5 Minute JournalClub

Key ASH Presentations

Issue 3, 2011

For more visit ResearchToPractice.com/5MJCASH2011

Research To Practice®

CME Information

LEARNING OBJECTIVES

- Apply updated results from the ENESTnd trial to the evidence-based selection between nilotinib and imatinib as front-line treatment for CML-CP.
- Inform patients with CML-CP who exhibit suboptimal responses or intolerance to front-line imatinib about reported rates of benefit from a switch to nilotinib.
- Apply updated results from the DASISION trial to the evidence-based selection between dasatinib and imatinib as front-line treatment for CML-CP.
- Explain the differential safety profiles of dasatinib and imatinib to patients with CML-CP.
- Refine or validate your current understanding of the comparative efficacy of BCR-ABL inhibitors in the treatment of newly diagnosed CML-CP.
- Compare and contrast the efficacy and safety of bosutinib and imatinib in the initial treatment of CML-CP.

CME Information (Continued)

CREDIT DESIGNATION STATEMENT

Research To Practice designates this educational activity for a maximum of 1 *AMA PRA Category 1 Credit*™. Physicians should only claim credit commensurate with the extent of their participation in the activity.

HOW TO USE THIS CME ACTIVITY

This CME activity contains slides. To receive credit, the participant should review the slide presentations and complete the Educational Assessment and Credit Form located at CME.ResearchToPractice.com.

FACULTY DISCLOSURES

The following faculty (and their spouses/partners) reported real or apparent conflicts of interest, which have been resolved through a conflict of interest resolution process:

Susan M O'Brien, MD
Professor of Medicine, Department of Leukemia
The University of Texas MD Anderson Cancer Center
Houston, Texas

CME Information (Continued)

Advisory Committee: Biogen Idec, Gemin X Pharmaceuticals Inc, Lilly USA LLC; *Consulting Agreements:* Allos Therapeutics, Calistoga Pharmaceuticals Inc, Celgene Corporation, Facet Biotech Corporation, Genentech BioOncology, Genmab, Genta Inc, GlaxoSmithKline, Sanofi-Aventis, Sunesis Pharmaceuticals Inc, Trubion Pharmaceuticals Inc; *Paid Research:* Bayer HealthCare Pharmaceuticals, Biogen Idec, Bristol-Myers Squibb Company, Gemin X Pharmaceuticals Inc, Genentech BioOncology, Genta Inc, Hana Biosciences Inc, Lilly USA LLC, Novartis Pharmaceuticals Corporation.

Neil P Shah, MD, PhD
Co-Leader, Hematologic Malignancies Program, UCSF Helen Diller Comprehensive Cancer Center
Assistant Professor of Medicine, Division of Hematology/Oncology, University of California, San Francisco
San Francisco, California

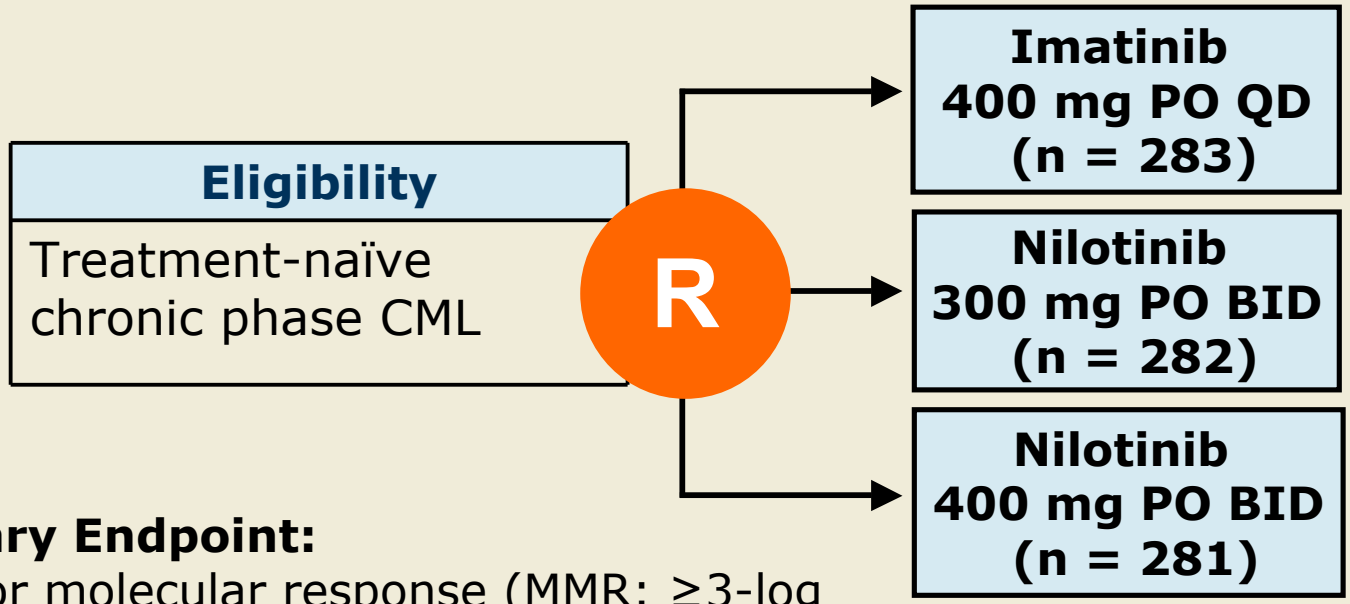
Advisory Committee: ARIAD Pharmaceuticals Inc, Bristol-Myers Squibb Company.

ENESTnd 24-Month Update: Continued Superiority of Nilotinib versus Imatinib in Patients with Newly Diagnosed Chronic Myeloid Leukemia in Chronic Phase (CML-CP)

Hughes TP et al.

Proc ASH 2010;Abstract 207.

