June 10, 2013

OUTPERFORM

Reason for report:

INITIATION

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HEALTHCARE EQUITY RESEARCH

AMBIT BIOSCIENCE

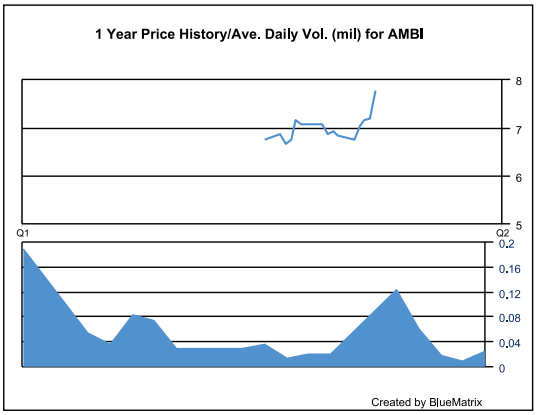
Advancing Targeted Therapy for AML -- Initiating at OP

• **Bottom Line**: We are initiating coverage on AMBI with an Outperform rating and $14 valuation based on DCF. In an area where chemotherapy remains as the standard of care with limited breakthrough, we see AMBI's quizartinib as the best-in-class FLT3 inhibitor which currently represents the mainstay for targeted therapy for acute myeloid leukemia (AML). The Phase III-ready wholly owned asset is expected to deliver data in 2015 while the possibility of filing based on the Phase II data could provide near-term upside to the stock.

• **Quizartinib is a wholly owned, late-stage and in our opinion best-in-class asset in an area with limited competition.** It has been tested in over 400 patients and has shown a promising and consistent efficacy and safety profile in 2nd and 3rd line therapies. MEDACorp KOLs do not view QTc prolongation associated with quizartinib to be limiting. In addition, KOL feedback indicates that complete response with incomplete neutrophil recovery (CRi), which represents the majority of responses seen on quizartinib, does enable stem cell transplant which is viewed as the only hope for relapsed / refractory AML patients. Therefore CRi may confer a clinically meaningful benefit.

• **While we advocate valuing AMBI based on the assumption of approval after the completion of Phase III, we believe the possibility of filing based on Phase II data exists and there is a realistic chance of approval, in our view, if the application gets to an FDA advisory panel review.** Although the FDA previously (in 2011) did not support filing for quizartinib based on early Phase II data, we believe the current data set is stronger. In addition, there has been at least one case (Marqibo) in which accelerated approval was obtained based on CRi, and data appeared far more limited, in our view. While there is considerable uncertainty about this upside scenario, at the current valuation we believe there is limited downside if Phase III is required and accelerated approval would be all upside.

Key Stats:	**(NASDAQ:AMBI)**
S&P 600 Health Care Index:	**982.44**
Price:	**$7.79**
52 Week High:	$8.24
52 Week Low:	$6.22
Shares Outstanding (mil):	21.5
Market Capitalization (mil):	$167.5
Book Value/Share:	$(0.38)
Cash Per Share:	$3.86
Dividend (ann):	$0.00
Dividend Yield:	0.0%
Valuation:	$14 on DCF analysis



Dec Yr	1Q	2Q	3Q	4Q	FY Rev	1Q	2Q	3Q	4Q	FY EPS	P/E
2012A	--	--	--	--	$17.6	--	--	--	--	($16,592.00)	NM
2013E	$6.6A	$6.5	$5.0	$3.0	$21.1	($3,019.30)A	($0.27)	($0.38)	($0.52)	($1.85)	NM
2014E	--	--	--	--	$15.0	--	--	--	--	($1.77)	NM

Source: Company Information and Leerink Swann LLC Research
Revenues in millions.
GAAP EPS. Estimates reflect May 2013 IPO.

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The Healthcare Investment Bank™

Ambit Biosciences

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Ambit Overview

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- Lead compound quizartinib, a selective potent FLT3 (FMS-like tyrosine kinase-3) inhibitor, showed promising Phase II data in acute myeloid leukemia (AML), where there have been few recent treatment advances
- Following the recent termination of the Astellas collaboration, quizartinib is now a wholly owned late-stage, best-in-class FLT3 inhibitor with data on nearly 400 patients.
- A strong platform supports internally developed pipeline programs to advance in oncology, autoimmune, and inflammatory diseases
- Key financials: 22M dilutive shares, $85M cash ($3.86/share)

Investment Thesis

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- Based on MEDACorp key opinion leader (KOL) feedback, we believe AMBI's lead candidate quizartinib is the best FLT3 (FMS-like tyrosine kinase-3) inhibitor in development and best currently available targeted agent for acute myeloid leukemia (AML), a devastating hematological cancer with few options and high unmet need.

- Quizartinib is a wholly owned, best-in-class FLT3 inhibitor, late-stage asset in an area with limited competition. It has been tested in over 400 patients and has shown a promising efficacy and safety profile. MEDACorp KOLs do not view QTc prolongation associated with quizartinib to be limiting. In addition, KOL feedback indicates that CRi, which represents the majority of responses seen on quizartinib, does enable stem cell transplant which is viewed as the only hope for relapsed / refractory AML patients. Therefore CRi confers a clinically meaningful benefit.

- While we advocate valuing AMBI based on the assumption of approval after the completion of Phase III, we believe the possibility of filing based on Phase II data exists and there is a realistic chance of approval if the application gets to an FDA advisory panel review. Although the FDA previously did not support filing for quizartinib based on early Phase II data, there has been at least one case (Marqibo) in which accelerated approval was obtained based on CRi, and data appeared far more limited, in our view. At the current valuation, we believe accelerated approval would be all upside.

Note: QTc – a corrected Q wave to T wave interval in heart electrical cycle

Valuation

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- We value AMBI at $14 per share based on an NPV methodology.
- We assume quizartinib launches in the second line setting for the treatment of FLT3-ITD AML in 2016 in the U.S., in 2017 in the EU, and in 2018 in Japan.
- Our projection for peak penetration is 50% in the U.S. and Japan and 45% in the EU. Our projection for probability weighted (60%) sales reaches $450M by 2029, one year after patent expiration.
- We use a discount rate of 10%, which we believe is appropriate given probability weighted sales projection.

Risks to Valuation

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- Clinical risk – although Phase II data are promising, these are single-arm studies and the controlled randomized Phase III trial may fail to show OS benefit vs. chemo therapy
- Regulatory risk -- achieving accelerated approval based on current Phase II data, which represents the upside scenario, faces considerable uncertainty given that the FDA previously appeared unsupportive of such filing based on early Phase II data.
- Commercial risk – quizartinib may face competition from other drugs targeting FLT3-ITD
- Financing risk – AMBI has cash of $85M, sufficient to fund operations through the Phase III trial

