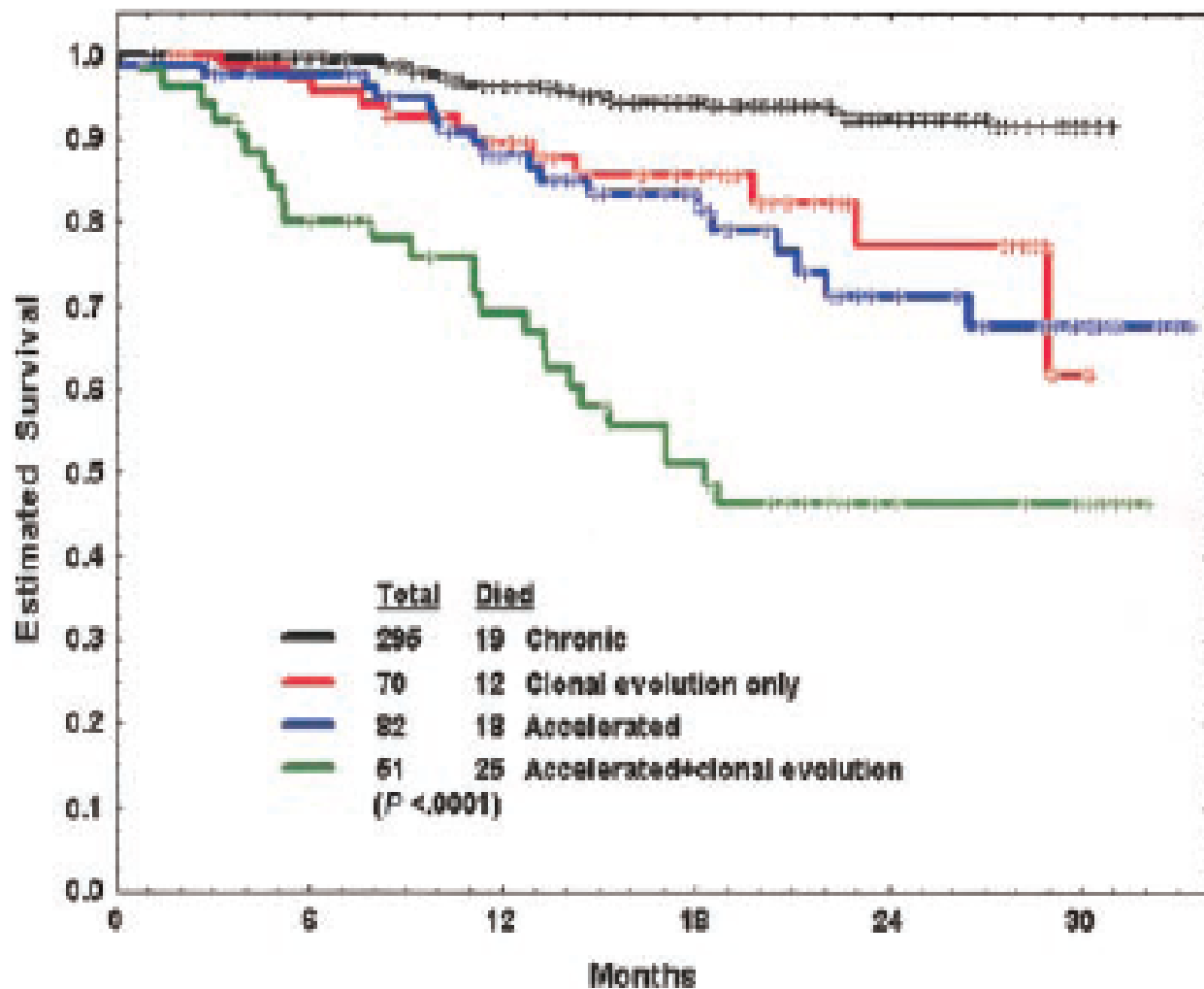


Figure 1. Survival of patients in chronic phase, with cytogenetic clonal evolution only, and in accelerated phase with or without cytogenetic clonal evolution.