ENESTnd Study Schema



Primary Endpoint:

- Major molecular response (MMR: ≥3-log reduction in BCR-ABL transcripts) at 12 months

Other Key Endpoints:

- Durable MMR (at 24 months)
- Complete cytogenetic response (CCyR)
- Progression to accelerated/blast phase (AP/BC)
- Progression-free survival (PFS), overall survival (OS)

Hughes TP et al. *Proc ASH* 2010;Abstract 207.

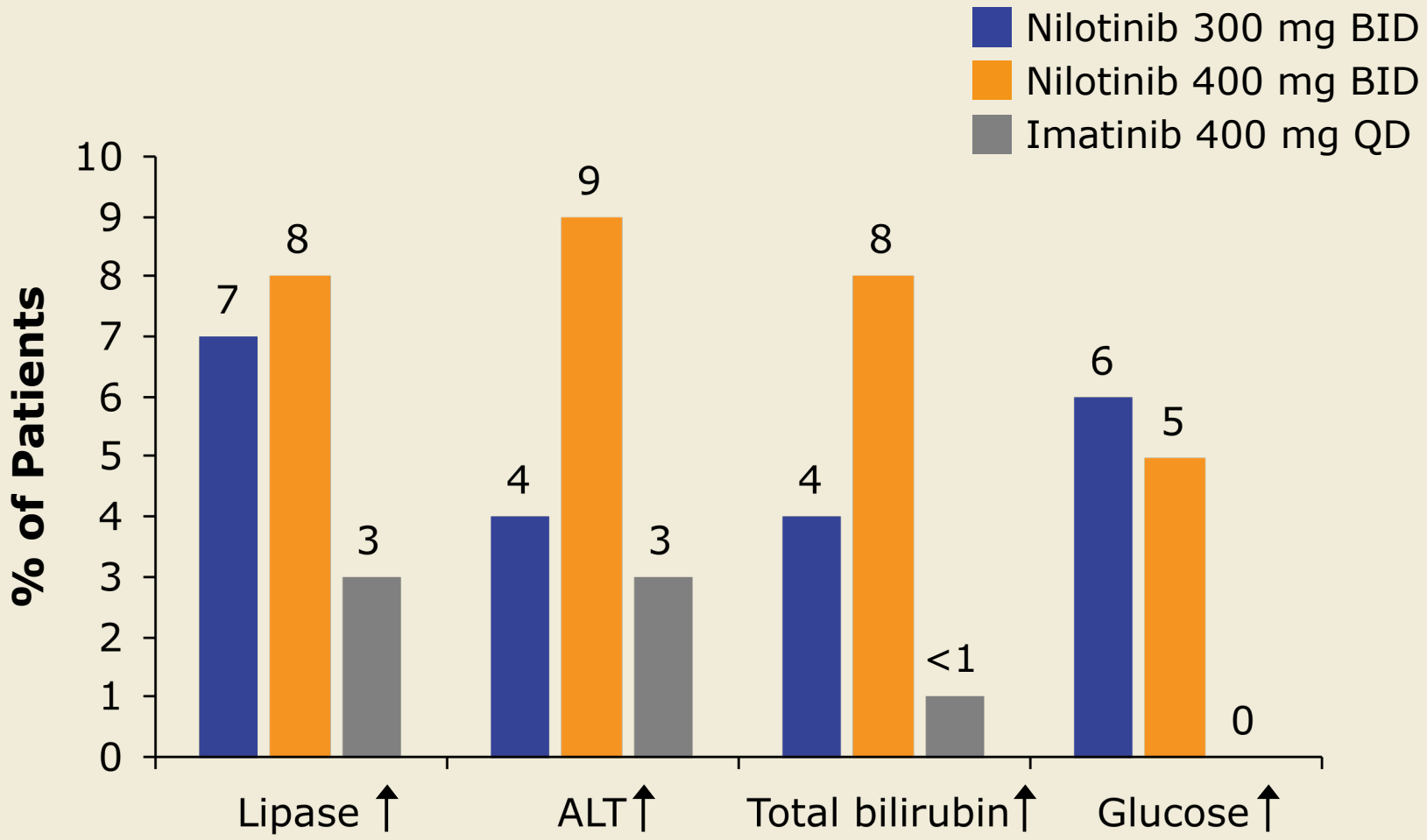
Efficacy Outcome

	Imatinib 400 mg QD	Nilotinib 300 mg BID		Nilotinib 400 mg BID	
With 24-month follow-up			***p*-value**		***p*-value**
Major molecular response	37%	62%	<0.001*	59%	<0.001*
Complete molecular response	6%	21%	<0.0001*	17%	0.0001*
CCyR	77%	87%	0.0018*	85%	0.016*
Progression to AP/BC	4.2%	0.7%	0.0059†	1.1%	0.0196†
CML-related deaths	3.5%	1.8%	—	1.1%	—
Estimated 24-month OS	96.3%	97.4%	0.65†	97.8%	0.21†

* CMH test stratified by Sokal vs imatinib
† Log-rank test stratified by Sokal vs imatinib for time to AP/BC and OS