Ambit – Internally Discovered Pipeline

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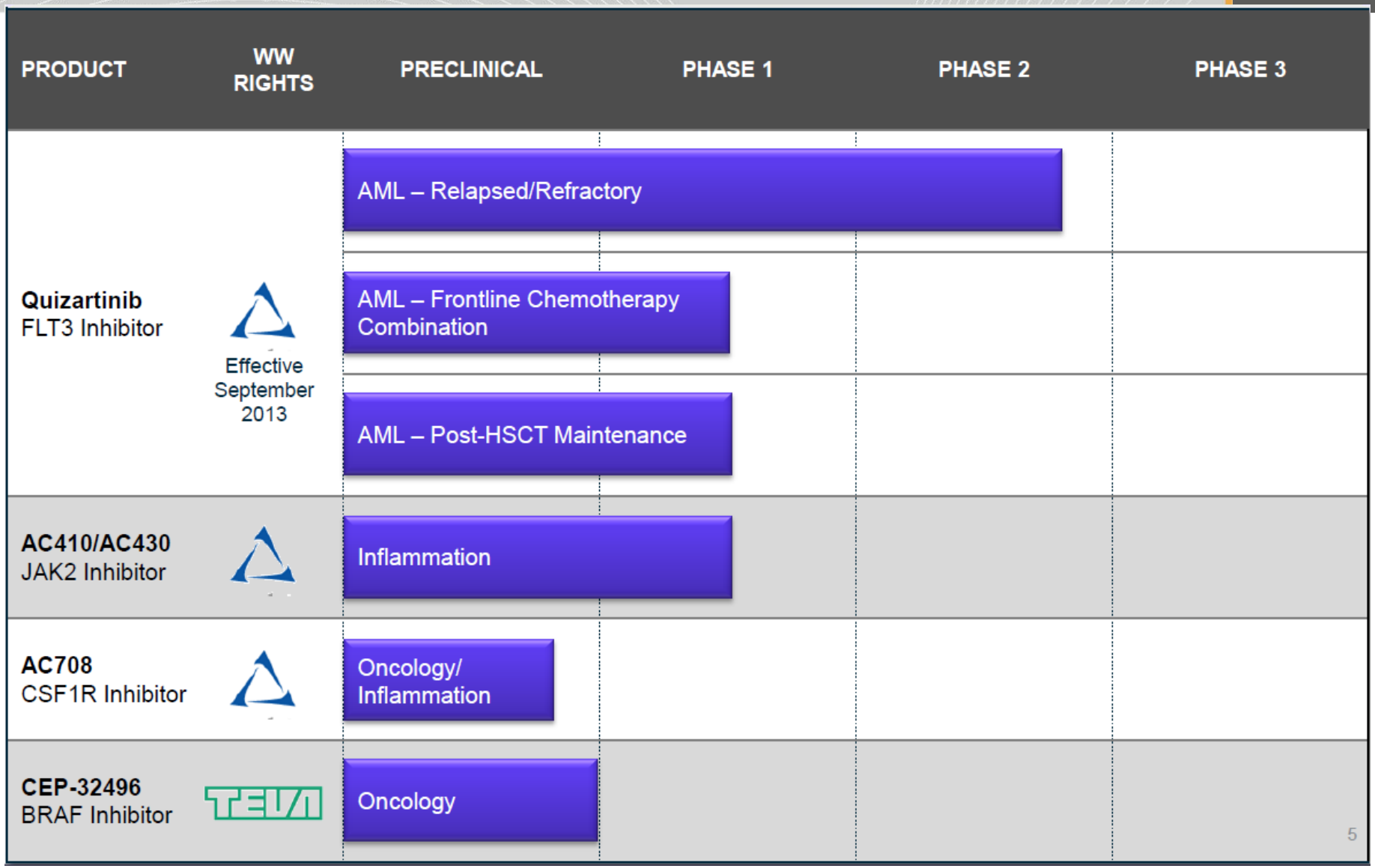

HSCT = Hematopoietic Stem Cell Transplantation

Source: Company Reports; Note: CSF1R – colony stimulating factor 1 receptor

Key Expected Events – Data News Flow

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Compound	Timing	Event
Quizartinib (FLT3i)	July, '13	Phase IIb data, Phase III dose selection
	Sept, '13	End of Phase II meeting with FDA
	Early '14	Phase III initiation
	YE:15	Phase III data
AC708 (CSF1Ri)	2H:13	Initiating IND-enabling studies

Source: Company reports and Leerink Swann

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KEY INVESTMENT CONSIDERATIONS

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DEFINING SUCCESS FOR THE PHASE III TRIAL

Quizartinib Proposed Phase III Trial

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- Monotherapy vs. physicians' choice of standard chemo
- Patient population: ≥ 18 y.o. FLT3-ITD + patients in 1st salvage
- Endpoint: Overall survival
- N= approximately 350 patients
- 2:1 randomization
- Dose determined by Phase 2b results
- Event driven interim analyses (considering adaptive design)
- Data by end of 2015

Source: Company Reports

OS and CR – Benchmarks for Chemotherapy

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- Analysis on 109 patients with FLT3-ITD mutation showed that following the first relapse, 36 patients received salvage chemo and achieved **24%** (8 out of 34 evaluable pts) in CR+CRp. Two of the 8 patients received an allogeneic stem cell transplant. The median OS was **13 weeks** from relapse*.

- In a study assessing lestaurtinib in combination with chemo therapy in 112 AML patients with FLT3 mutant after first relapse, the control arm (salvage chemo therapy in 2nd line) showed a CR+CRp rate of **21%** (23) and a median OS of **~3.9 months** from relapse**.

- A study on 594 patients (including all genotypes) in 3rd line therapy (receives second salvage therapy) showed a **13%** (76) CR rate and median OS of **1.5 months**. Subgroup analysis showed a CR rate of **26%** (50) and median OS of **4.9 months** for low risk patients (0-2 AEs), or **8%** (10) and **2.6 months** for intermediate risk (3 AEs), and **2%** (3) and **1.6 months** for high risk patients (4-7 AEs)***.

*Source: *Ravandi et al, (2010) 34:752-756; **Levis et al, (2011) 117:3294-3301; ***Giles et al, Cancer (2005) 104:547-554*

