

# Concepts in AML Treatment

## The AMLSG Genotype-adapted Approach

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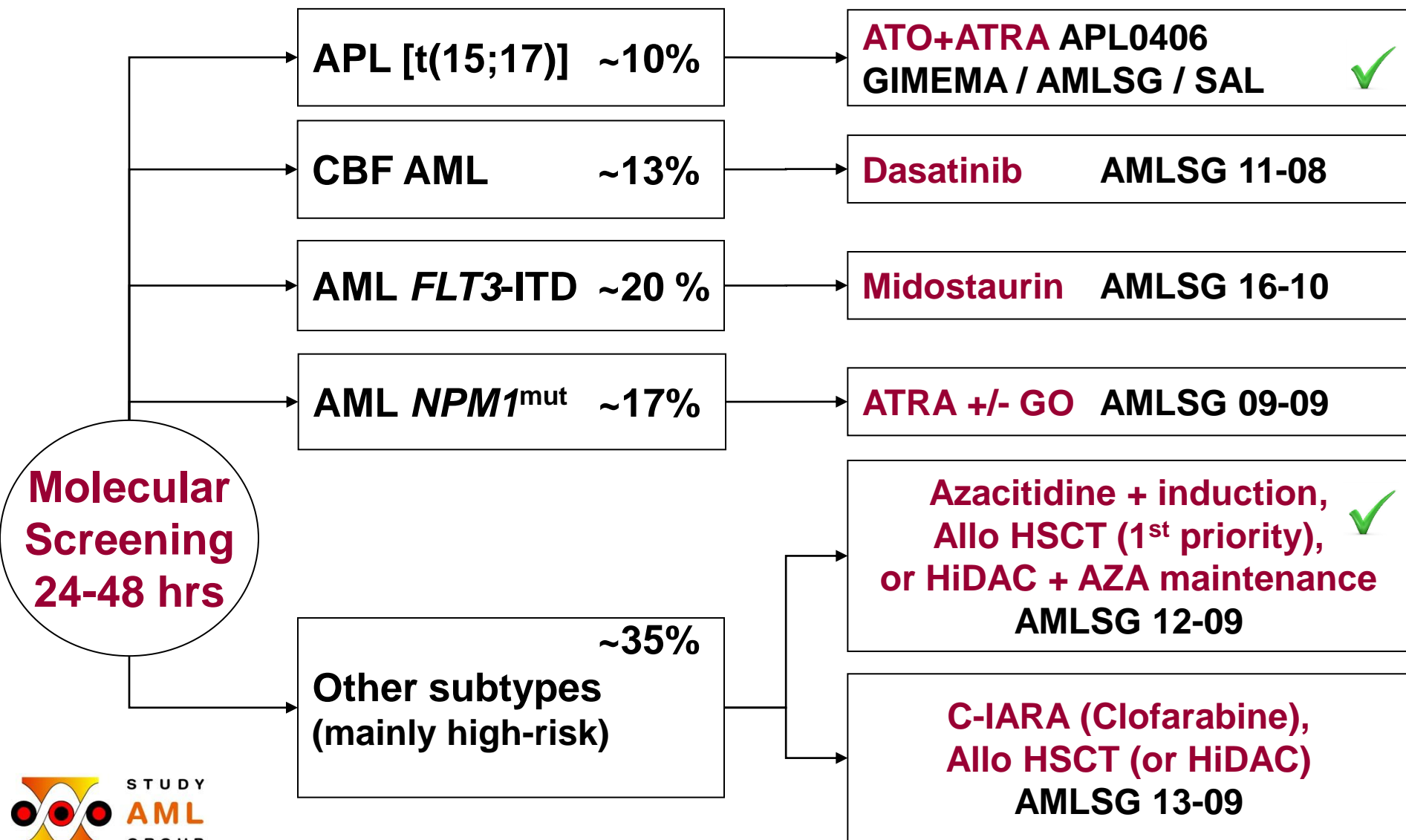
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Co-Chair German MPN-SG**