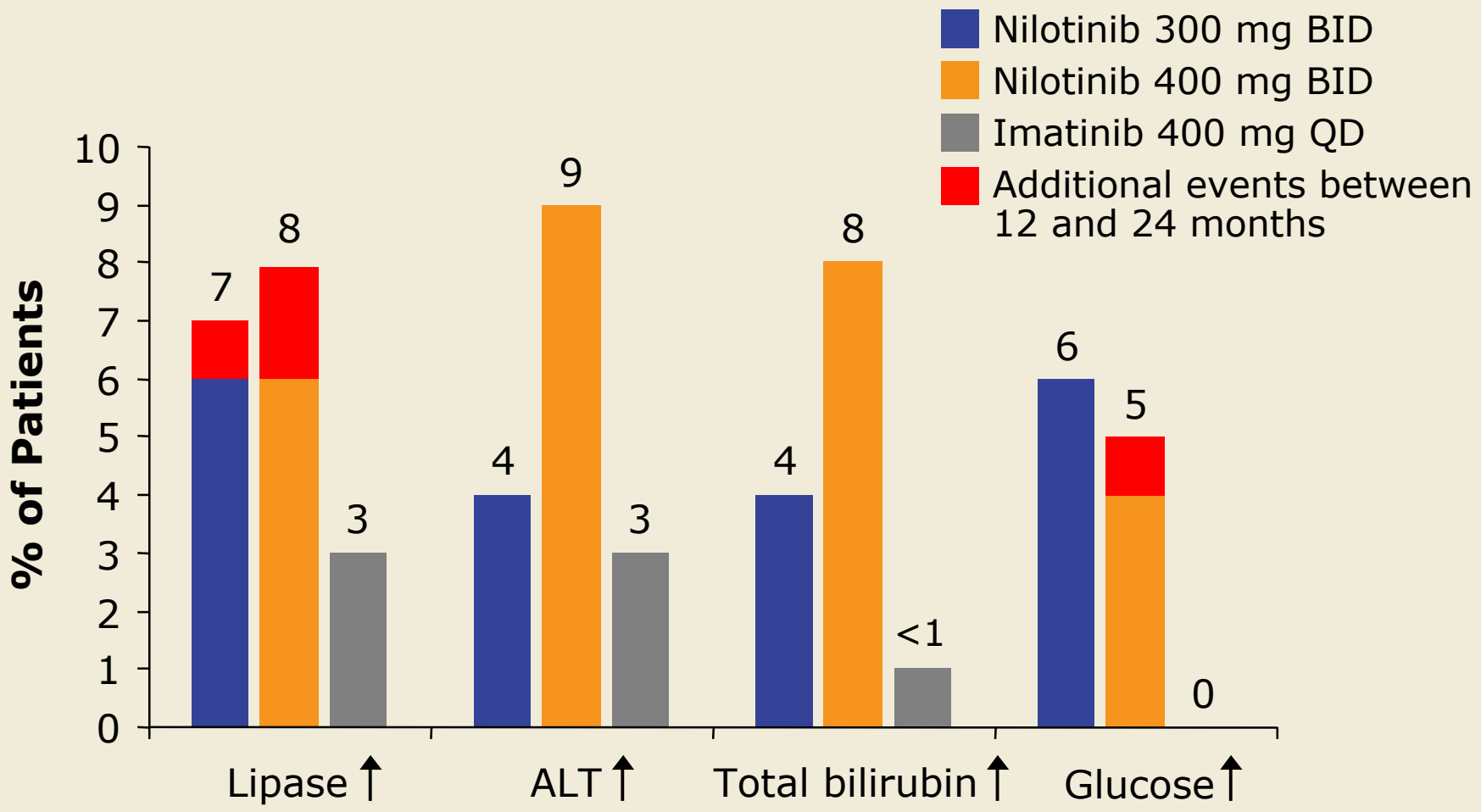
Hughes TP et al. *Proc ASH* 2010;Abstract 207.

Selected Grade 3 and 4 Biochemical Abnormalities



Hughes TP et al. *Proc ASH* 2010;Abstract 207.

Selected Grade 3 and 4 Biochemical Abnormalities



Hughes TP et al. *Proc ASH* 2010;Abstract 207.

Author Conclusions

- With longer follow-up, nilotinib continues to demonstrate superior efficacy compared to imatinib.
  - Higher rates of MMR and CCyR
  - Lower rates of transformation to accelerated/blast phase
- Nilotinib resulted in fewer CML-related deaths compared to imatinib.
- Longer follow-up does not show any change in the adverse-event profile of nilotinib.
- Taken together, these data support nilotinib as a new standard of care for patients with newly diagnosed chronic phase CML.