Quizartinib Showed Median OS of 6.35 Months in 2nd Line Phase 2 Monotherapy

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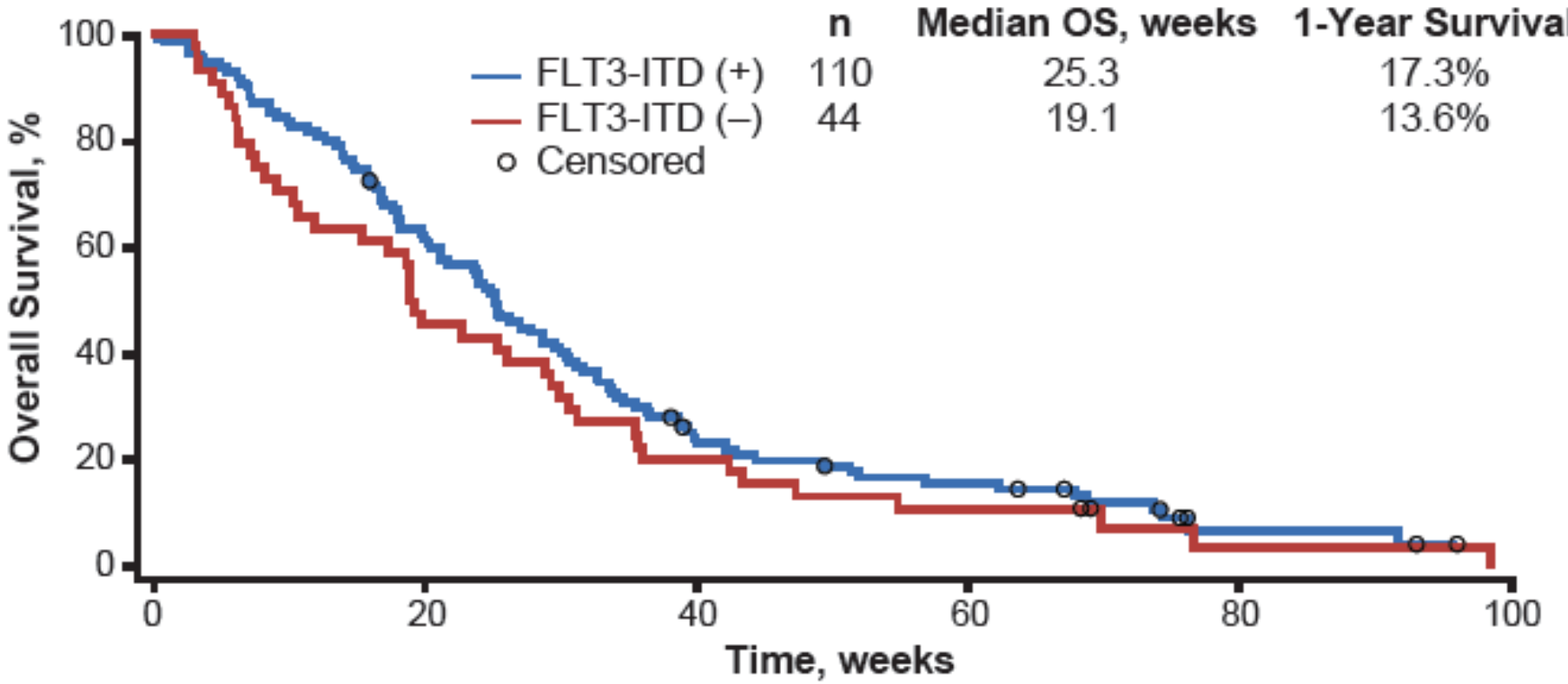
- Median age – 69 years old
- 10% of patients bridged to stem cell transplant



FLT3-ITD=FMS-like tyrosine kinase 3 internal tandem duplication; OS=overall survival.

Source: Martinelli et al, 2013 ASCO, #7021

Quizartinib Median OS Maintained at 6 Months in 3rd Line Phase II Monotherapy

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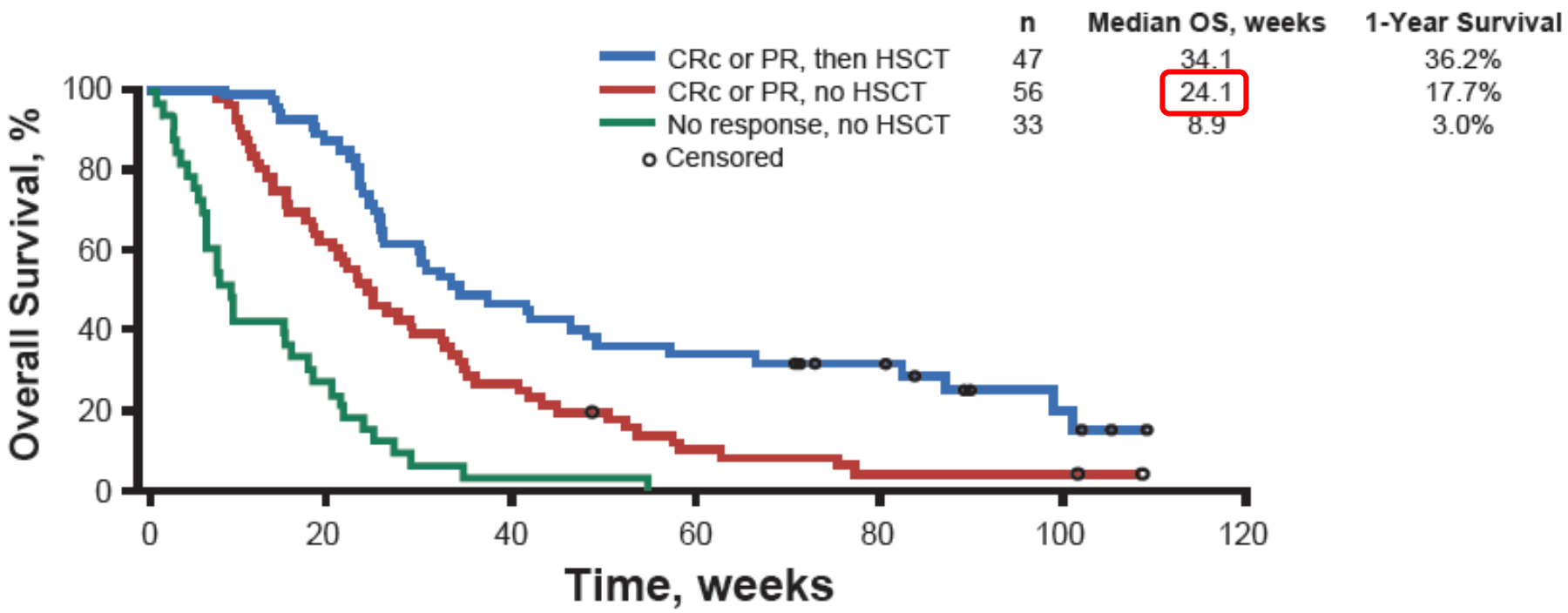
- Median age – 51 years old
- 35% of patients bridged to stem cell transplant



CRc=composite complete remission (CR + CRp + CRi); FLT3-ITD=FMS-like tyrosine kinase 3 internal tandem duplication; HSCT=hematopoietic stem cell transplantation; OS=overall survival; PR=partial remission.

