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Welcome & Introductions

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Update on Chronic Myeloid Leukemia

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Tuesday, February 3, 2015

CML: Epidemiology and Etiology

- Approximately 5000 new cases annually in the U.S.
- 15% of all adult leukemias
- Incidence increases significantly with age
  - Median age: ~ 67 years
  - Prevalence increasing due to current therapy
- Presentation
  - Asymptomatic (50%)
  - Constitutional symptoms, abdominal pain/early satiety, bleeding/bruising
- Natural history
  - Most patients (85-90%) present in CP
  - Majority of CML-related deaths due to progression to AP/BC
- Risk factors: Radiation exposure

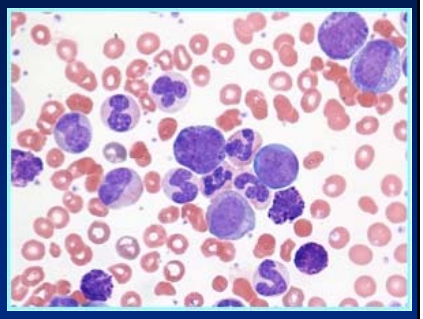
CML = chronic myeloid leukemia; CP = chronic phase; AP = accelerated phase; BC = blast crisis.
NCCN, 2011; Jemal et al, 2009; Richardson et al, 2009; Bacarrani, Cortes, et al, 2009.

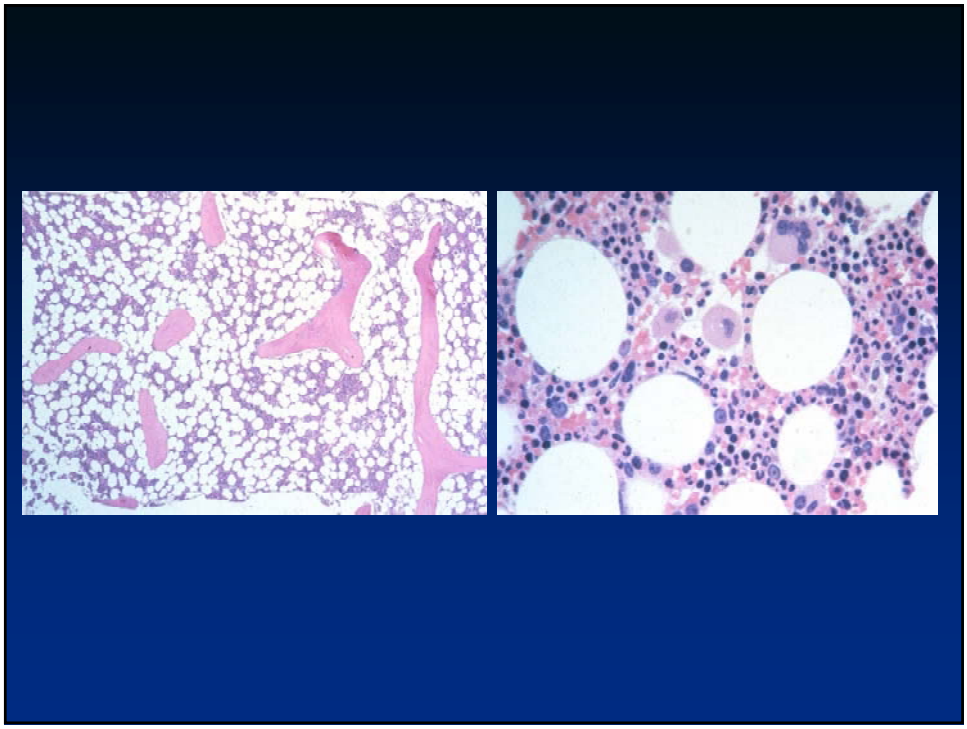
Diagnostic Considerations in CML

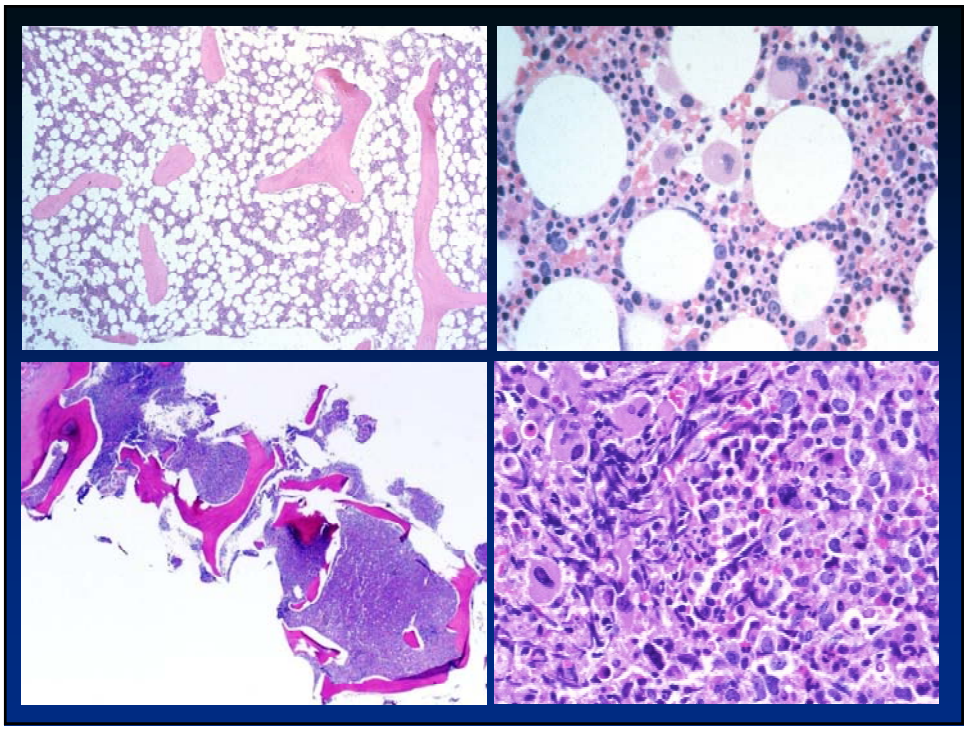
- A peripheral blood smear or bone marrow aspirate can only give a presumptive diagnosis of CML – one still needs to confirm the presence of the Philadelphia chromosome and/or fusion of the BCR and ABL1 genes

Common Peripheral Blood Findings

1) Leukocytosis with a 'left shift'
2) Normocytic anemia
3) Thrombocytosis in ~ 50% of patients
4) Absolute eosinophilia with a normal percentage of eosinophils
5) Absolute and relative increase in basophils