**Head of Phase I/II Unit  
Head of Clinical Trials Office  
Head of Hematology Lab  
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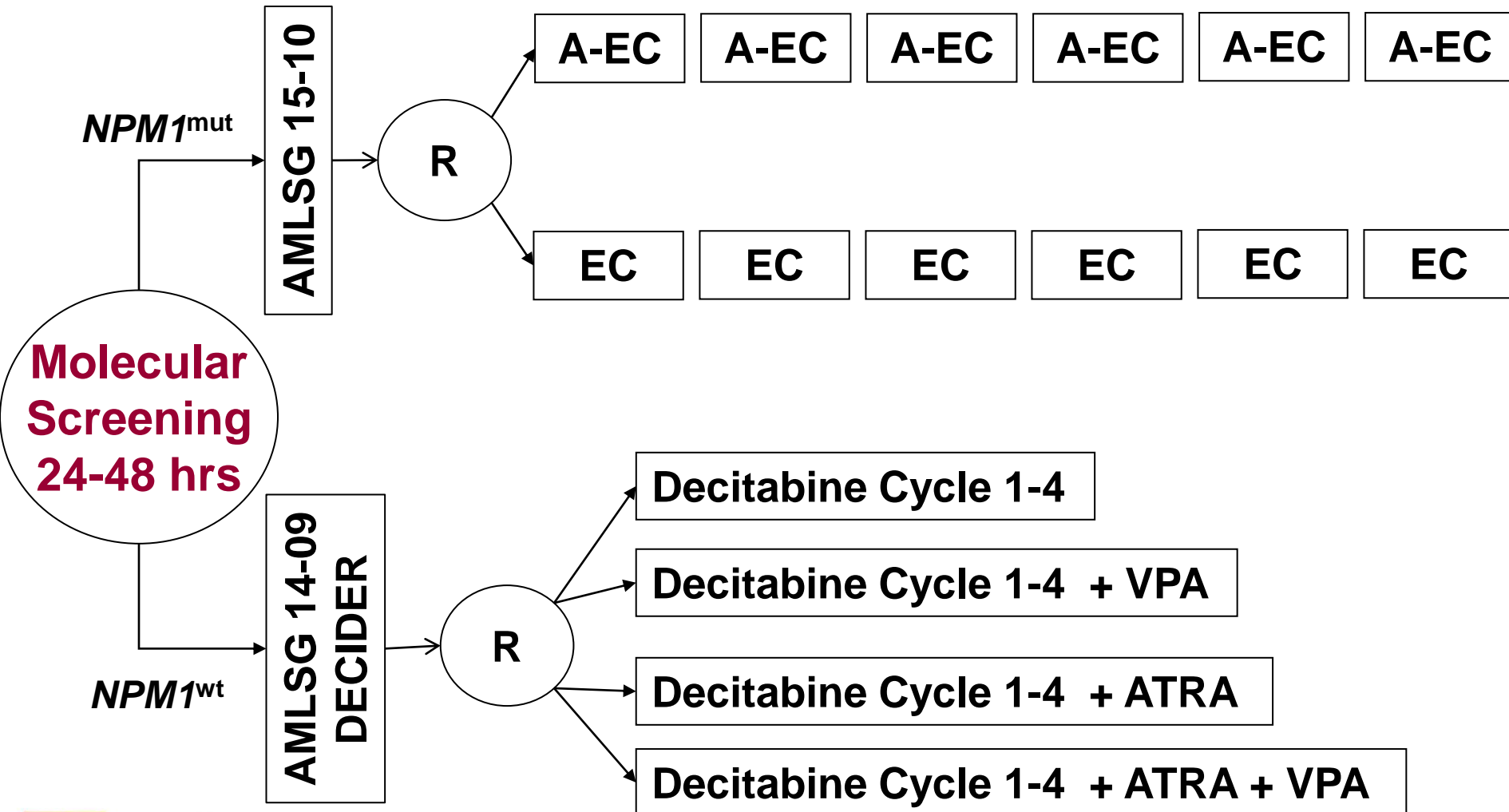
# AMLSG Biomarker-Driven Treatment Trials