Source: Cortes et al, ASCO 2013, #7012

Study Assumption for Overall Survival Appears Conservative

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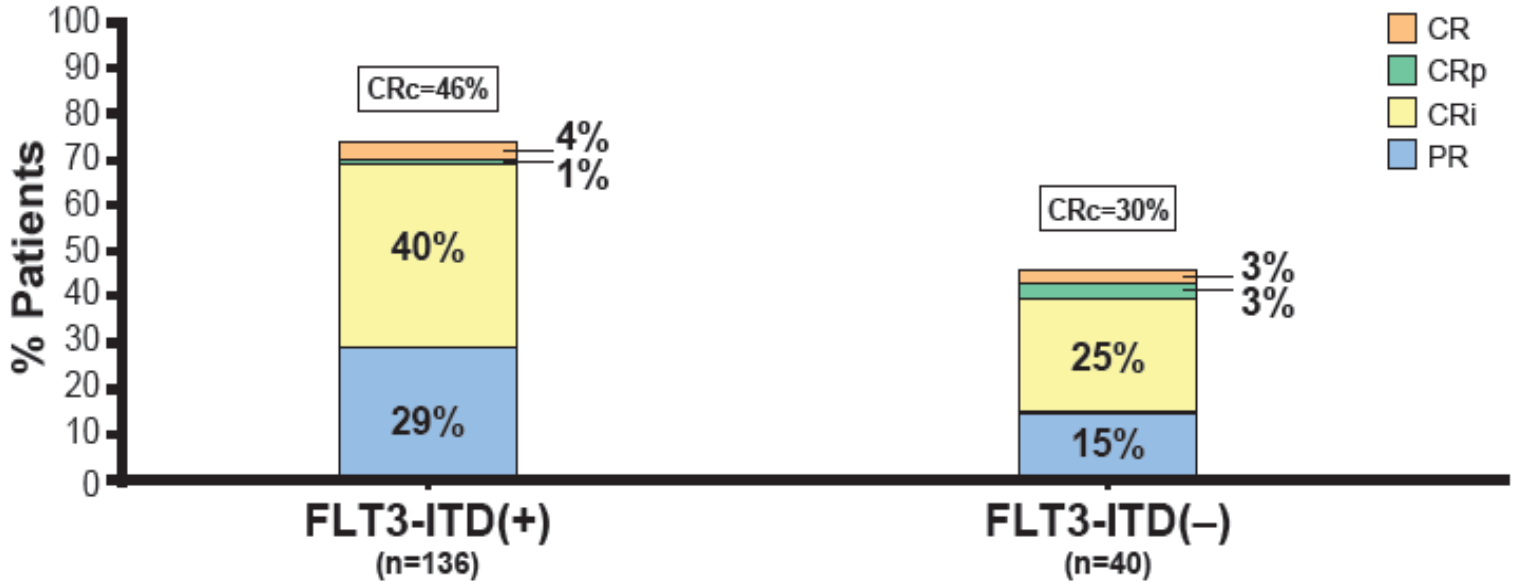
- The assumption for the Phase III trial was 3.9 months for the physician's choice of standard of care (chemotherapy) vs. 6 months in quizartinib monotherapy
- Based on historical data, we believe the assumption for both the control arm and the drug arm is conservative, providing some upside for the potential positive outcome

However, Quizartinib CR+CRp Rate (6% in 2nd Line) Lower than Benchmark (21-24%)



	FLT3-ITD(+)	FLT3-ITD(–)
Median (range) duration CRc, weeks	10.6 (0.1+–102.1+)	7.0 (0.1–8.1)
Median time (range) to CRc, weeks	4.1 (0.1+–102.1+)	4.2 (0.1–8.1)

CI=confidence interval; CR=complete remission; CRc= composite CR (CR + CRp + CRi); CRi=complete remission with incomplete hematologic recovery; CRp=complete remission with incomplete platelet recovery; FLT3-ITD=FMS-like tyrosine kinase 3 internal tandem duplication; PR=partial remission.

Source: Cortes et al, ASCO 2013, #7012

Instead, Quizartinib Has High CRi Rates Across All Phase II Cohorts

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Phase 2 Comparison

Response	Phase 2b 30 mg Cohort	Phase 2b 60 mg Cohort	Phase 2 Cohort 2
CRc+PR	44%	78%	74%
CRc	38%	39%	46%
CR+CRp	0%	11%	5%
Bridge to Transplant	25%	33%	35%

Response Definitions

CRc	CR + CRp + CRi
CR	Reduction of bone marrow blasts to < 5% Full hematologic recovery
CRp	Reduction of bone marrow blasts to < 5% Incomplete platelet recovery
CRi	Reduction of bone marrow blasts to < 5% Incomplete neutrophil recovery with or without platelet recovery
PR	Reduction of bone marrow blasts to between 5% - ≤ 25% and ≥ 50% reduction from baseline

Source: Company Reports

Phase II Follow-up Data Show That Cri Results in Frequent HSCT and Potentially OS Benefit

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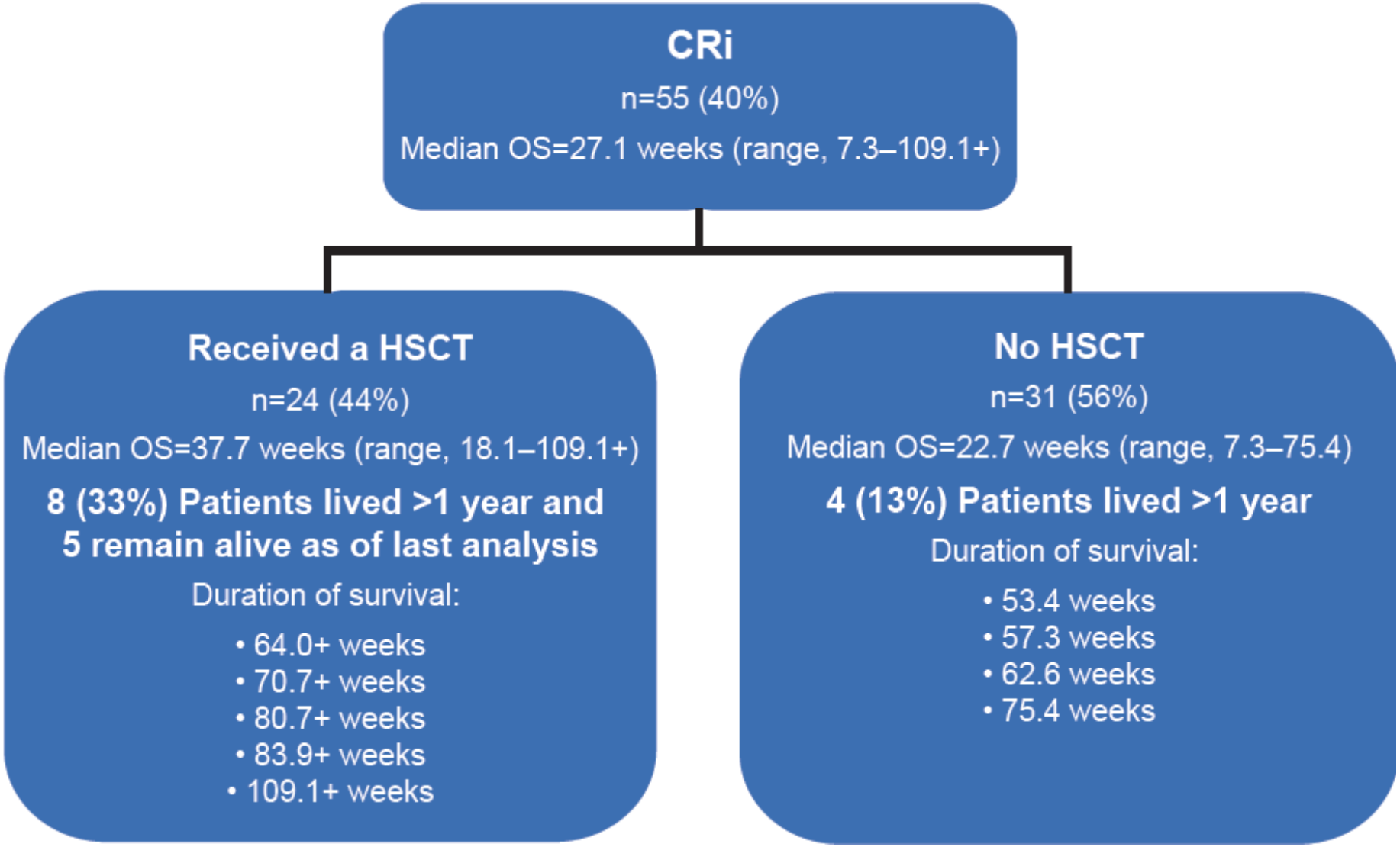