# **BONE MARROW BIOPSY**

## **fibrosis**

**CELLS**

**DNA**

**RNA**



**For subsequent analysis**

## Fibrosis and response to Imatinib

110 patients post-IFN failure, chronic phase  
67 (61 %) severe reticulin (grade 3-4) fibrosis

	<b>Yes</b>	<b>No</b>
<b>Complete cytogenetic response</b>	<b>67 %</b>	<b>58 %</b>
<b>4 year survival rates</b>	<b>80 %</b>	<b>88 %</b>
<b>Failure free survival rates</b>	<b>69 %</b>	<b>77 %</b>

(Leukemia Lymphoma, 2005)

## Myelofibrosis in early chronic phase

198 patients

75 patients (38 %) severe reticulin (grade 3-4) fibrosis

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	<b>Yes</b>	<b>No</b>	
<b>Complete cytogenetic response</b>	<b>76 %</b>	<b>89 %</b>	<b>p=0.07</b>
<b>3 year survival rates</b>	<b>87 %</b>	<b>97 %</b>	<b>p=0.04</b>

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15 % of patients with grade 4 = worse outcome

(Cancer, 2005)

# Before starting the treatment with Imatinib

**Yes**

**No**

**Bcr-Abl transcript level**

**\* point mutation**

**% of BM Ph + cells**

**\*Crkl phosphorylation**

**\*genomic profile**

**\*Wilms tumor gene  
expression**

**9q+**

**\*phosphotyrosine  
levels in CD34+ cells**

**Bone marrow biopsy**

# Warning situation

- High risk patients
- Additional chromosomal abnormalities
- 9q+

Warnings imply that the patient should be monitored very carefully and may become eligible for other treatments.

# Pre therapeutic assessment

- **Performance status**
- **Relevant past medical history (psychiatric disorder)**
- **Biochemistry (renal and liver functions)**
- **Platelet dysfunction**
- **Concomitant medications**

# 3 phases

**Chronic phase**

**Accelerated phase**

**Blastic phase**

⇒ **Physical exam**

⇒ **Peripheral blood count ; differential**

⇒ **Bone marrow aspiration**

⇒ **Cytogenetic analysis**

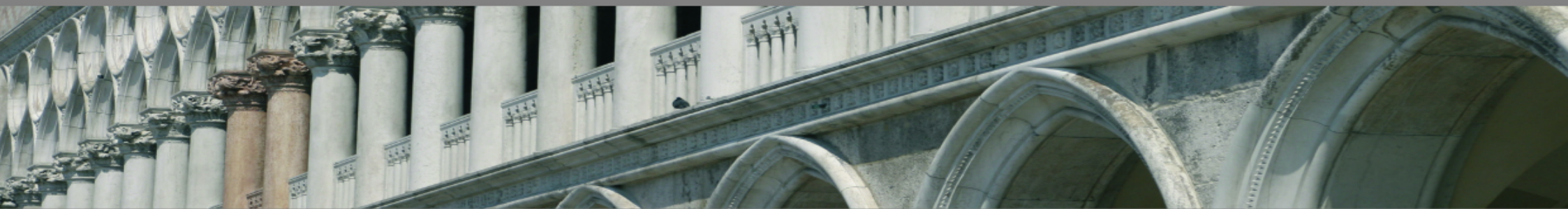
⇒ **Scan. = spleen size**

# **Conclusion: panel recommendations**

- 1. Spleen assessment, complete blood test before any treatment**
- 2. Sokal/Hasford prognostic subcategories**
- 3. Bone marrow aspiration with cytogenetic analysis**
- 4. Cases with warning features**



EVOLVING CONCEPTS IN THE MANAGEMENT OF CHRONIC MYELOID LEUKEMIA



RECOMMENDATIONS FROM AN EXPERT PANEL ON BEHALF OF THE EUROPEAN LEUKEMIANET