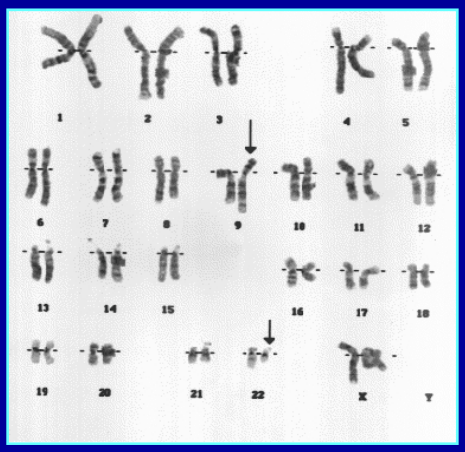




Diagnostic Considerations: Cytogenetic Analysis

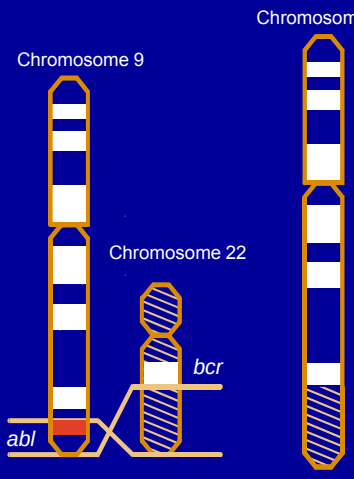
1) Allows for the diagnosis of CML
2) Requires a bone marrow aspirate for optimal metaphases
3) Allows for evaluation of clonal evolution as well as additional chromosomal abnormalities in Ph negative clones
4) Occasionally, cryptic and complex translocation events may result in the missed identification of the t(9;22)

46,XX,t(9;22)(q34;q11.2)

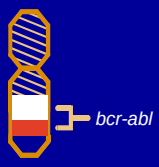


Ph = Philadelphia.
Forrest et al, 2009; Bakshi et al, 2008; Sismani et al, 2008.
Courtesy of Larry Beauregard, Jr., PhD.

The Ph Chromosome and the *bcr-abl* Gene: The t(9;22) translocation



Philadelphia Chromosome (or 22q-)



Fusion protein with constitutively active tyrosine kinase activity

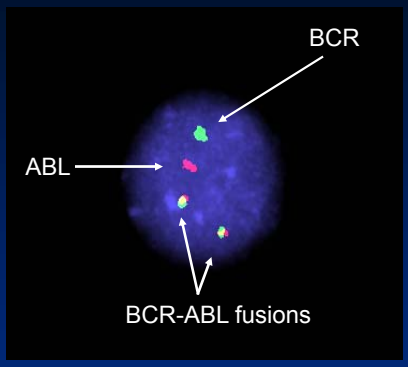
↓

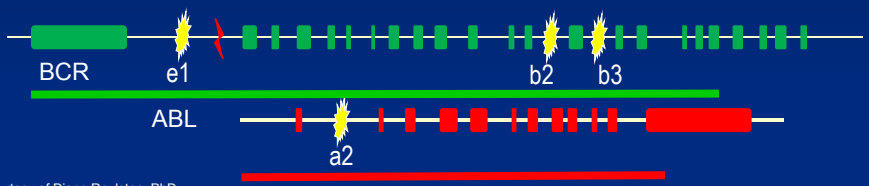
Bcr/abl is necessary and sufficient to cause CML in murine HSCT model

Melo. *Blood*. 1996;88:2375.
Pasternak et al. *J Cancer Res Clin Oncol*. 1998;124:643.

Diagnostic Considerations: FISH

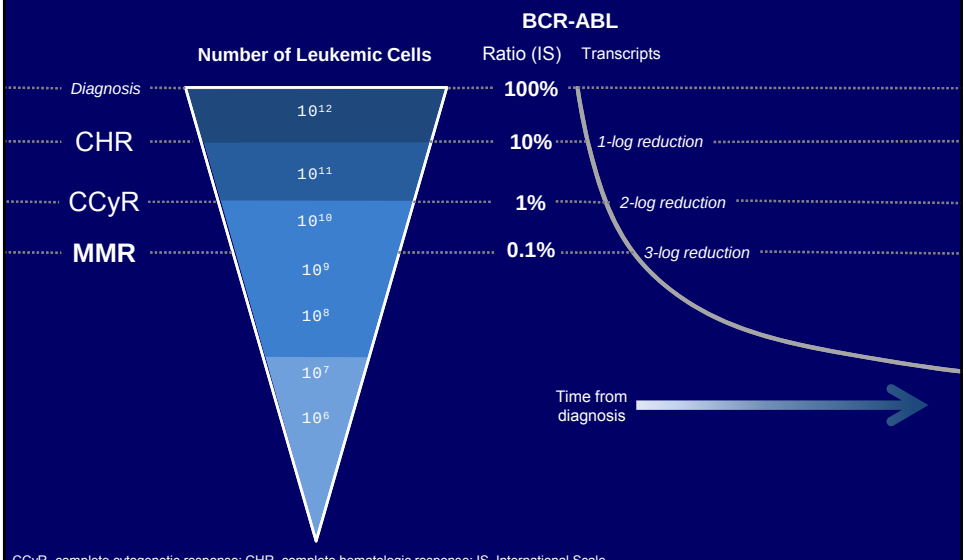
1) Allows for the diagnosis of CML
2) Does not require a bone marrow aspirate for optimal results
3) More sensitive than karyotype
4) Identification of Ph duplications
5) Identification of deletion of der (9) chromosome
6) Identification of cryptic insertions or translocations involving BCR-ABL





Courtesy of Diane Roulston, PhD.

BCR-ABL Transcript Levels by PCR Correlate with CML Disease Burden



CCyR, complete cytogenetic response; CHR, complete hematologic response; IS, International Scale.
Adapted from Aguayo A, Couban S. *Leuk Lymphoma*. 2009;50(Suppl 2):1-8; Radich JP. *Blood*. 2009;114(16):3376-3381.

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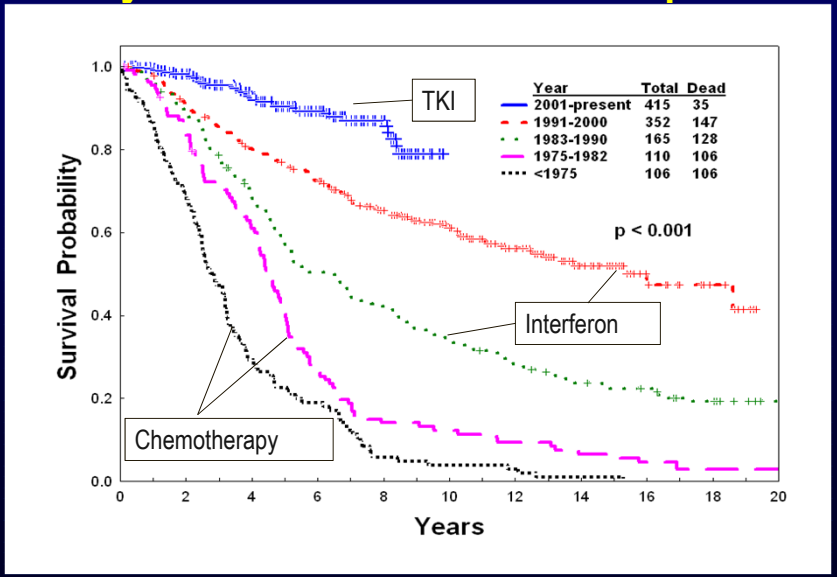
Definition of Response in CML

Response by Type	Definitions
Hematologic	
Complete (CHR)	WBC < 10×10^9/L Basophils < 5% No myelocytes, promyelocytes, myeloblasts in the differential Platelet count < 450×10^9/L Spleen nonpalpable
Cytogenetic*	
Complete (CCgR)	No Ph+ metaphases
Partial (PCgR)	1% to 35% Ph+ metaphases
Minor (mCgR)	36% to 65% Ph+ metaphases
Minimal (minCgR)	66% to 95% Ph+ metaphases
None (noCgR)	> 95% Ph+ metaphases
Molecular†	
Complete (CMolR)	Undetectable *BCR-ABL* mRNA transcripts by real time quantitative and/or nested PCR in two consecutive blood samples of adequate quality (sensitivity > 10^4)
Major (MMolR)	Ratio of *BCR-ABL* to *ABL* (or other housekeeping genes) ≤ 0.1% on the international scale

Baccarani, Cortes, et al, 2009.