## Intensive Treatment

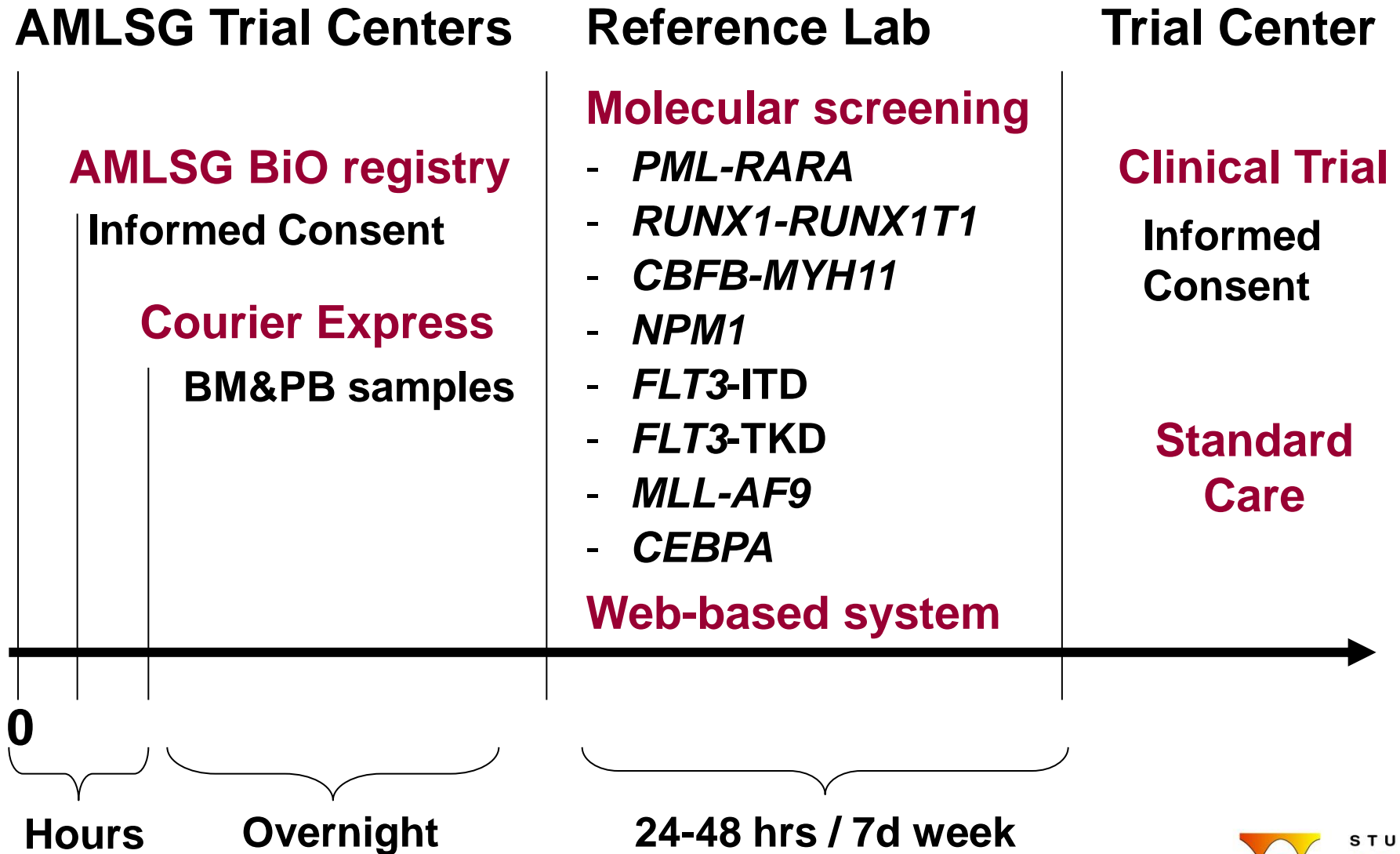


# AMLSG Biomarker-Driven Treatment Trials

## Non-Intensive Treatment



# AMLSG BiO Registry: Fast Biomarker Screening



# AMLSG BiO Registry: Fast Screening

## Within 48 hours

### 1. Flowcytometry

- 8 - 10 color analyses

### 2. Molecular screening

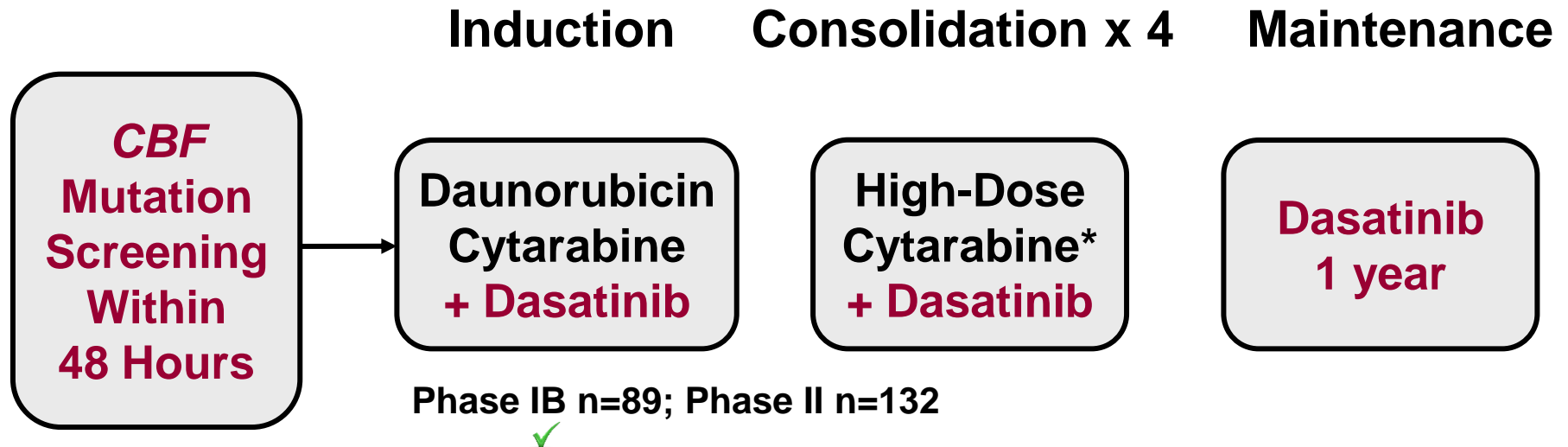
- *PML-RARA*
- *RUNX1-RUNX1T1*
- *CBFB-MYH11*
- *NPM1*
- *FLT3-ITD*
- *FLT3-TKD*
- *MLL-AF9*
- *CEBPA*

- All Reports are available directly in advance by Fax