Source: Cortes et al, ASCO 2013, #7012

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CASE FOR APPROVAL BASED ON PHASE II DATA

The FDA Previously Did Not Support Filing of Quizartinib on Phase II data

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- AMBI approached the FDA in 2011 with early Phase II data on potential accelerated approval
- Among 63 patients, 17 were dosed at 200mg where high QTc signal was reported
- According to the FDA, these were not sufficient to support CRi as a surrogate endpoint

Two Phase II Trials with Over 400 Patients on Quizartinib

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- Substantially more patients were on quizartinib vs. Marqibo, which was approved in Ph-ALL based on a single-arm 65 patient study
- CRc rates were in a range of 38-56%, higher than historical data
- OS data from both cohort 1 (2nd line) and cohort 2 (3rd line) were over 6 months, suggesting sustainable activity

Quizartinib Safety Profile Improved

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- Phase IIb trial with reduced doses (30mg and 60mg) showed comparable efficacy vs. high dose data while toxicity profile was improved substantially

Comparing Grade 3 QT Prolongation in Phase 2b Versus Phase 2				
	Phase 2b*		Phase 2	
Adverse Event	30 mg N=20 n (%)	60 mg N=19 n (%)	90/135 mg N=316 n (%)	200 mg N=17 n (%)
QT Prolongation	0 (0%)	1 (5%)	50 (16%)	6 (35%)

Source: Company Reports

During the Past Few Years, FDA Appears More Open to Approval on Single Arm Studies

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- The FDA approved seven oncology drugs based on single arm studies due to large magnitude of benefit and unmet medical needs

Drug	Indication	Approval Date
Iclusig (ponatinib)	Chronic myeloid leukemia	December 2012
Synribo (omacetaxine mepesuccinate)	Chronic myeloid leukemia	October 2012
Bosulif (bosutinib)	Chronic myeloid leukemia	September 2012
Marqibo (liposomal vincristine)	Acute lymphoblastic leukemia	August 2012
Kyprolis (carfilzomib)	Multiple myeloma	July 2012
Erivedge (vismodegib)	Basal cell carcinoma	February 2012
Xalkori (crizotinib)	Non-small cell lung cancer	August 2011

Source: Company Reports

Bridging to Transplant Is Considered by KOLs a Clinically Meaningful Benefit

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- Transplant is considered the key method to potentially cure AML
- MEDACorp KOLs believe transplant could translate into survival benefit, serving as a meaningful clinical endpoint
- CRi is considered sufficient for stem cell transplant, therefore could serve as a meaningful surrogate endpoint

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APPROVAL OF MARQIBO SUGGESTS CRi MAY BE AN APPROVABLE ENDPOINT

Marqibo Was a 505(b)(2) Filing

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- Marqibo is a liposomal formulation of vincristine designed to increase the therapeutic window
  - Compounded in the pharmacy by mixing vincristine sulfate and sphingomyelin/cholesterol liposomes into the sodium phosphate buffer vial
  - Vial is inverted 5 times, the floatation ring is attached, then kept in 65 degree Celsius water bath for 10 minutes
- The filing was based on the results of a Phase II single arm study, supported by a Phase I/II single arm dose finding study
  - Phase II study was in Ph- ALL or lymphoblastic lymphoma. 2nd or greater relapse, or whose disease progressed after 2 or more treatment lines

Source: Marqibo Label; Note: Ph-ALL – ***Philadelphia-positive subtype of acute lymphoblastic leukemia***

Marqibo Phase II Eligibility Criteria

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- Phase II study was in Ph- ALL or lymphoblastic lymphoma. 2nd or greater relapse, or whose disease progressed after 2 or more treatment lines
- Achieved CR to at least 1 prior, but not necessarily the immediate prior therapy
- Not eligible for immediate HSCT

34% of Patients in the Marqibo Phase II Did Not Receive Asparaginase Products Prior to Enrollment

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Chemotherapy used	first-line	second-line
vincristine	100%	93.8%
cyclophosphamide	93.8%	81.5%
methotrexate	92.3%	78.5%
cytarabine	89.2%	84.6%
doxorubicin	89.2%	72.3%

22 out of 65 patients did not receive asparaginase products prior to enrollment, which is an approved and therefore available therapy for the treatment of Ph- ALL

Source: FDA Briefing Documents and Slides

CR + CRi Was 15% Including Unconfirmed Responses

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	CR+CRi FDA Assessment Based on CRFs Review (N=65)	
	Confirmed + Unconfirmed*	Confirmed
Complete Remission (CR) [n(%)] 95% CI	3 (4.6) (1.0, 12.9)	2 (3.1) (0.4, 10.7)
CRi (including CRp) [n(%)] 95% CI	7 (10.8) (4.5, 21.0)	6 (9.2) (3.5, 19.0)
CR+CRi [n(%)] 95% CI	10 (15.4) (7.6, 26.5)	8 (12.3) (5.5, 22.8)

Source: FDA Briefing Slides for the Oncologic Drugs Advisory Committee (ODAC) Panel

Duration of CR/CRi was 28 Days According to FDA Analysis

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Subject	Response By FDA	CR/CRi Duration (days)		
		FDA	Until next treatment/relapse/death	Applicant
1	CRi	7	23	42
2	CRi	26	50	135
3	CR	28	61	162
4*	CR	28	146	166
5	CRi	28	62	210
6	CRi	36	39	463
7	CRi	63**	65	162
8	CRi	144	144	144
9	CR	Unable to assess	35	35
10	CRi	Unable to assess	9	132
11	Pending**	Unable to assess	-	32
Median (95% CI)		**28 (7 , 36)**	**56 (9 , 65)**	**144 (35 , 166)**

*Extramedullary ALL in kidney, negative bone marrow examination
**These cases are under review based on further information from applicant.

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Source: FDA Briefing Slides for the ODAC Panel

Marqibo FDA Advisory Panel on March 21, 2012

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- FDA panel voted 7-4 (with 2 abstentions) in favor of the agent in response to the following question:
  - Given the following risk/benefit profile of Marqibo:
    - a 5% Complete Response (CR) rate; a 15% CR + CRi (CR with incomplete blood count recovery) rate
    - a safety profile, including 33% neuropathy adverse events (AEs) of Grade 3 or higher and 10% discontinuation due to peripheral neuropathy.
    - **VOTE: Has Marqibo demonstrated a favorable risk-benefit for the treatment of adult patients with Philadelphia chromosome negative acute lymphoblastic leukemia in second or greater relapse or whose disease has progressed following two or more treatment lines of anti-leukemia therapy?**

Marqibo

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- Statements from the panel were mixed. Comments from the minutes of the panel:
  - Some members concurred that successfully bridging a patient to transplant did represent a real clinical benefit to those patients.
  - Several members discussed a lack of treatment options for the patient population which was studied, and stated that these patients will often receive only supportive therapies.
  - Members who voted “yes” cited a feeling that the response rate in the trial was similar to the limited options that could otherwise be used in these patients, but with less toxicity. Some of these members expressed that this, combined with a subset of patients being successfully bridged to transplant, represented a clinical benefit. Another member mentioned a possible benefit to patients in receiving a single agent rather than the multi-drug regimen that would otherwise be used. One member stated that the “yes” vote was more an indictment of the lack of other options than enthusiasm about Marqibo.