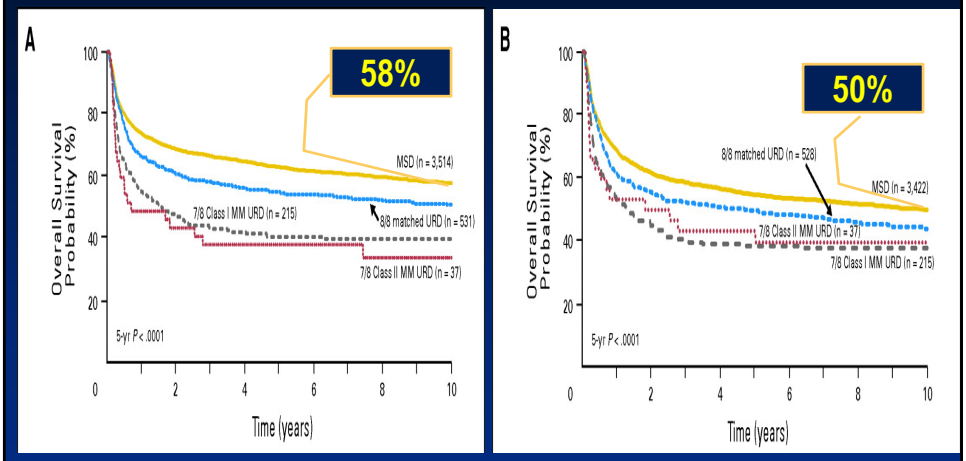
Overall Survival of Patients with Early Chronic Phase CML Has Improved



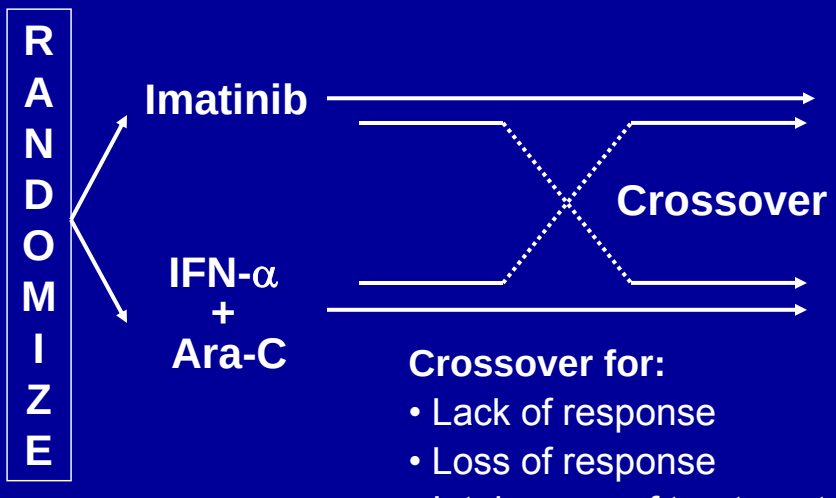
Kantarjian et al. *Blood* 2012; 119: 1981-7. Reproduced with permission of AMERICAN SOCIETY OF HEMATOLOGY.

Allogeneic Hematopoietic Stem Cell Transplant is Curative For (Some) CML Patients

Overall Survival | Leukemia-Free Survival



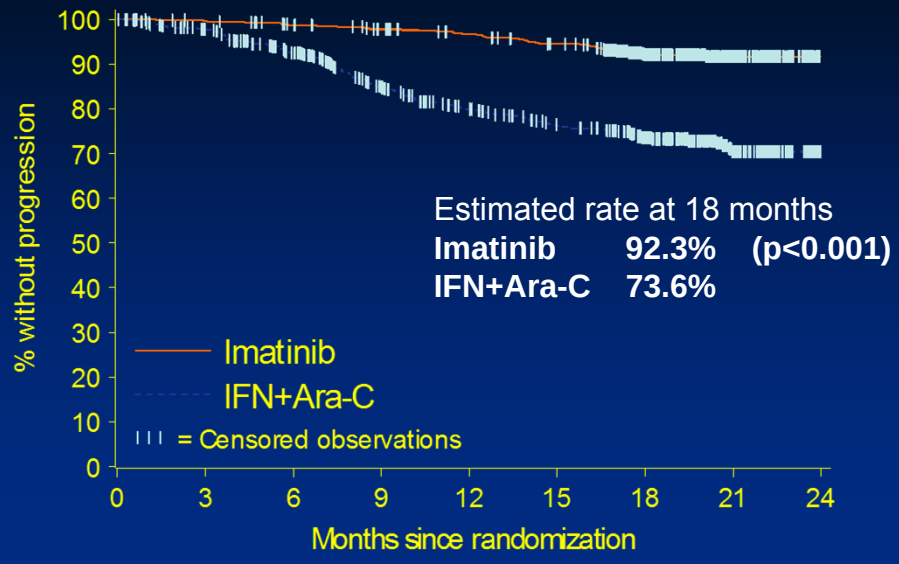
International Randomized Study of Interferon + Ara-C versus STI571 (IRIS)



Crossover for:

- Lack of response
- Loss of response
- Intolerance of treatment

IRIS Trial: Progression-free Survival (Intention to Treat)



Progression of CML-CP to AP/BC by CyR after 12 Months of Imatinib (IRIS)