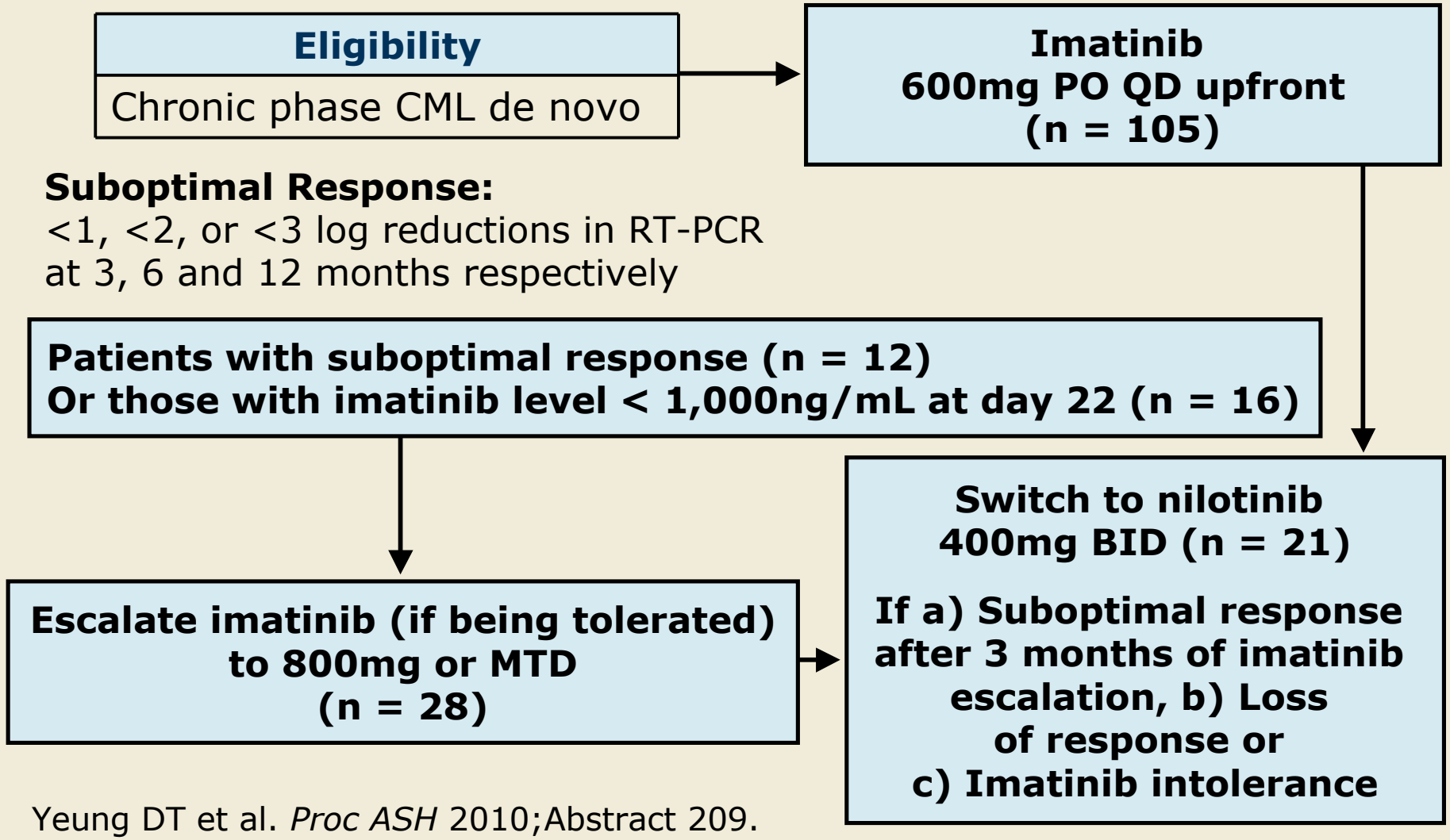
Hughes TP et al. *Proc ASH* 2010;Abstract 207.

Selective Escalation of Imatinib Therapy and Early Switching to Nilotinib in De Novo Chronic Phase CML Patients: Interim Results from the TIDEL-II Trial (Abstract Only)

Yeung DT et al.

Proc ASH 2010;Abstract 209.

TIDEL-II Trial Design



Yeung DT et al. *Proc ASH* 2010;Abstract 209.

Treatment Outcome (from Abstract)

N = 105, median follow-up 18.9 months

Response at 12 months in patients with a minimum of 12 months of follow-up (n = 80/105*)	
Complete cytogenetic response (CCyR)	92%
Major molecular response (MMR: ≥3-log reductions at 12 months)	66%
Complete molecular response	11%

Efficacy endpoints in patients who switched to nilotinib (n = 21)	
Achieved or maintained CCyR (20/21)	95%
MMR† (10/19 not in MMR prior to switch) Imatinib intolerant (9/12) Suboptimal imatinib responders (1/7)	53% 75% 14%

* Includes all patients regardless of imatinib dose or switch to nilotinib
† MMR evaluated at median follow-up 295 days after switch

Yeung DT et al. *Proc ASH* 2010;Abstract 209.

Author Conclusions

- A strategy of selective intensification of BCR-ABL inhibitor therapy (either imatinib dose escalation or switch to second-generation TKI) based on molecular response and PK values resulted in a 66% MMR rate and 92% CCyR rate by 12 months.
- Only a minority (20%) of patients required a switch to nilotinib.
  - Patients experiencing imatinib intolerance (n = 14) demonstrated excellent response rates after switching to nilotinib.

Yeung DT et al. *Proc ASH* 2010;Abstract 209.

Investigator comment on the ENESTnd trial in CML

Just like the dasatinib front-line trial, the update of the nilotinib ENESTnd trial by Hughes shows the second-generation TKIs to be more effective front-line treatments than imatinib. The 24-month follow-up presentation from the ENESTnd trial, comparing nilotinib to imatinib as first-line therapy for CML, talks about the best MMR and CCyR. The 24-month CCyR, and not MMR, is a validated endpoint in predicting longer-term outcomes.

I believe what is probably more compelling is the difference in transformation. Even though the numbers are low, the rate of progression to accelerated or blast phase was significantly lower in patients treated with nilotinib, and that is a clinically relevant endpoint. If a patient experiences disease transformation, then they would generally have a poorer survival. The overall trend is definitely in favor of nilotinib.

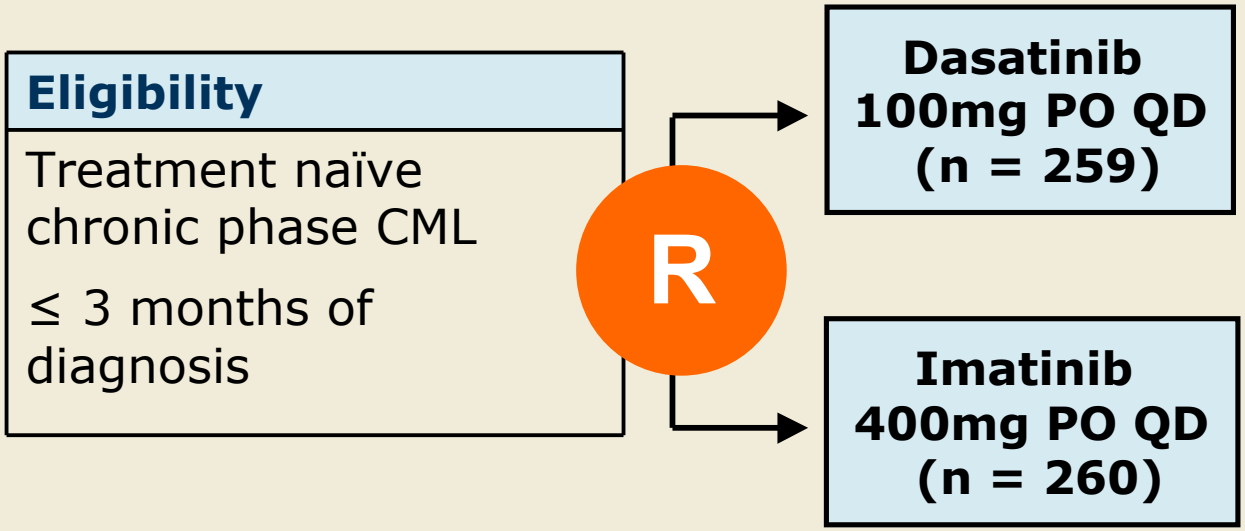
Interview with Susan M O'Brien, MD, January 4, 2011