- Final reports are send out by regular mail
- Bone marrow cytology will be integrated into the concept in mid 2013

## Within 7 days

### 3. Cytogenetics

# Phase IB/II Study of Chemotherapy + Dasatinib in Patients with Newly Diagnosed Core-Binding Factor (CBF) AML - AMLSG 11-08



Companion studies, e.g.:

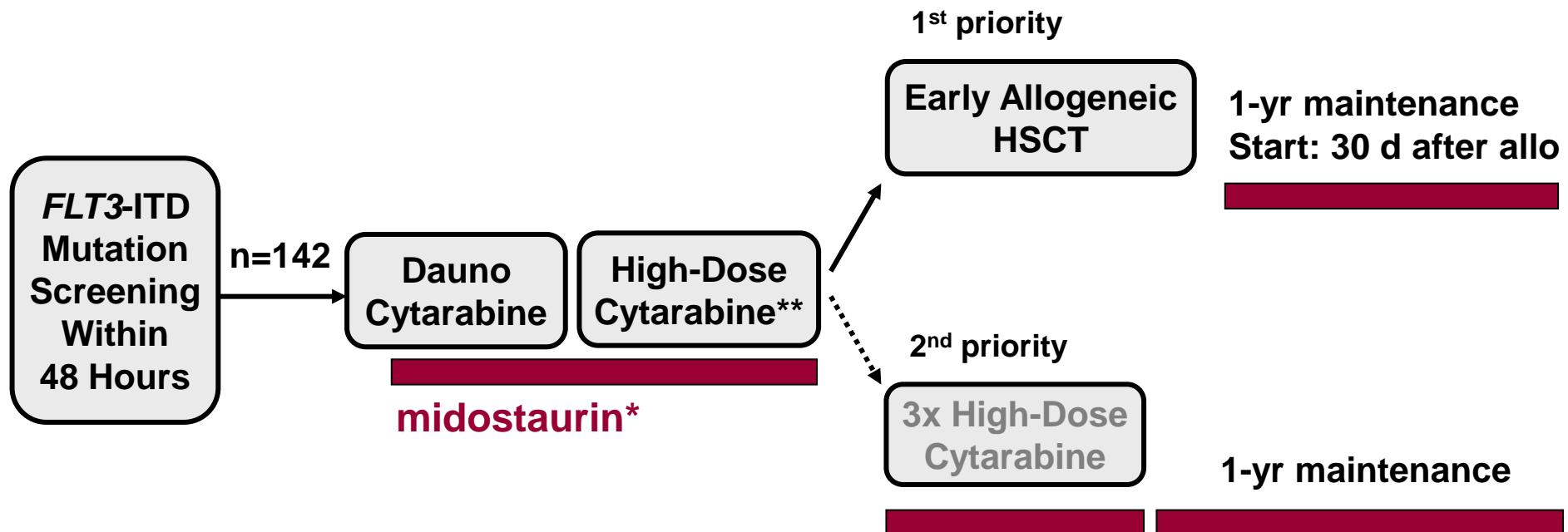
- Gene mutation analyses
- Minimal residual disease assessment (RQ-PCR)
- Pharmacodynamics studies (KIT plasma inhibitory activity)