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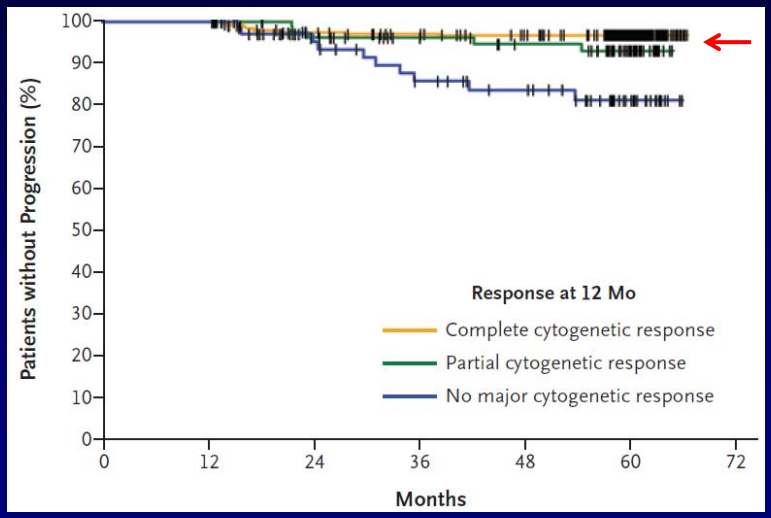
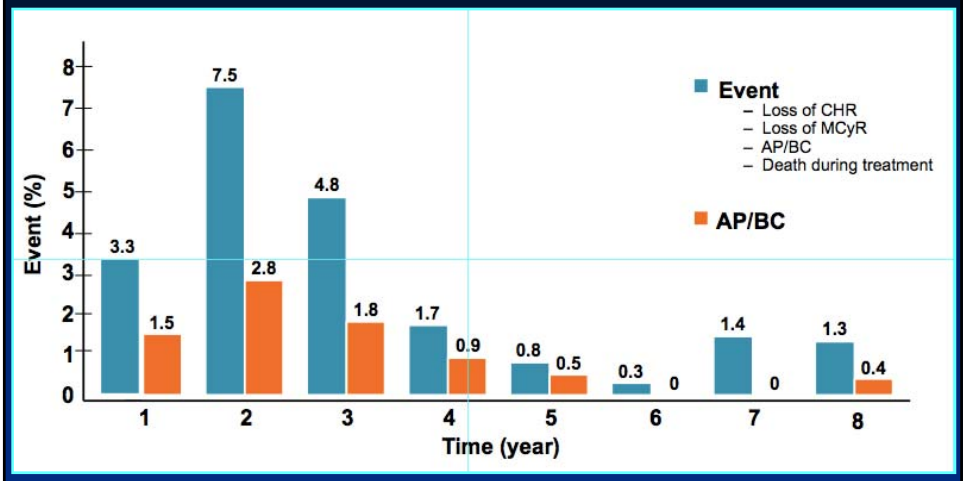


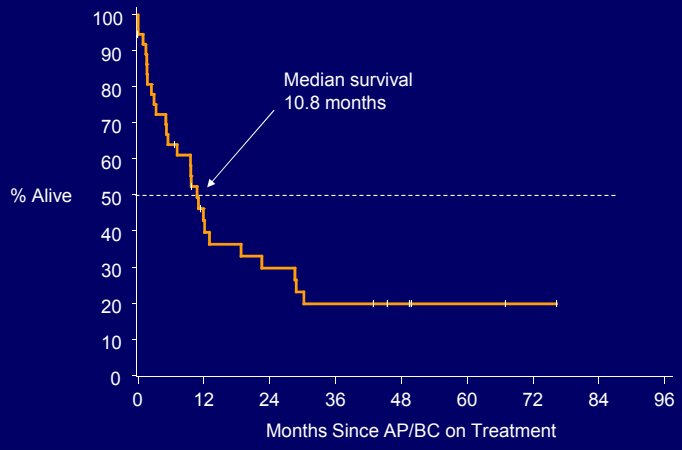
Druker et al. *N Engl J Med* 2006;355:2408

Decreasing Event Rate Over Time in the IRIS Trial: Imatinib Arm



Deininger. et al. ASH 2009. Abs # 1126

Survival Decreases After CML Progression to Accelerated Phase or Blast Crisis (IRIS)



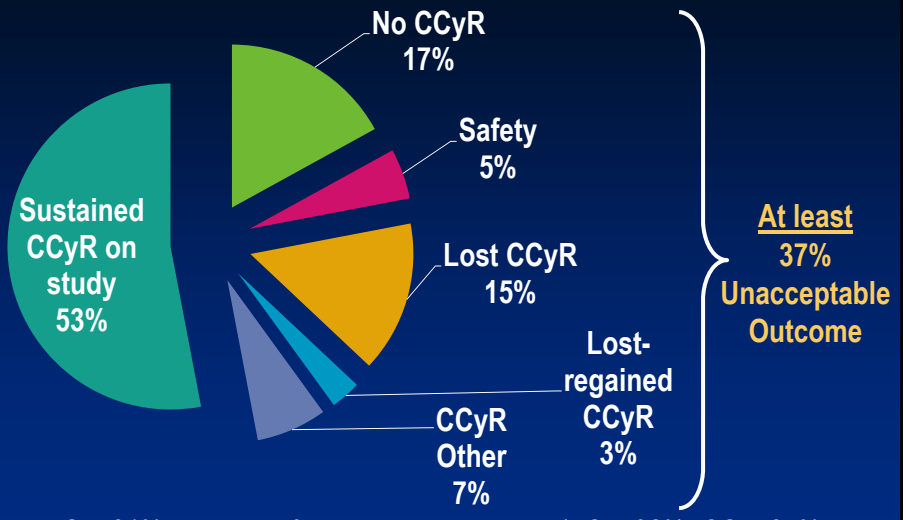
Given the poor prognosis of patients with advanced disease, preventing progression is a key goal in Ph+ CML treatment

Side Effects of Imatinib

Imatinib: Common or Frequent Complaints	
Neutropenia	Musculoskeletal complaints
Thrombocytopenia – mainly during yr 1	Hypophosphatemia
GI disturbances / Diarrhea	Rash
Edema and fluid retention	Pediatrics: growth retardation
Occasional bone mineral metabolism problem	
Long Term Toxicities of Imatinib	
Liver, kidney, cardiac toxicity and immunosuppression.	
CHF: • 1276 patients at MDACC were studied with median follow up at 47 mos • 22 patients, or 1.7% have CHF, however 13/22 had received cardio toxic drugs in the past.	
Management of Acute Toxicities	
Management of anemia and neutropenia includes use of erythropoietin and filgrastim	

Atallah et al, *Blood* 2007; 110: 1233–1237; NCCN Guidelines v4.2013.

IRIS 8-Year Update



- EFS = 81%; Freedom from progression to AP/BC = 92%; OS = 85%

Deininger M, et al. *Blood* . 2009;114(22): 1126.

ENESTnd: Nilotinib vs Imatinib in CML-CP

ENESTnd Study Design and Endpoints

- N = 846
- 217 centers
- 35 countries

RANDOMIZED*

- Nilotinib 300 mg BID (n=282)
- Nilotinib 400 mg BID (n=281)
- Imatinib 400 mg QD (n=283)

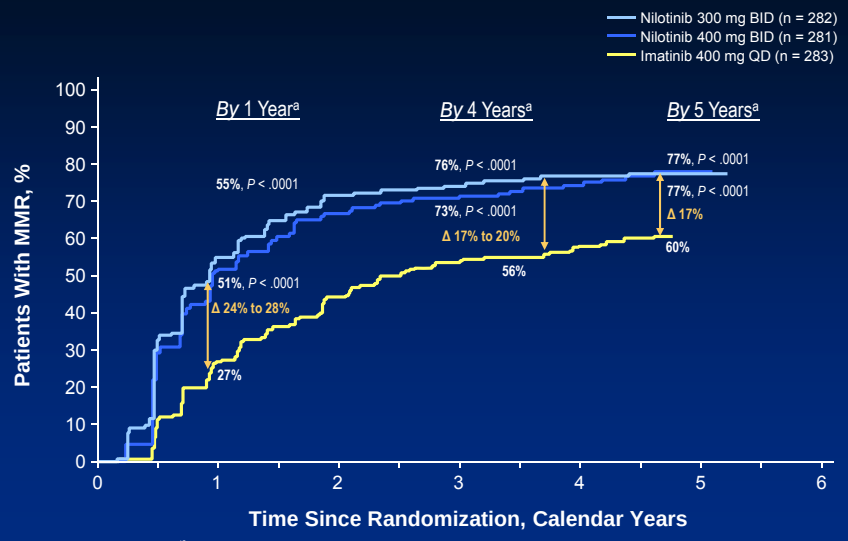
*Stratification by Sokal risk score

Follow-up 5 years

- Primary endpoint: MMR at 12 months
- Secondary endpoint: CCyR by 12 months
- Other endpoints: Time to and duration of MMR and CCyR, EFS, PFS, time to AP/BC, OS