Dasatinib versus Imatinib in Patients with Newly Diagnosed Chronic Myeloid Leukemia in Chronic Phase (CML-CP) in the DASISION Trial: 18-Month Follow-Up

Shah N et al.

Proc ASH 2010;Abstract 206.

DASISION Study Schema



Primary Endpoint:
Confirmed complete cytogenetic response (confirmed CCyR) by 12 months

Other Key Endpoints:
Rate of CCyR, time to CCyR, duration of CCyR, rate of major molecular response (MMR), time to MMR, progression-free survival (PFS), overall survival (OS)

Shah N et al. *Proc ASH* 2010;Abstract 206.

Confirmed Complete Cytogenetic Response*

	Imatinib (n = 260)	Dasatinib (n = 259)	*p*-value
Confirmed CCyR (by 12 months)	67%	77%	0.0086
Confirmed CCyR (by 18 months)	70%	78%	0.0366

*CCyR = No Philadelphia chromosome-positive metaphases in bone marrow samples (FISH not allowed). Confirmed CCyR at 12 months = CCyR detected in two consecutive assessments at least one month apart.

Shah N et al. *Proc ASH* 2010;Abstract 206.

Secondary Endpoints

	Imatinib	Dasatinib
CCyR (at any time)	80%	85%
Time to CCyR	5.8 months	3.1 months
MMR* (12 months)	28%	46%
MMR (at any time)	41%	57%
Time to MMR	11.8 months	8.3 months
Transformation to advanced phase CML	3.5%	2.3%
OS (at 18 months)	97.9%	96%
PFS (at 18 months)	93.7%	94.9%

*MMR = BCR-ABL ≤ 0.1% on International Scale.

Shah N et al. *Proc ASH* 2010;Abstract 206.

Select Drug-Related Adverse Events

	Imatinib (n = 258)		Dasatinib (n = 258)	
Adverse event	**All grades**	**Grades 3-4**	**All grades**	**Grades 3-4**
Fluid retention Pleural effusion	43% 0%	1% 0%	23% 12%	1% < 1%
Myalgia*	38%	1%	22%	0%
Nausea	21%	0%	9%	0%
Vomiting	10%	0%	5%	0%
Thrombocytopenia	Not reported	10%	Not reported	19%

Grade 3 to 4 bleeding occurred in three imatinib-treated patients and two dasatinib-treated patients.

*Includes myalgia, muscle inflammation and musculoskeletal pain.

Shah N et al. *Proc ASH* 2010;Abstract 206.

Conclusions

- With longer follow-up, dasatinib continues to demonstrate superior efficacy compared to imatinib in CML-CP.
  - Higher and faster rates of CCyR and MMR
- Few patients transformed to accelerated or blast phase in either group.
- Dasatinib continues to be generally well tolerated.
  - Pleural effusion (12%) was seen only with dasatinib but it did not impact efficacy.
- Based on the predictive value of early CCyR, further follow-up may demonstrate better long-term outcomes, such as PFS or OS, for first-line dasatinib versus imatinib.

Shah N et al. *Proc ASH* 2010;Abstract 206.

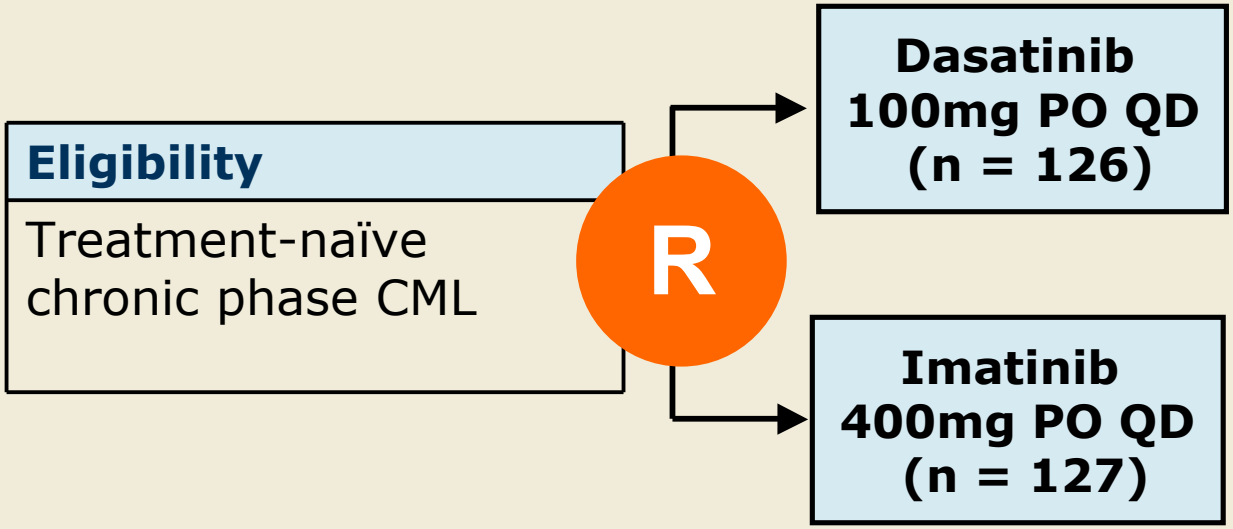
A Randomized Phase II Trial of Dasatinib 100 Mg Vs Imatinib 400 Mg in Newly Diagnosed Chronic Myeloid Leukemia in Chronic Phase (CML-CP): The S0325 Intergroup Trial

Radich JP et al.