\* Cytarabine: 18-60yrs: 3g/m<sup>2</sup>, q12hr, d1-3; >60yrs: 1g/m<sup>2</sup>, q12hr, d1-3

ClinicalTrials.gov Identifier: NCT00850382 (AMLSG), NCT01238211 (CALGB)

PI: H. Döhner; supported by BMS

# Phase II Study of Chemotherapy + Midostaurin Followed by Allogeneic HSCT and Midostaurin Maintenance in AML with *FLT3*-ITD (18-70 yrs) AMLSG 16-10 Trial



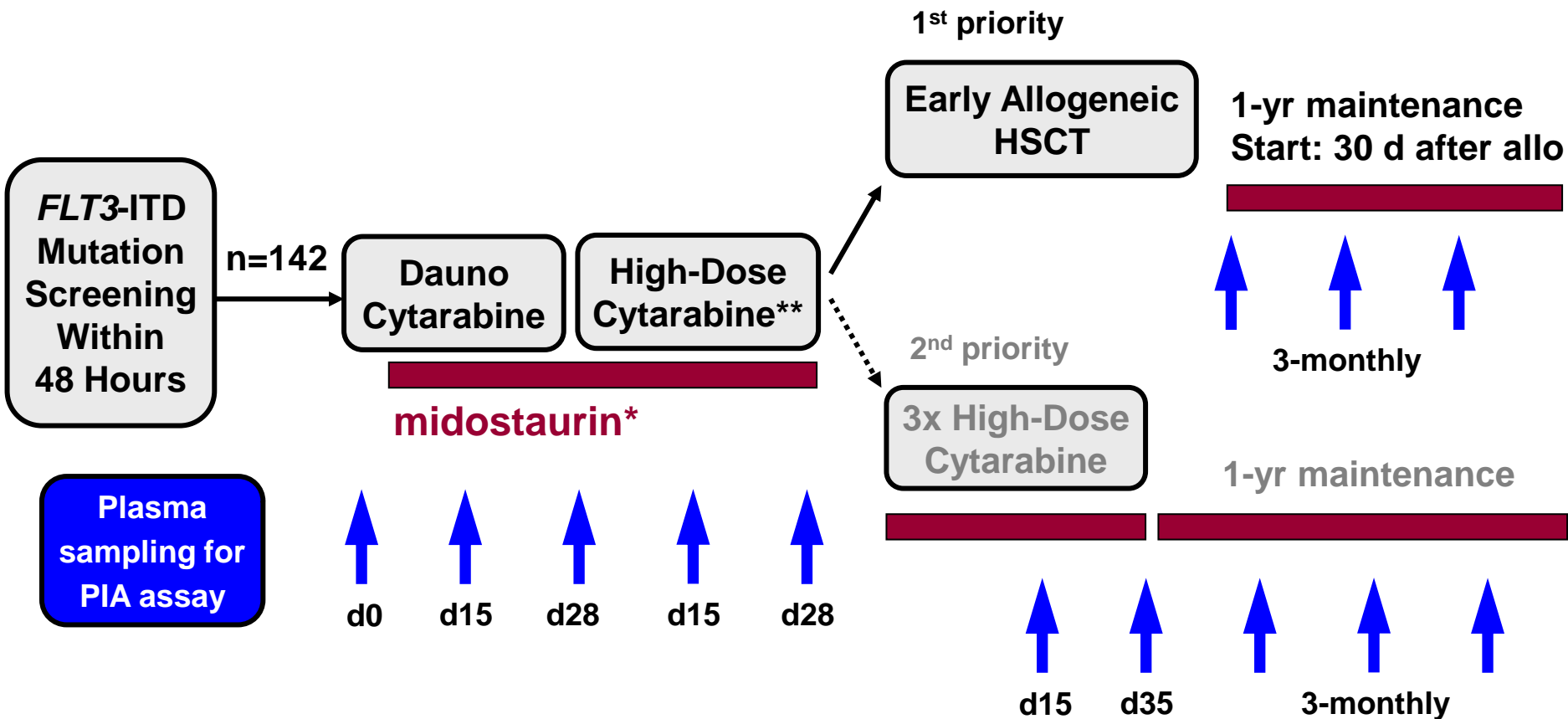
\* Midostaurin: start on day 8, thereafter continuous dosing