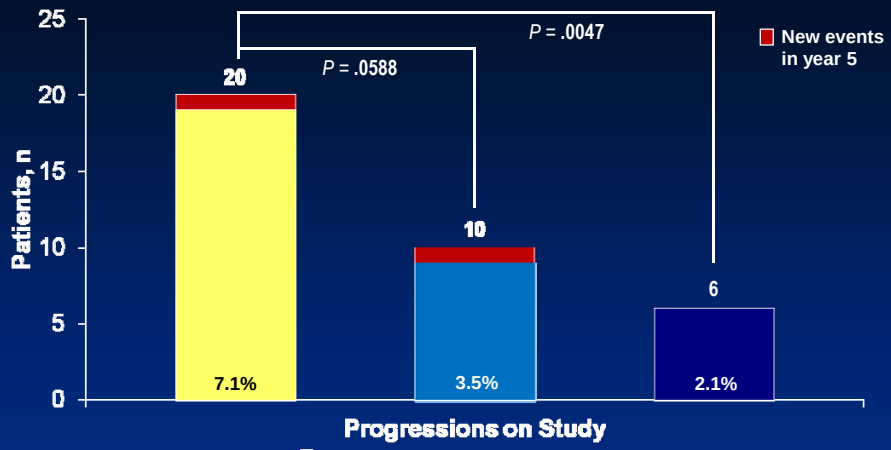
Saglio G, et al. *ASH 2009*. Abs # LBA-1 (oral).

ENESTnd 5 Years: Cumulative Incidence of MMR



MMR, major molecular response (BCR-ABL^{IS} ≤ 0.1%).
[a] Cumulative response rates reported consider each year to consist of twelve 28-day cycles.

ENESTnd 5 Years: Progression to AP/BC on Study[a] (Including After Treatment Discontinuation)



- Two new progressions on study in year 5 (1 in the nilotinib 300 mg BID arm and 1 in the imatinib arm)
- Both patients had BCR-ABL > 10% at 3 months

[a] Includes progression to AP/BC (excluding clonal evolution) or deaths in patients with advanced CML occurring on study (on core or extension treatment or during follow-up after treatment discontinuation).

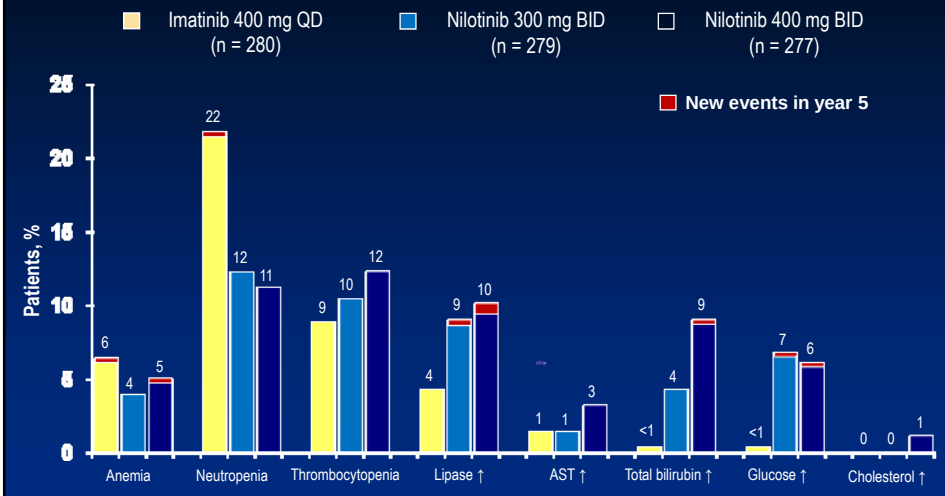
ENESTnd 5 Years: PFS and OS on Study (Including After Treatment Discontinuation)[a]

	Imatinib 400 mg QD (n = 283)	Nilotinib 300 mg BID (n = 282)	Nilotinib 400 mg BID (n = 281)
Estimated 5-year PFS, %	**91.1**	**92.0**	**95.3**
Progressions and deaths, n	23	22	11
Hazard ratio (95% CI)	—	0.92 (0.51-1.65)	0.46 (0.23-0.95)
P value		.77	.03
Estimated 5-year OS, %	**91.6**	**93.6**	**96.0**
Total deaths, n	21	18	10
Deaths in patients with advanced CML, n[b]	15	6	4
Hazard ratio (95% CI)	—	0.84 (0.45-1.58)	0.46 (0.22-0.98)
P value	—	.58	.04

- There were 6 newly reported deaths in year 5
  - Imatinib (n = 2): both due to study indication
  - Nilotinib 300 mg BID (n = 3): study indication, rectal cancer, and pneumonia
  - Nilotinib 400 mg BID (n = 1): sepsis

[a] Includes events occurring on core or extension treatment or during follow-up after treatment discontinuation.
[b] Patients for whom the principle cause of death was either "study indication" or "unknown" or not reported but occurred subsequent to a documented progression to AP/BC.

ENESTnd: Newly Occurring or Worsening Grade 3/4 Hematologic and Selected Biochemical Abnormalities



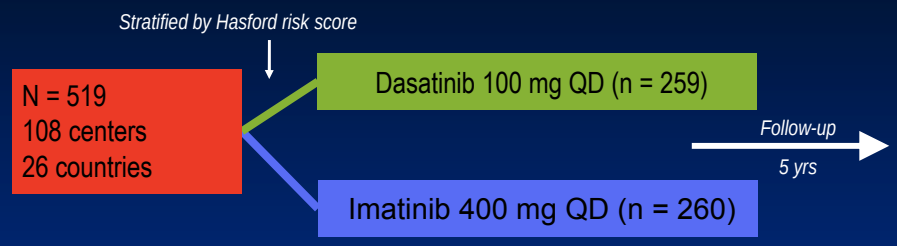
ENESTnd: Selected Cardiovascular Events by 5 Years (All Cause*, All Grades)

Patients With an Event, n	Imatinib 400 mg QD n = 280			Nilotinib 300 mg BID n = 279			Nilotinib 400 mg BID n = 277		
	Total, n	Y1-4, n	Y5, n	Total, n	Y1-4, n	Y5, n	Total, n	Y1-4, n	Y5, n
IHD	5	3	2	11	11	0	21	14	7
ICVE	1	1	0	4	3	1	8	5	3
PAD	0	0	0	4	4	0	6	5	1

- Due to the discontinuation rate, patients had longer exposure to nilotinib than imatinib
- Approximately 85% of patients with a cardiovascular event had at least 1 risk factor and were not optimally managed for hyperglycemia and hypercholesterolemia

*All cause indicates all events, not only those deemed study drug-related by the investigator.
IHD, ischemic heart disease; ICVE, ischemic cerebrovascular events;
PAD, peripheral arterial disease.