Proc ASH 2010;Abstract LBA-6.

S0325 Trial Design

Stratified by Hasford risk category



Primary Endpoint:

- Level of BCR-ABL transcript at 12 months, >4 log reduction (central PCR labs)

Other Key Endpoints:

- Best cytogenetic response by 12 months (local cytogenetics)
- Best hematologic response by 12 months
- Adverse events

Radich JP et al. *Proc ASH* 2010;Abstract LBA-6.

Treatment Outcomes

	Imatinib (n = 123)	Dasatinib (n = 123)	*p*-value
Molecular response at 12 months*			
3 log reduction	43%	59%	0.042
4 log reduction	20%	27%	0.31
Cytogenetic CR within 12 months†	69%	82%	0.097
Hematologic CR within 12 months	90%	86%	0.25
PFS at 12 months	96%	99%	0.20

*BCR-ABL mRNA levels were available for 90 imatinib- and 99 dasatinib-treated patients at 12 months.

†Cytogenetic data were available for 58 imatinib- and 67 dasatinib-treated patients at 12 months.

Radich JP et al. *Proc ASH* 2010;Abstract LBA-6.

Non-Hematologic Toxicities

	Imatinib 400 mg/d N = 123		Dasatinib 100 mg/d N = 122	
	All grades	Grades 3-4	All grades	Grades 3-4
Fluid retention Edema (any) Pleural	 59 2	 3 1	 24 14	 1 2
Diarrhea	49	2	41	6
Nausea	59	0	32	0
Vomiting	23	0	19	1
Muscle pain	44	1	12	0
Rash	34	2	40	0
Headache	19	2	34	3
Fatigue	63	1	61	1
Prolonged QTc	1	0	2	1

Radich JP et al. *Proc ASH* 2010;Abstract LBA-6.

Author's Conclusions

- The study provides further evidence that dasatinib appears more efficacious than imatinib for patients with treatment-naïve chronic phase CML.

- Dasatinib and imatinib have different toxicity.
  - Dasatinib — more thrombocytopenia (data not shown) and pleural effusions
  - Imatinib — more fluid retention and nausea

Radich JP et al. *Proc ASH* 2010;Abstract LBA-6.

Investigator comment on the trials investigating comparative efficacy of dasatinib versus imatinib as initial treatment of CML

The data from the pivotal IRIS trial of imatinib in first-line CML have shown that if a patient does not have a complete cytogenetic response at 18 months, then they have a worse outcome, and thus 18-month cytogenetic response is a validated endpoint in the initial treatment of CML. The presentation by Shah details the 18-month cytogenetic response data with dasatinib as 78 percent versus 70 percent with imatinib in CML. To me, this update makes it more convincing and compelling than the original paper that the long-term outcome will likely be better for patients with CML receiving up-front dasatinib.

The SWOG study by Radich has the primary endpoint of a four-log reduction of BCR-ABL molecular transcripts at 12 months. Only fifty percent of the patients had cytogenetic data. The study did not meet the primary endpoint, though there was a trend in favor of dasatinib. In my view, this endpoint is not validated and is not known to be correlated with long-term outcomes.

Interview with Susan M O'Brien, MD, January 4, 2011

Comparative Efficacy of First-Line Treatment of Chronic Myeloid Leukemia: A Systematic Review and Meta-Analysis

Mealing S et al.

Proc ASH 2010;Abstract 3436.

Objectives

- Use meta-analysis to evaluate the relative efficacy of the oral BCR-ABL inhibitors imatinib, dasatinib and nilotinib in patients with newly diagnosed chronic-phase CML (CML-CP).
- The analyses were conducted using mixed treatment-comparison meta-analytical techniques.
  - In the absence of randomized head-to-head trials, a Bayesian mixed treatment-comparison meta-analysis provides a means to indirectly estimate the treatment effect of 1 intervention relative to another.

Mealing S et al. *Proc ASH* 2010;Abstract 3436.

Methods

- Abstracts were independently reviewed by 2 members of the project team for inclusion in the network meta-analysis (NMA).
- Criteria for inclusion of study data in the NMA:
  - English-language, randomized controlled trials that included adult patients (>18 years of age) with newly diagnosed CML-CP
    - Evaluated dasatinib, imatinib, nilotinib, interferon alpha* or hydroxyurea*
    - Major molecular response (MMR), complete cytogenetic response (CCyR), partial cytogenetic response, minor cytogenetic response, no cytogenetic response, and overall and progression-free survival outcomes data

*Non-BCR-ABL inhibitors were also included to increase the available data network.

Mealing S et al. *Proc ASH* 2010;Abstract 3436.

Trials Included in the NMA

Citation	Study Design	Treatments (N)
N Engl J Med 2010;362:2260-70	R, MC, phIII	Dasatinib 100 mg QD (n=259) Imatinib 400 mg QD (n=260)
Blood 2009;113:4497-504	P, R	Imatinib 400 mg QD (n=108) Imatinib 800 mg QD (n=108)
N Engl J Med 2010;362:2251-9	MC, R, phIII	Nilotinib 300 mg BID (n=282) Nilotinib 400 mg BID (n=281) Imatinib 400 mg QD (n=283)

R = randomized; MC = multicenter; phIII = Phase III;
P = prospective

Mealing S et al. *Proc ASH* 2010;Abstract 3436.