Marqibo Is a Liposomal Formulation of a Product Already on the Market – Vincristine

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- ODAC panel members expressed concern over the formulation
  - Members also discussed the liposomal formulation of the product and its possible impact on the effectiveness of the drug.
  - One member expressed skepticism that the formulation would make a significant improvement on the activity of the parent drug, vincristine. Because the biologically active drug is identical between the products, some members stated that Marqibo may simply be an alternate mechanism to deliver vincristine to the patient.

Marqibo Label Favorable – Includes the Higher 15% CR/CRi and 56-Day Duration Data

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	Study 1 (N=65) n (%)
Complete remission (CR)	3 (4.6)
CR with incomplete blood count recovery (CRi)	7 (10.8)
CR + CRi (95% CI[a])	10 (15.4) (7.6 – 26.5)
MEDIAN DURATION of CR or CRi:	**Days (95% CI)**
Based on the first date of CR or CRi to the date of the last available histologic assessment of the same response (n=8)	28 (7, 36)
Based on the first date of CR or CRi to date of documented relapse, death, or subsequent chemotherapies including hematopoietic stem cell transplant (HSCT) (n=10)	56 (9, 65)

[a] CI = Confidence interval (Clopper-Pearson).

Source: Marqibo Label

Implications for Quizartinib

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- Positive read-through:
  - The FDA appears willing to accept CRi as an endpoint and to accept the limitations with duration of response as patients will go on HSCT if possible
  - The response rate with quizartinib appears to be higher than that seen with Marqibo, implying a potentially easier approval pathway
- Caveats in extrapolation:
  - Marqibo was a 505(b)(2) application, using a reformulation of an existing agent, which may have led the FDA to be more willing to grant it accelerated approval
  - ALL (Acute Lymphoblastic Leukemia) and AML are somewhat different diseases, and the FDA may view the unmet medical need differently

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QUIZARTINIB LOOKS TO BE THE MOST POTENT INHIBITOR OF FLT3 (FMS-LIKE TYROSINE KINASE-3) AND THE BEST FLT3 INHIBITOR FOR TARGETED THERAPY IN AML

FLT3 – A Validated Target with Poor Prognosis in AML

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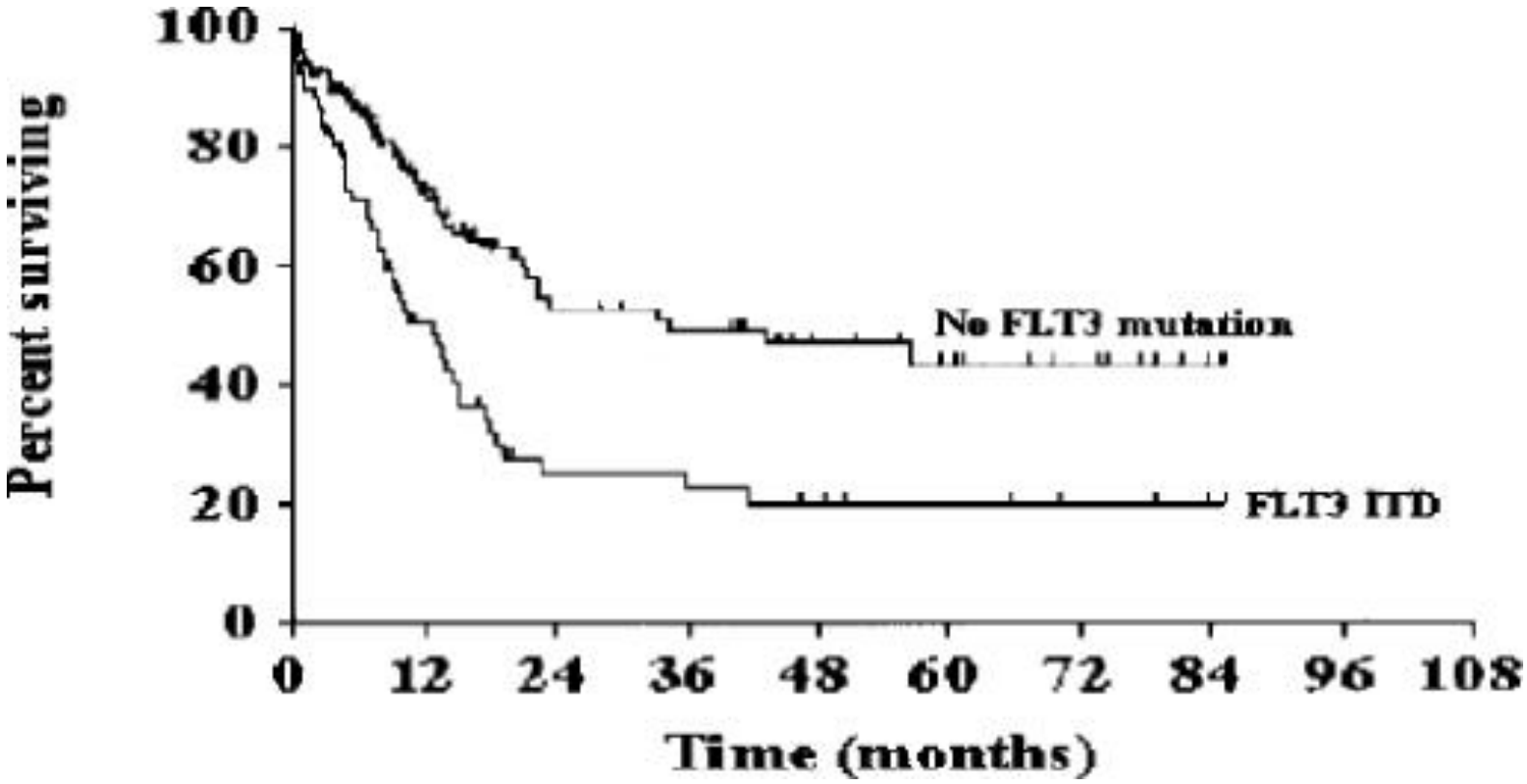
- Lower OS in AML pts with FLT3-ITD mutation vs. no mutations
- Over 35% of AML pts over age 55 have FLT3-ITD mutation
- FLT3-ITD mutation is routinely tested as a standard diagnosis