Dasatinib vs Imatinib in Treatment-Naive CML (DASISION)



- Primary endpoint: confirmed CCyR by 12 mos
- Secondary/other endpoints: rates of CCyR and MMR; times to confirmed CCyR, CCyR, and MMR; time in confirmed CCyR and CCyR; PFS; OS

Kantarjian H, et al. N Engl J Med. 2010;362:2260-2270.

DASISION 3-Yr Update

Cumulative Molecular Responses

Outcome, %		Dasatinib 100 mg QD (n = 259)	Imatinib 400 mg QD (n = 260)
Cumulative MMR	1 yr	46*	23
	2 yrs	64*	46
	3 yrs	68*	55
Cumulative MR[4]	3 yrs	35†	22
Cumulative MR[4.5]	3 yrs	22‡	12

*P < .0001 vs imatinib. †P = .00635 vs imatinib. ‡P = .00069 vs imatinib.

OS and PFS

3-Yr Survival Outcome	Dasatinib (n = 259)	Imatinib (n = 260)	HR (95% CI)
PFS, %	91.0	90.9	1.00 (0.55-1.80)
OS, %	93.7	93.2	0.86 (0.45-1.65)
Deaths, n	17	20	-

Hochhaus A, et al. ASCO 2012. Abstract 6504.

DASISION 3-Year Update

Hematologic AEs and Biochemical Abnormalities

Grade 3/4 AEs, %	Dasatinib 100 mg BID (n = 281)	Imatinib 400 mg QD (n = 283)
Neutropenia	24.0	20.9
Thrombocytopenia	19.4	11.2
Anemia	11.6	8.5
Decreased phosphorus	7.0	28.3
Decreased calcium	3.1	1.9
Elevated creatinine	1.2	0.8
Elevated total bilirubin	1.2	0
Elevated ALT	0.4	1.6
Elevated AST	0.4	1.2
Decreased potassium	0	2.3

Toxicities

- Impaired platelet aggregation and bleeding
- Pleural effusion (up to 29% of pts)
- Reversible pulmonary arterial HTN
- Dose interruption in 83% of patients
- Dose reduction in 71% of patients

Hochhaus A, et al. ASCO 2012. Abstract 6504; Sprycel Prescribing information 2013; NCCN Guidelines v4.2013.

The Goal of Therapy in Ph+ CML Is Prevention of Progression to Advanced Phases

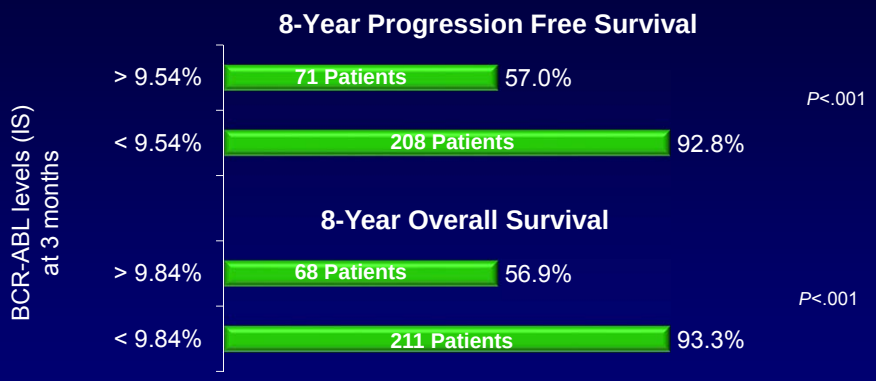
Updated NCCN Clinical Practice Guidelines in Oncology

Month	Recommended Response	Monitoring Test
(diagnosis)	–	• IS RQ-PCR and bone marrow cytogenetics
3	≤10% BCR-ABL IS transcripts (or PCyR)	• IS RQ-PCR • Bone marrow cytogenetics if IS RQ-PCR is unavailable
6	≤10% BCR-ABL IS transcripts (or PCyR)	• IS RQ-PCR • Bone marrow cytogenetics if IS RQ-PCR is unavailable
12	CCyR	• IS RQ-PCR • Bone marrow cytogenetics if neither CCyR nor MMR
18	CCyR	• IS RQ-PCR • Bone marrow cytogenetics if not in MMR and lack of CCyR at 12 months

To be confident with a patient's molecular response:

- Monitor patients by RQ-PCR (IS only) every 3 months for 3 years following CCyR, then every 3 to 6 months thereafter
  - Assay sensitivity is recommended to be at least 4.5 logs below the standardized baseline
- Reducing BCR-ABL to ≤10% by 3 months is an important clinical consideration

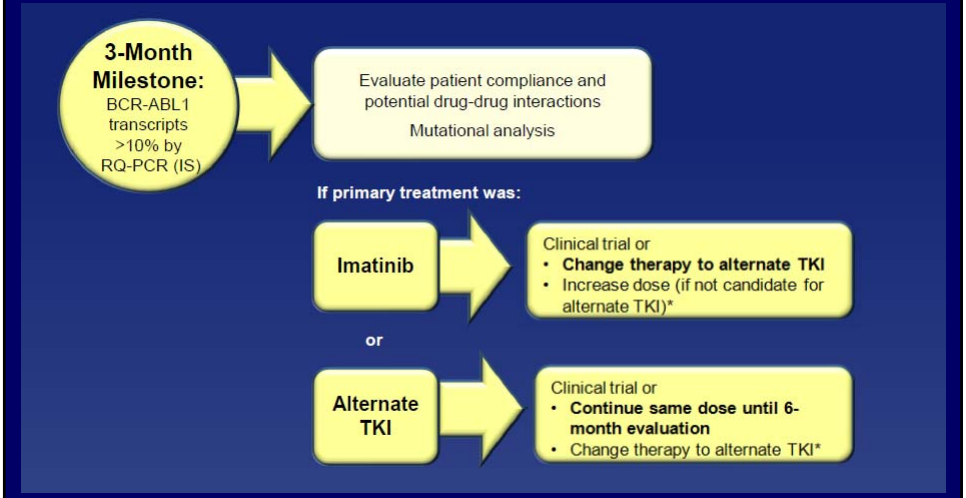
Depth of Early Molecular Response at 3 Months Correlates with PFS and OS



- 282 CML-CP patients treated with imatinib were evaluated at the Hammersmith Hospital between 2000 and 2010
- Cutoffs in transcript levels at 3, 6, and 12 months predictive of patient outcome were identified by ROC

Marin D et al. *J Clin Oncol.* 2012;30(3):232-238.

NCCN Practice Guidelines Recommendations based on 3 Month Milestone Molecular Result



Compliance to Imatinib (Adagio)

Adherence ratings (visual analogue scale) by physician, patient and family members were very high (94.9-97.1 on a 0-100 scale)

Actual Imatinib Taken (assessed by pill count)	n	%
As prescribed	23	14.2
> the prescribed dose	24	14.8
< prescribed dose	115	71.0

NCCN recommends evaluating compliance whenever a milestone is not achieved

Noens L, et al. *Blood.* 2009;113:5401-5411.
NCCN Guidelines. CML 3.2014.