\*\* Optional 1<sup>st</sup> consolidation before allo HSCT

ClinicalTrials.gov Identifier: NCT01477606

PI: R.F. Schlenk; supported by Novartis

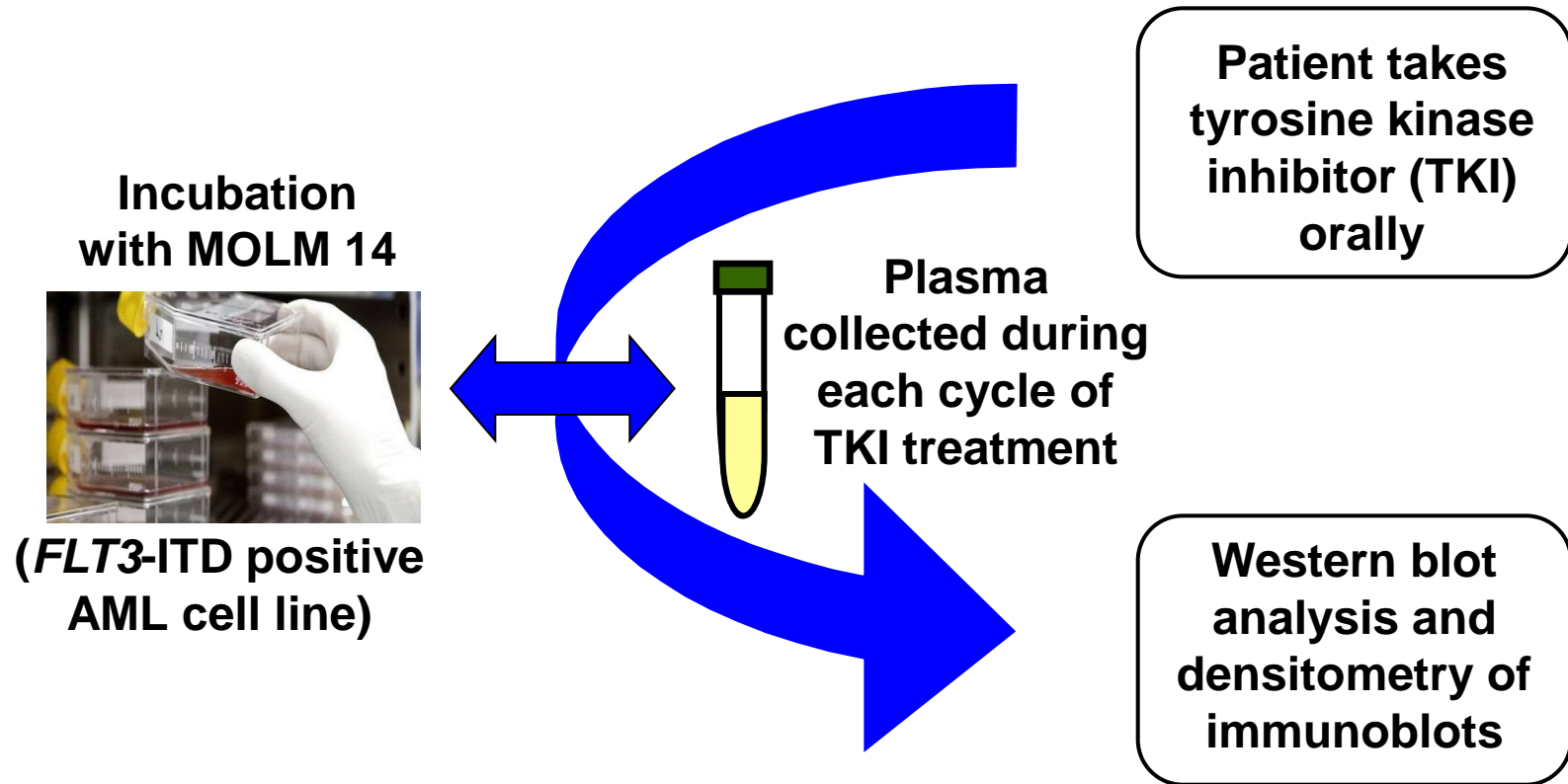
# AML SG 16-10 Trial: Pharmacodynamic Study of FLT3 Plasma Inhibitory Activity (PIA)\*



\* Levis M, et al. Blood. 2006;108:3477-3483.