Data Used in the NMA

Citation	Treatments	CCyR 6 mo (%)	CCyR 12 mo (%)	MMR 12 mo (%)
N Engl J Med 2010;362:2260-70	Dasatinib 100 mg QD Imatinib 400 mg QD	73.0 59.2 (P=NR)	83.4 71.5 (P=0.0011)	45.9 28.1 (P<0.0001)
Blood 2009;113:4497-504	Imatinib 400 mg QD Imatinib 800 mg QD	50.0 51.9 (P=NS)	58.3 63.9 (P=0.435)	33.3 39.8 (P=NS)
N Engl J Med 2010;362:2251-9	Nilotinib 300 mg BID Nilotinib 400 mg BID Imatinib 400 mg QD	67.0 63.0 44.9 (P=NR)	80.1 77.9 65.0 (P<0.001)*	44.0 43.1 21.9 (P<0.001)*

*P-*value is for both nilotinib arms vs imatinib. NR = not reported; NS = not significant*

Mealing S et al. *Proc ASH* 2010;Abstract 3436.

Relative Treatment Effects: CCyR at 12 Months

	Imatinib 400 mg QD OR (95% CI*)	Dasatinib 100 mg QD OR (95% CI*)	Nilotinib 300 mg BID OR (95% CI*)	Nilotinib 400 mg BID OR (95% CI*)
Imatinib 400 mg QD	—	0.51 (0.33, 0.76)	0.47 (0.31, 0.67)	0.53 (0.36, 0.76)
Dasatinib 100 mg QD	2.06 (1.31, 3.06)	—	0.96 (0.52, 1.63)	1.10 (0.60, 1.85)
Nilotinib 300 mg BID	2.22 (1.49, 3.21)	1.13 (0.61, 1.93)	—	1.17 (0.76, 1.71)
Nilotinib 400 mg BID	1.94 (1.31, 2.78)	0.99 (0.54, 1.67)	0.89 (0.58, 1.31)	—

**95% CI = Bayesian equivalent of a 95% confidence interval*

Mealing S et al. *Proc ASH* 2010;Abstract 3436.

Efficacy Results

- The evaluation of efficacy using 6-month and 12-month CCyR and 12-month MMR:
  - Significantly higher responses in the dasatinib 100 mg QD and nilotinib 300 mg BID groups compared with imatinib 400 mg QD ($P<0.05$).
  - Response odds for dasatinib 100 mg QD and nilotinib 300 mg BID were >2-fold higher than those of imatinib 400 mg QD
- Indirect comparisons of dasatinib vs nilotinib showed no significant differences in relative efficacy.
- Evidence networks could not be constructed for survival endpoints due to a paucity of events in the publications.

Mealing S et al. *Proc ASH* 2010;Abstract 3436.

Conclusions

- Dasatinib and nilotinib were associated with significant improvements in CCyR and MMR compared with imatinib 400 mg QD.
- Using the CCyR at 6 and 12 months and the MMR at 12 months, there were no significant differences in the relative efficacy of dasatinib and nilotinib.
- CCyR at 18 months, survival and safety-related outcomes could not be evaluated in this study.
- The addition of data from future randomized controlled trials will strengthen the present meta-analysis.

Mealing S et al. *Proc ASH* 2010;Abstract 3436.

Investigator comment on the meta-analysis and systematic review of the comparative efficacy of first-line treatment of CML

This review tells us something that we already knew from the two randomized trials of second generation TKIs published earlier this year in the *New England Journal of Medicine.* Both the controlled trials had primary endpoints at 12 months of treatment, though the well-established endpoint with imatinib is complete cytogenetic response at 18 months. With the earlier endpoints at 12 months, the second-generation TKIs looked better.

We currently do not know if these earlier endpoints are going to be associated with better event-free or overall survival in the long run.

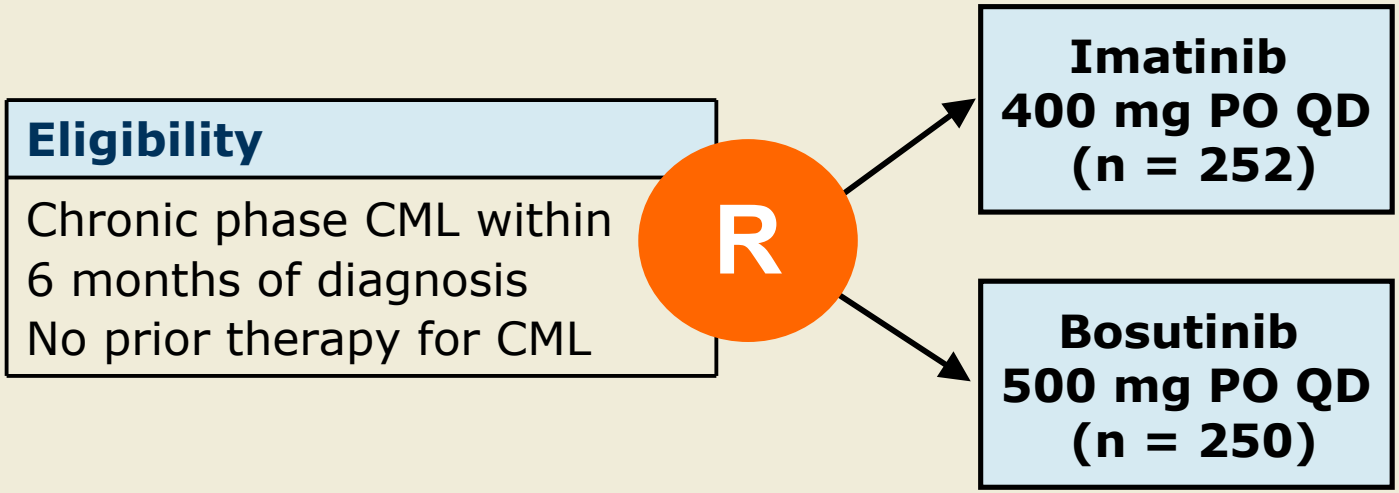
Interview with Susan M O'Brien, MD, January 4, 2011

An Ongoing Phase 3 Study of Bosutinib (SKI-606) versus Imatinib in Patients with Newly Diagnosed Chronic Phase Chronic Myeloid Leukemia

Gambacorti-Passerini C et al.