Source: Company Reports, Frohling et al, Blood 2001, 100:4372-4380

FLT3 – A Validated Target with Poor Prognosis in AML

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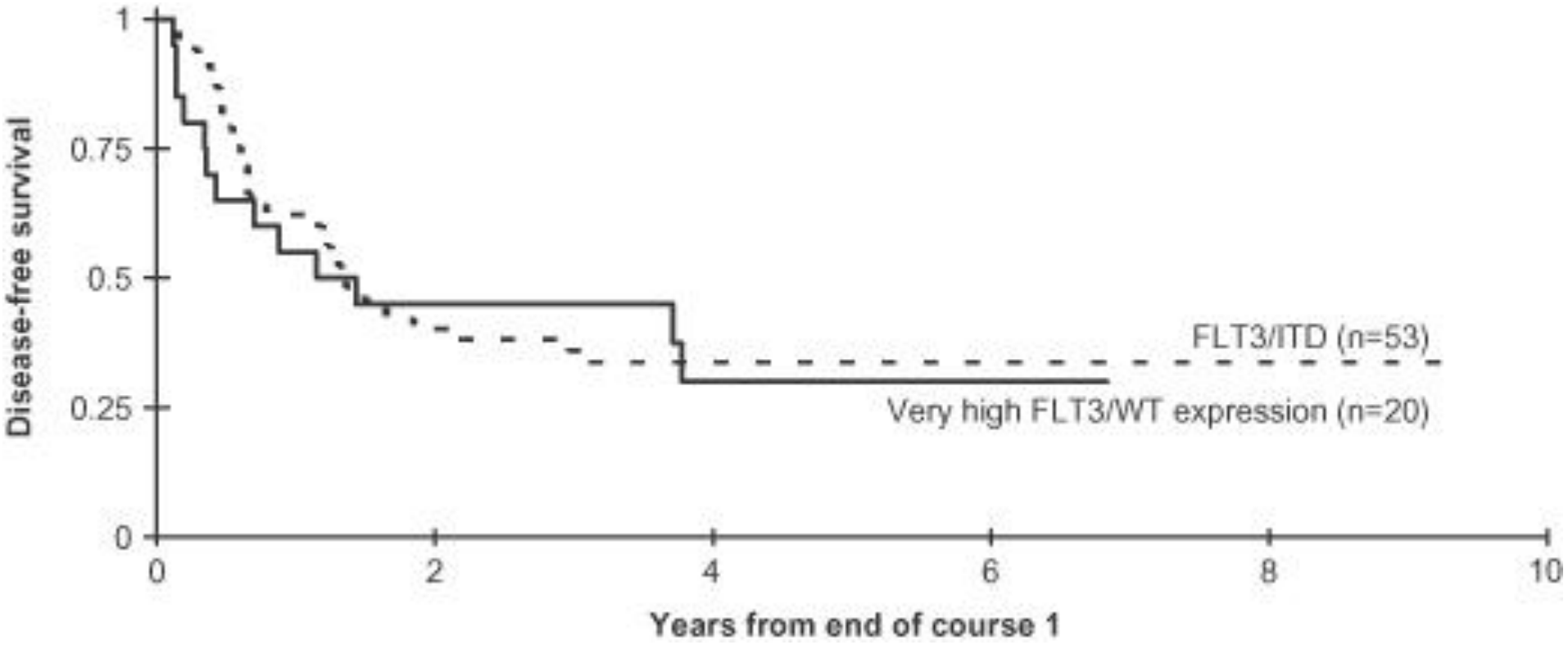
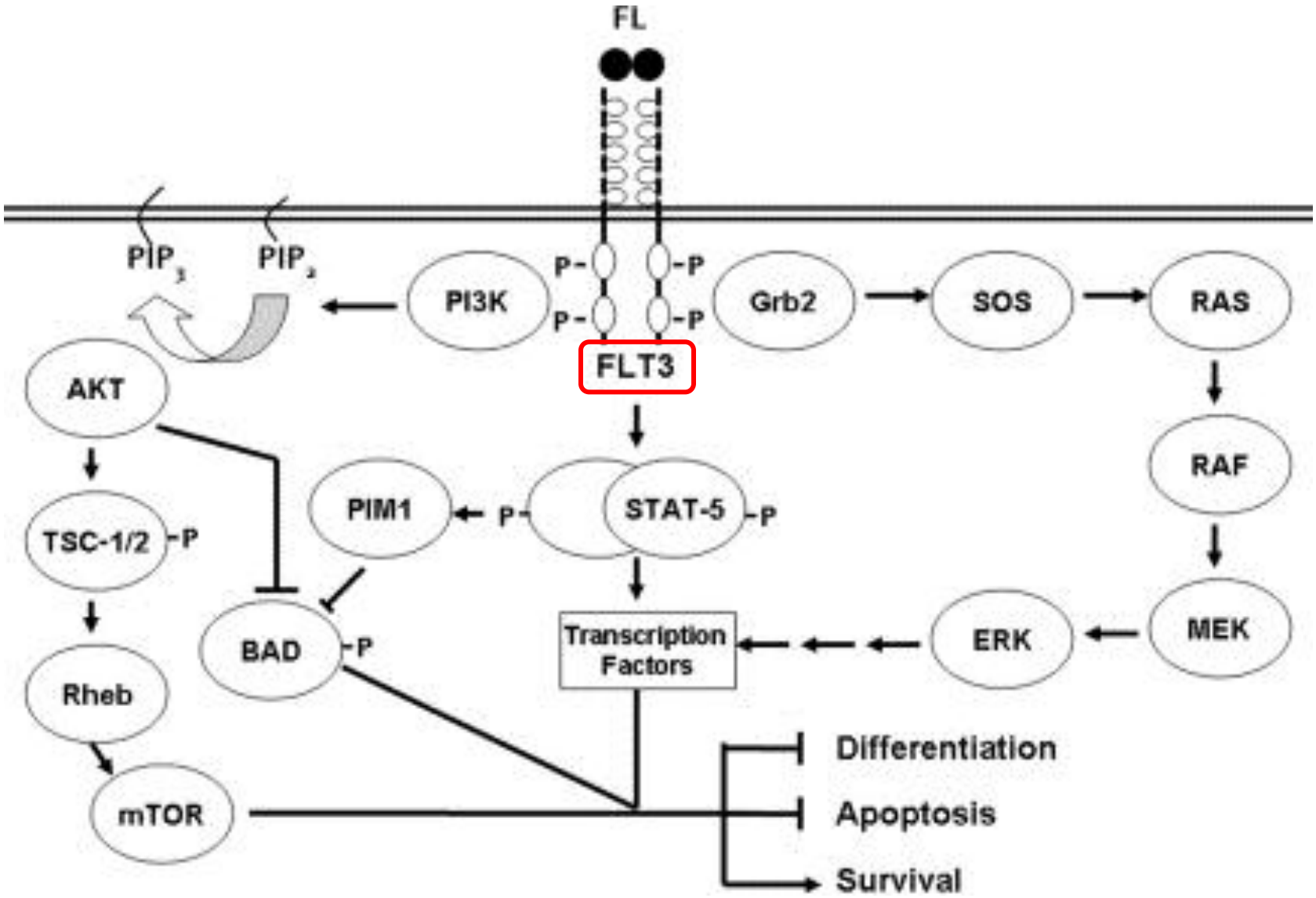
- Lower OS in pts with high expression of wild-type (WT) FLT3 w/o FLT3-ITD
- 25% of FLT3-ITD negative pts have high level of WT FLT3



Source: Company Reports, Brown et al, Blood 2008, 112:abstract 147

FLT3 Pathway Critical for Leukemogenesis



Source: Fathi et al, Oncologist (2011) 16:1162

Kinase Inhibitors in Development for the Treatment of AML

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Target	Inhibitors	Reported Single-Agent Composite Remission Rate (CR + CRi)	AML Patient Population
FLT3	AC220	44-54%[17,18]	FLT3-ITD+
	Sorafenib	Anecdotal[22]; 92%[20]	FLT3-ITD+
	PLX397	NA	FLT3-ITD+
	Crenolanib	NA	Any FLT3 mutation
KIT	Imatinib	Anecdotal[32]; *10%[33]	KIT overexpression
	SU5416	Anecdotal[31]	KIT overexpression
JAK2	Ruxolitinib	8%[39]	Post-MPN AML
mTOR	Rapamycin	None[43]	Unselected
	Everolimus	None[44]	Unselected
	Deforolimus	None[45]	Unselected
MEK	Trametinib	19%[46]	RAS-mutant leukemia (includes other leukemias)
Aurora Kinase	AZD1152	14%[48]	Unselected
	MLN8237	1 patient[49]	Unselected
CDK	Dinaciclib	None[53]	Unselected
PLK1	Volasertib	3%[53]	Unselected