Reasons for Lack of Compliance

Intentional	Unintentional
Side effects	Forgetting
Socializing/dining out/drinking alcohol	Accidentally taking too much
Travelling	Prescribing error
Diversion from planned activities	No imatinib available at pharmacy
Temporary illness	Delays in drug delivery from specialty pharmacy
Risk of pregnancy	
Negative emotions and feelings	
“No real reason/lack of discipline”	
Bad taste	

Noens et al. *Haematologica*. 2014;99(3):437-47, Eliasson et al. *Leuk Res.* 2011;35(5):626-30.

Strategies to Improve Adherence

- Encourage patients to discuss barriers to compliance with physician
- Educate patients on the clinical impact of non-adherence
  - The occasional missed dose has a consequence
  - Involve family members
- Educate on early recognition of adverse events
- Provide clear, simple, written instructions for dosing and timing
  - Use simple tools, use technology
- Frequent follow-up calls, office visits, or email/text reminders
  - Reiterate the importance of dose adherence

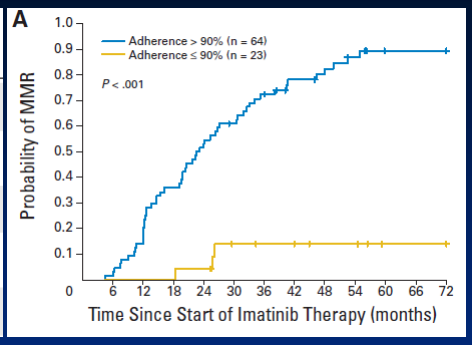
Imatinib Compliance (Pill Counts) Correlates with Achievement of CCyR in CML-CP

	N	% imatinib doses not taken in 90 day period (mean)	p
Patients treated with imatinib > 12 months			0.012
Complete CyR	98	9.0%	
Incomplete CyR	9	26.0%	
All patients			0.004
Complete CyR	109	9.1%	
Incomplete CyR	15	23.9%	

Noens et al. (ADAGIO Study). *Blood* 2009; 113: 5401-5411

Adherence is the Critical Factor for Achievement of MolR in CML-CP Patients in CCyR on Imatinib

Adherence Rate (%)	No. of Patients	MMR		
		No.	%	*P*
≥ 100	36	20	55.5	.1
≤ 99	51	19	37.2	
> 95	57	34	59.6	.002
≤ 95	30	5	16.7	
> 90	64	37	57.8	< .001
≤ 90	23	2	8.7	
> 85	69	38	55.1	< .001
≤ 85	18	1	5.6	
> 80	75	39	52	< .001
≤ 80	12	0	0	



- Hammersmith Hospital, April 2008 – February 2009
- 87 patients with CML-CP in CCyR on imatinib
- Compliance monitored for median 91 days by MEMS and pill count

Marin et al. *J Clin Oncol* 2010; 28: 2381-2388

Higher Copayments (Cost Sharing) Adversely Effects Adherence to ABL TKI Therapy in CML-CP Patients

	Discontinuation			Non-adherence		
	Adjusted Proportion (%)	Adjusted relative risk	95% CI	Adjusted Proportion (%)	Adjusted Relative Risk	95% CI
Lower copayment	10%	1.00		21%	1.00	
Higher copayment	17%	1.70	1.30 – 2.22	30%	1.42	1.19 – 1.69

Dusetzina SB et al. *J. Clin. Oncol.* **2014**

Second Generation ABL TKI in CML

Parameter	Dasatinib	Nilotinib	Bosutinib
Potency (fold vs IM)	325	30	20-50
Target	Src & Abl	Abl	Src & ABL
BCR-ABL binding	Active + Inactive	Inactive	Intermediate
Resistant mutations	T315I	T315I	T315I
Mutations with intermediate sensitivity	E255K/V, V299L, F317L	E255K/V, Y253F/H, Q252H, F359V	E255V/K, V299L, F317L
Standard dose (CP)	100mg QD	400mg BID	500mg QD
Grade 3-4 neutropenia & thrombocytopenia	33% / 22%	31% / 33%	12% / 21%
Other notable toxicities	Pleural effusion, bleeding	Bilirubin, lipase elevation	Diarrhea, rash, transaminase elevation
C-KIT inhibition (vs imatinib)	Increased	Similar	None
PDGFR inhibition (vs imatinib)	Increased	Similar	None
Clinical activity	Highly active	Highly active	Highly active

Sprycel®, Tasigna®, Bosulif® prescribing information (2013).

Second Generation ABL TKI in CML CP Post-Imatinib Resistance

Response	Percentage		
	Dasatinib	Nilotinib	Bosutinib
FU (mo)	>24	>24	24*
CHR	89	77	86
MCyR	59	56	54
CCyR	44	41	41
24 mo PFS**	80%	64%	79%
24 mo OS**	91%	87%	92%

* Median
** All patients

Shah et al. *Haematologica* 2010; 95: 232-40; Kantarjian et al. *Blood* 2011; 117: 1141-45; Cortes et al. *Blood* 2011; 118; 4567-76

Second Generation ABL TKI in CML CP Post- Imatinib Failure

Toxicity	Dasatinib	Nilotinib	Bosutinib
Pleural effusion	++	-	-
Liver	+	+	+
Transaminases	+	+	++
Bilirubin	-	++	-
Rash	+	+	++
Diarrhea	-	-	++
Lipase	- (+)	++	-
Glucose	-	++	-
Hypophosphatemia	++	++	+
Bleeding	+	-	-
QTc	++	++	-

Response to Bosutinib as Third-Line Therapy

- 114 pts who failed imatinib (600mg) & dasatinib or nilotinib
- Minimum 24 mo F/U

Response, %	IM + D resistant (n = 37)	IM + D intolerant (n = 49)	IM + NI resistant (n = 27)
CHR	62	80	76
MCyR	33	48	39
CCyR	19	43	27
PCyR	14	5	12
MMR	3	25	11
2-yr progression or death	21	12	49

IM, imatinib; D, dasatinib; NI, nilotinib.