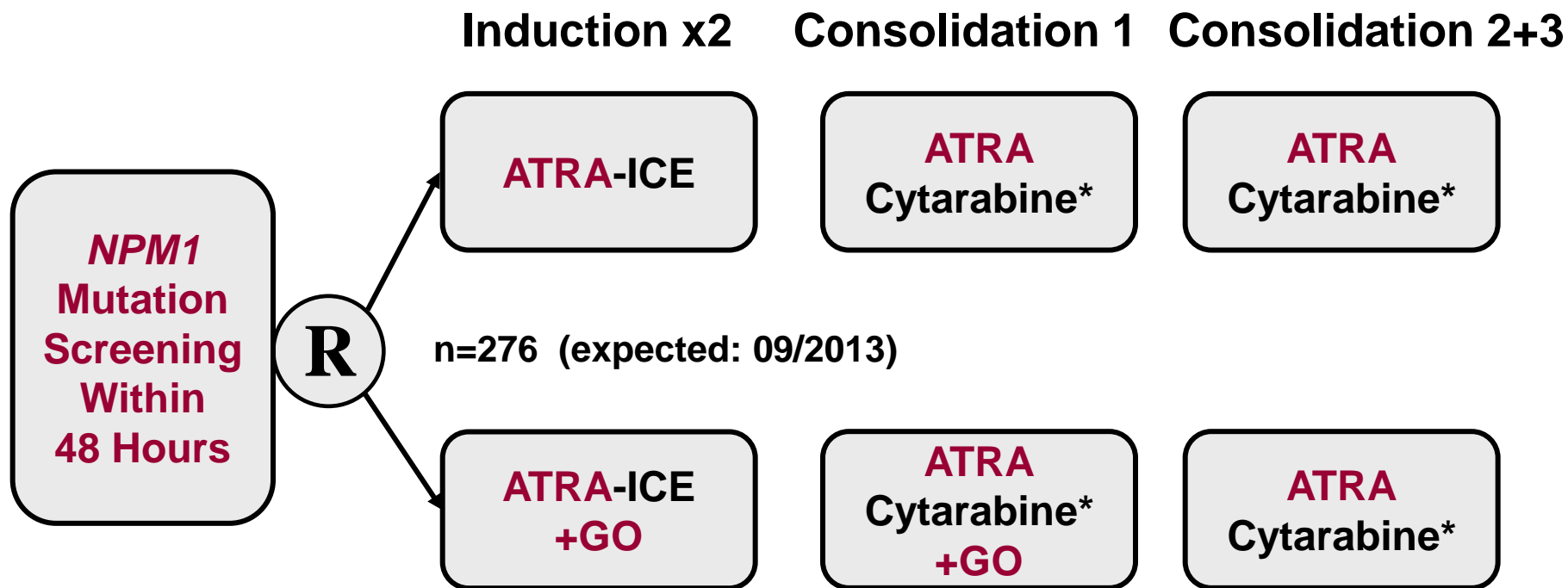
# Plasma Inhibitory Activity (PIA) Assay



## Advantages:

- *in vitro* target monitoring using surrogate biological material
- independent from myeloid blast cells
- read out for individual variable protein binding

# Phase III Study of Chemotherapy in Combination with ATRA with or without Gemtuzumab Ozogamicin (Mylotarg) in Patients with *NPM1*<sup>mut</sup> Acute Myeloid Leukemia AMLSG 09-09

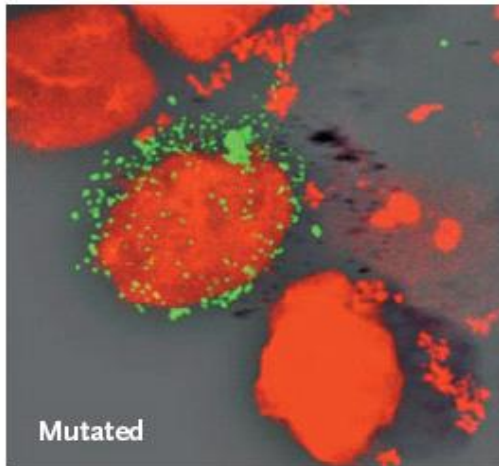
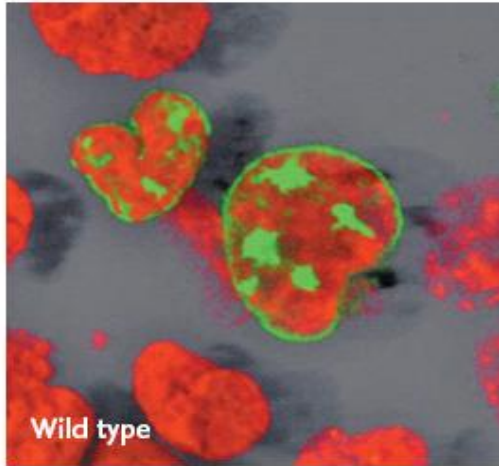