Proc ASH 2010;Abstract 208.

BELA Study Schema



Primary Endpoint:
Complete cytogenetic response (CCyR) rate at 12 months

Other Key Endpoints:
Major molecular response (MMR) rate at 12 months
Duration of CCyR, MMR and complete hematologic response (CHR)
Time to and rate of progression to accelerated/blast phase (AP/BP)
Safety and tolerability

Gambacorti-Passerini C et al. *Proc ASH* 2010;Abstract 208.

Efficacy Outcomes

	Imatinib	Bosutinib	*p*-value
CCyR at 12 months ITT population (n = 252; 250) Evaluable population (n = 241; 219)	 68% 68%	 70% 78%	 0.601 0.026
MMR at 12 months ITT population (n = 252; 250) Evaluable population (n = 241; 219)	 26% 27%	 39% 43%	 0.002 <0.001
Median time to CCyR	24.6 weeks	12.9 weeks	<0.0001
Median time to MMR	72.3 weeks	37.1 weeks	<0.0001
Transformation to AP/BP (n = 252; 250)	4%	2%	0.053
CML-related deaths (n = 252; 250)	3%	1%	0.056

Gambacorti-Passerini C et al. *Proc ASH* 2010;Abstract 208.

Nonhematologic Safety Events

	Imatinib (n = 251)		Bosutinib (n = 248)	
	All Grades	**Grade 3-4**	**All Grades**	**Grade 3-4**
Diarrhea	21%	1%	68%	10%
Vomiting	13%	0%	32%	3%
Bone pain	10%	1%	4%	0%
Muscle cramps	20%	0%	2%	0%
Peri-orbital edema	14%	0%	<1%	0%
Increased ALT	Not Reported	3.2%	Not Reported	20.6%
Increased AST	Not Reported	2.8%	Not Reported	10.1%

Gambacorti-Passerini C et al. *Proc ASH* 2010;Abstract 208.

Hematologic Adverse Events

	Imatinib (n = 251)	Bosutinib (n = 248)
Grade ≥3 anemia	6.4%	6.0%
Grade ≥3 neutropenia	22.7%	8.9%
Grade ≥3 thrombocytopenia	13.1%	12.5%

Gambacorti-Passerini C et al. *Proc ASH* 2010;Abstract 208.

Treatment Summary: Dose Interruption, Reduction, Discontinuation

Parameter	Imatinib (n = 251)	Bosutinib (n = 248)
Dose interruption secondary to adverse event	42%	61%
Dose reduction secondary to adverse event	18%	39%
Discontinued patients (total)	20%	29%
Discontinuation secondary to adverse event	5%	19%
Discontinuation secondary to treatment failure	10%	3%

Gambacorti-Passerini C et al. *Proc ASH* 2010;Abstract 208.

Author's Conclusions

- Bosutinib did not demonstrate a superior rate of CCyR at 12 months based on the ITT population, but was higher based on the evaluable population.
- Bosutinib treatment did result in a superior rate of MMR at 12 months compared to imatinib based on the ITT and evaluable populations.
- Patients on bosutinib appear to have lower rates of deaths due to CML progression, transformation to AP/BP and discontinuations due to treatment failure compared to those on imatinib.

Gambacorti-Passerini C et al. *Proc ASH* 2010;Abstract 208.

Investigator comment on the Phase III study of bosutinib versus imatinib in CML

This was a study comparing another second-generation TKI, bosutinib, to imatinib in the up-front management of CML. Bosutinib is an interesting drug because the putative advantage of this drug is that it doesn't interfere with the PDGF receptor or with c-Kit. The hypothesis has been that one of the reasons dasatinib causes pleural effusions is by interfering with PDGF receptor signaling, and all the currently available TKIs cause myelosuppression by inhibiting c-Kit. Thus there was a theoretical rationale that bosutinib might cause fewer pleural effusions and less myelosuppression.

The general expectation was that this would be another positive randomized trial of a second-generation TKI in first-line chronic phase CML. Unfortunately, the results were rather disappointing as the complete cytogenetic responses were similar in both arms in the intent-to-treat analysis. Additionally, a high percentage of patients came off study because of toxicity in response to bosutinib.

Interview with Susan M O'Brien, MD, January 4, 2011

Investigator comment on the Phase III study of bosutinib versus imatinib in CML

The primary endpoint of this study was complete cytogenetic response (CCyR), and in viewing the intent-to-treat population at 12 months no significant difference was observed in the CCyR rate between the two arms. Seventy percent of patients receiving bosutinib versus 68 percent receiving imatinib achieved CCyR. The major molecular response rate seemed to be superior for bosutinib at 39 percent versus 26 percent, but this was not the primary endpoint.

One of the most important observations of this trial was that 19 percent of patients discontinued bosutinib due to adverse events compared to only five percent of patients receiving imatinib. The most common cause for discontinuation of imatinib was treatment failure, at 10 percent compared to three percent with bosutinib.

So this study, unfortunately, missed its primary endpoint. I believe this agent has significant activity. However, whether it will obtain approval in the front-line setting, now that nilotinib and dasatinib have already established a high bar, remains to be seen.

Interview with Neil P Shah, MD, PhD, January 4, 2011