Khoury et al. ASH 2012; Abstract #3785

Ponatinib Phase 2 PACE Study Responses at Any Time

	CP-CML			AP-CML	BP-CML	Ph+ ALL
	MCyR	CCyR	MMR	MaHR*	MaHR	MaHR
R/I to das/nil	56%	48%	31%	62%	32%	50%
T315I	72%	70%	58%	61%	29%	36%
Total**	60%	54%	38%	61%	31%	41%
Median time to response, months						
	2.8	2.9	5.5	0.7	1.0	0.7

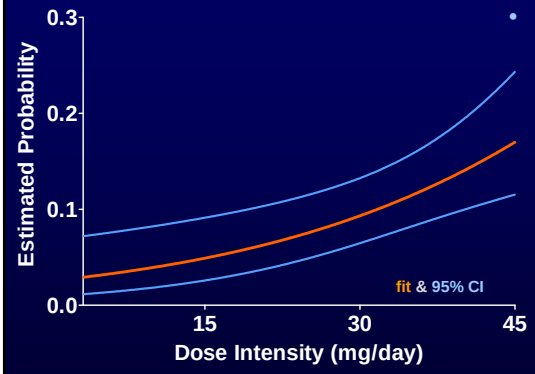
*14 AP-CML patients with baseline MaHR and 1 AP-CML patient with no baseline MaHR assessment counted as non-responders
**Total comprises all eligible patients treated with ponatinib. It excludes 5 patients (3 CP-CML, 2 AP-CML) who were non-cohort assigned (post-imatinib, non-T315I), but treated; all 5 achieved MCyR

Ponatinib Phase 2 PACE Study Incidence of Vascular Occlusive Events Over Time

	N=449 n (%)			
Data as of:	23 July 2012 (USPI)		03 Sep 2013	
Median Follow-up [exposure]	12 months [340 patient-yrs]		24 months [578 patient-yrs]	
Category	SAE	AE	SAE	AE
Cardiovascular	21 (5)	29 (6)	28 (6)	41 (9)
Cerebrovascular	8 (2)	13 (3)	18 (4)	25 (6)
Peripheral vascular	7 (2)	17 (4)	16 (4)	28 (6)
Total Arterial Thrombosis	34 (8)	51 (11)	53 (12)	77 (17)
Venous Thromboembolism	10 (2)	15 (3)	13 (3)	23 (5)
Vascular Occlusion[a]				
Method 1[b]	41 (9)	62 (14)	62 (14)	91 (20)
Method 2[c]	47 (10)	81 (18)	67 (15)	109 (24)

[a]Combined incidence of cardiovascular, cerebrovascular, peripheral vascular, venous thromboembolism events; [b]EMA press release, Nov 22, 2013; [c]FDA drug safety communication, Oct 31, 2013; SAE = AE reported as serious by the investigator, per standard criteria

Ponatinib Phase 2 PACE Study
Multivariate Analysis of Arterial Thrombotic AEs



- **Risk factors significantly associated with arterial thrombotic AEs:**
  - Older age (p<0.0001)
  - History of diabetes (p=0.0003)
  - Higher dose intensity to time of first event (p=0.0009)
  - History of ischemia (p=0.0087)
  - Longer time since diagnosis (p=0.0228)
  - Higher baseline neutrophils (p=0.0276)
  - Higher baseline platelets (p=0.0466)

- **Each 15 mg/day reduction in dose intensity results in a predicted reduction of ~40% in the risk of an arterial thrombotic event**

Data are similar for vascular occlusive events

Omacetaxine for CML CP After Failure of ≥2 ABL TKI

- 122 pts with CML CP (n=81) or AP (n=41) with ≥2 prior TKI
- Omacetaxine 1.25 mg/m^2 BID x14d, then x7d

Response, %	CP N=81	AP N=41
Primary endpoint	MCyR 20% CCyR 10%	MaHR 27% CHR 24%
Median duration, mo	17.7	9
Median PFS, mo	9.6	4.7
Median OS, mo	33.9	16

- 11 pts (9 CP, 2 AP) ongoing response
- Median 35 cycles over median 39 months
- Median response duration: 14 mo CP, 24 mo AP

Cortes et al. *Clin Lymphoma Myeloma Leuk* 2013 [Epub ahead of print]

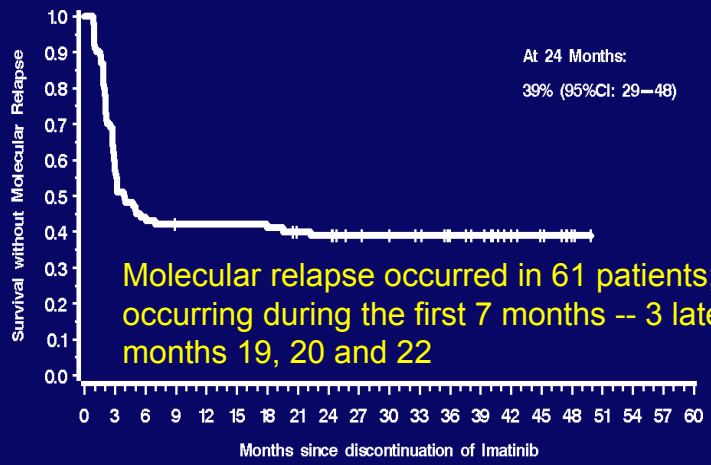
STIM Trial Update

- 100 patients; CML-CP; CMR x 2 years on imatinib; median age 63
- Median follow up 30 months (range 9-45 months)
- 61 relapses: 58 during first 7 months, 3 relapses at 19, 20 and 22 months
- Maintenance of CMR at 24 and 36 months = 39%
- 56 of 61 regained CMR on imatinib
  - Median time to achieved CMR again = 4 months (0-21 mo)
  - One patient lost CCyR (based on BCR/ABL:ABL ratio 6.6%) and received dasatinib; four have unmaintained CCyR
  - 5 of 39 without confirmed molecular relapse had fluctuation in BCR/ABL:ABL ratio
- Unsustained CMR was more likely in low risk patient and with longer duration of imatinib therapy (> 60 mo)

Mahon FX et al. *Blood* 2011;118:Abstract #603

Kaplan-Meier estimates of CMR After imatinib discontinuation in STIM trial

The overall probability of maintenance of CMR at 24 and 36 months was 39% (95% CI 29-48).



Molecular relapse occurred in 61 patients; 58 relapses occurring during the first 7 months -- 3 late relapses at months 19, 20 and 22

Mahon FX et al. *Blood* 2011;118:Abstract #603

Management of CML-CP with ABL TKI

- Encourage dialogue with patients re barriers to compliance
- Close monitoring per standard guidelines (ELN, NCCN) required
- Failure (not warning or suboptimal responses) is indication to change therapy
- Mutation analysis when failure; informative in some patients
- Review compliance, toxicities, drug-drug interactions at visit
- Avoid rapid succession of ABL TKI
- Manage adverse events effectively
- Consider all your options

Update on Chronic Myeloid Leukemia

someday is today

LEUKEMIA & LYMPHOMA SOCIETY
fighting blood cancers

Question and Answer Session

Dr. Erba's slides are available for download at
www.LLS.org/programs

Update on Chronic Myeloid Leukemia

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The Leukemia & Lymphoma Society (LLS) offers:

- **Live, online chats** that provide a friendly forum to share experiences with others. Living with CML chat held on Tuesday and Thursday nights, 8:00-10:00 pm ET, and Caregiver Chat held on Tuesday nights from 8:00-10:00 pm ET
  - **WEBSITE: www.LLS.org/chat**
- **What to ask:** For a list of suggested questions to ask about certain topics, download and print any of the following guides.
  - **WEBSITE: www.LLS.org/whattoask**
- **Co-Pay Assistance Program** offers financial assistance to qualified cancer patients to help with treatment-related expenses and insurance premiums.
  - **WEBSITE: www.LLS.org/copay** **TOLL-FREE PHONE: (877) 557-2672**
- **Information Resource Center:** Speak one-on-one with an Information Specialist who can assist you through cancer treatment, financial, and social challenges.
  - **EMAIL: infocenter@LLS.org** **TOLL-FREE PHONE: (800) 955-4572**