All adult patients eligible for intensive therapy, no upper age limit

\* Cytarabine: 18-60yrs: 3g/m<sup>2</sup>, q12hr, d1-3; >60yrs: 1g/m<sup>2</sup>, q12hr, d1-3

PI: R.F. Schlenk; supported by Pfizer and Else Kröner-Fresenius-Foundation

# AML with Mutated *NPM1* in Older Patients >60 yrs



- **Incidence**

- **24% all, 43% CN-AML**

Schlenk RF, Döhner K, et al. *Haematologica*. 2009

- **52% probably CN-AML**

Büchner T, et al. *J Clin Oncol*. 2009

- **56% CN-AML**

Becker H, et al. *J Clin Oncol*. 2009

- **Response to intensive induction**

- **OR, 3.17; 95%-CI, 1.37–7.35**

Schlenk RF, Döhner K, et al. *Haematologica*. 2009

- **84% CR rate**

Becker H, et al. *J Clin Oncol*. 2009

# Treatment Schedules: AMLSG 15-10

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**Arm A-EC\*:** Cytarabine 20 mg s.c. bid on days 1 to 7  
Etoposide 50 mg/m<sup>2</sup> cont. i.v. on days 1 to 3#  
ATRA 45 mg/m<sup>2</sup> p.o. on days 8 to 28

**Arm EC\*:** Cytarabine 20 mg s.c. bid on days 1 to 7  
Etoposide 50 mg/m<sup>2</sup> cont. i.v. on days 1 to 3#

\* For a maximum of 6 cycles in the absence of progressive disease, repeated between day 29 and 43.

# Starting with cycle 2 etoposide 100mg/die p.o. day 1-3

Ubbo-Emmius-Klinik Aurich  
 HELIOS Klinikum Bad Saarow  
 Charité Berlin  
 Vivantes Klinikum Neukölln, Berlin  
 Klinikum Bochum  
 Marienhospital Herne, Bochum-Herne  
 University of Bonn  
 Städtisches Klinikum Braunschweig  
 Klinikum Bremen  
 Klinikum Darmstadt  
 University of Düsseldorf  
 Klinikum Essen-Werden  
 Klinikum Esslingen  
 St. Franziskus-Hospital Flensburg  
 Klinikum Frankfurt Höchst  
 University of Freiburg  
 Klinikum Fulda  
 University of Gießen  
 Wilhelm-Anton-Hospital Goch  
 University of Göttingen  
 University of Hamburg  
 Krankenhaus Altona, Hamburg  
 Klinikum Hamm  
 Klinikum Hanau  
 Klinikum Hannover Siloah  
 Hannover Medical School  
 SLK Kliniken Heilbronn  
 University of Homburg  
 University of Innsbruck  
 Klinikum Karlsruhe  
 University of Kiel  
 Caritas Krankenhaus, Lebach  
 Klinikum Lemgo  
 Krankenhaus der Barmherzigen Schwestern Linz  
 Krankenhaus der Elisabethinen Linz  
 Klinikum Lüdenscheid  
 University of Magdeburg  
 University of Mainz  
 Klinikum Minden  
 Technical University of München  
 Klinikum Schwäbisch-Gmünd  
 Lukaskrankenhaus Neuss  
 Klinikum Oldenburg  
 Pius-Hospital Oldenburg  
 Klinikum Passau  
 Elisabeth Krankenhaus Recklinghausen  
 Caritas-Klinik St. Theresia, Saarbrücken  
 Salzburger Landeskliniken  
 Klinikum Sindelfingen-Böblingen  
 Klinikum Stuttgart  
 Diakonie-Klinik, Stuttgart  
 Klinikum Traunstein  
 Krh. der Barmherzigen Brüder, Trier  
 University of Tübingen  
 University of Ulm  
 Klinikum Villingen-Schwenningen  
 Hanuschkrankenhaus, Wien  
 HELIOS Klinikum Wuppertal

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 Dr. Teschendorf, Prof. Dr. Schmiegel  
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