Abbreviations: AML, acute myeloid leukemia; CR, complete remission; CRi, incomplete recovery of blood counts; NA, not assessed; MPN, myeloproliferative neoplasms; CDK, cyclin dependent kinase; PLK1, polo-like kinase 1.
*Patients with less than 5% blasts at start of treatment

- Clear evidence suggests that FLT3 is a validated target in AML
- Selective potent FLT3 inhibitors (quizartinib and sorafenib) have shown most promising bone marrow response; however, most with incomplete recovery of blood counts
- Anecdotal bone marrow response has been observed for other targets including c-KIT,JAK2,RAS; however, it is unclear whether these are valid targets in AML
- Combination with other targeted agent or chemotherapy may prove to be more efficacious

Source: Smith et al, 2013 ASCO Education Book

FLT3 Mutations

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- FLT3 (FMS-like tyrosine kinase-3) gene plays an important role in survival and proliferation of hematopoietic progenitor cells
- Two major types of FLT3 mutations have been identified in ~30% of AML patients
  1. ITD (internal tandem duplications) in the juxtamembrane (JM) domain – 15-25%
  2. Point mutations of residue 835 in the active loop of FLT3 – 7%
- Prognosis for FLT3-ITD mutations is significantly worse than wild type

Source: MD Anderson Cancer Center

Chemical Property of FLT3 Inhibitors

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Compound	Chemical class	FLT3 IC_{50}	Other targets
Sexamanib (SU5416)	3-Substituted indolinone	100 nM	c-KIT, VEGFR
Sunitinib (SU11248)	3-Substituted indolinone	50 nM	c-KIT, PDGFR, VEGFR
Lestaurtinib (CEP701)	Indolocarbazole	3 nM	TrkA, VEGFR, JAK2
Midostaurin (PKC412)	Indolocarbazole	10 nM	c-KIT, PDGFR, c-FMS
Tandutinib (MLN518)	Piperazinyl quinazoline	30 nM	c-KIT, PDGFR
Sorafenib (BAY 43-9006)	Bi-aryl urea derivative	3 nM	c-RAF, PDGFR, VEGFR, c-KIT
KW-2449	n/a	13 nM	Aurora kinase, ABL
AC220	Bis-aryl urea derivative	1 nM	c-KIT, PDGFR, RET, CSF1R

Source: Knapper, Expert Opin Investig Drugs (2011) 20:1377

Chemical Structure of FLT3 Inhibitors

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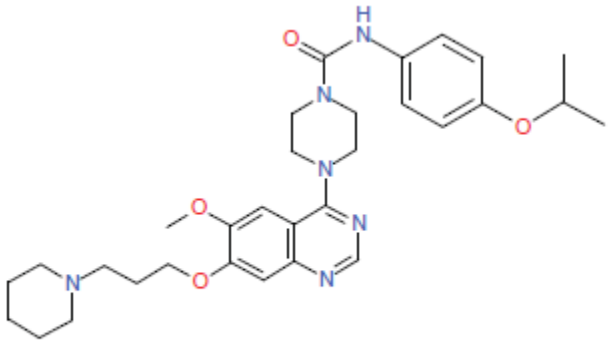
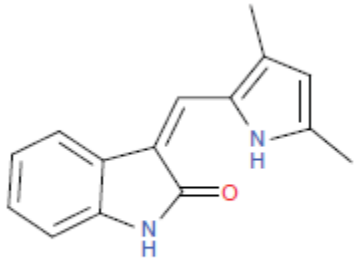
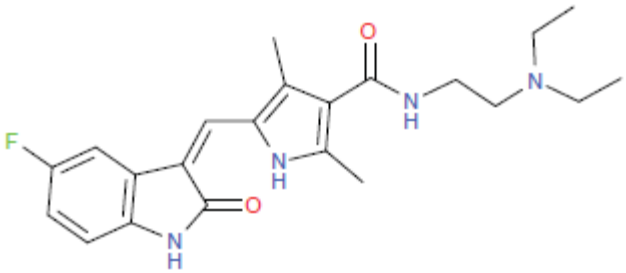


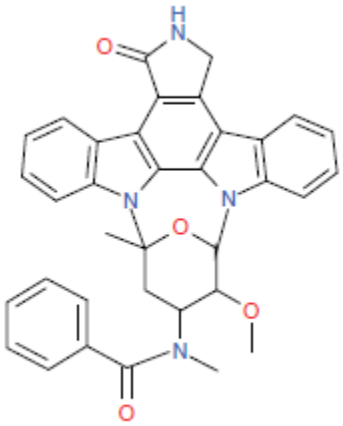
MLN518 (Tandutinib)



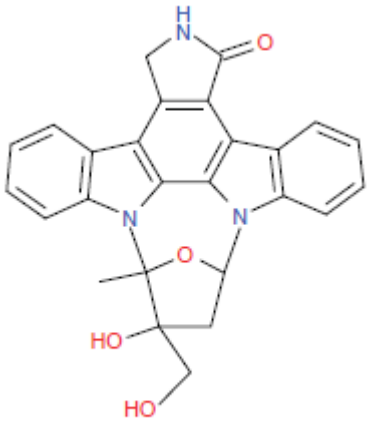
SU5416 (Semaxanib)



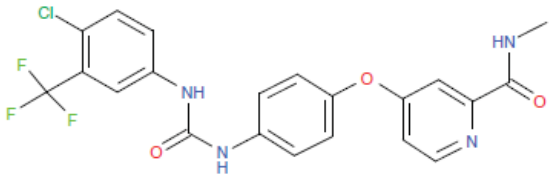
SU11248 (Sunitinib)



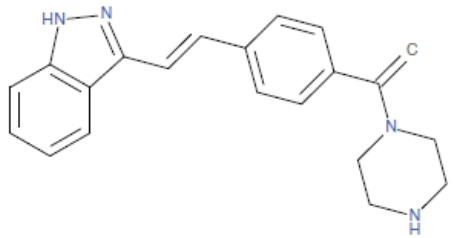
PKC412 (Midostaurin)



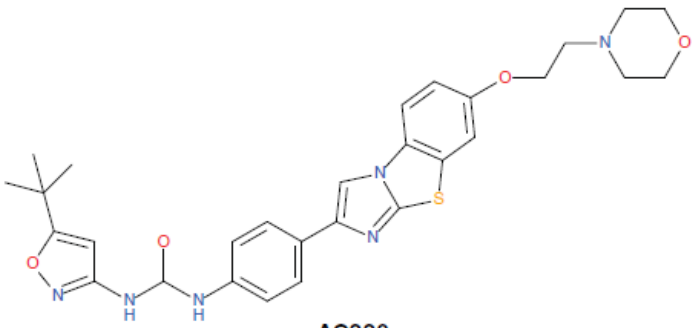
CEP701 (Lestaurtinib)



Sorafenib



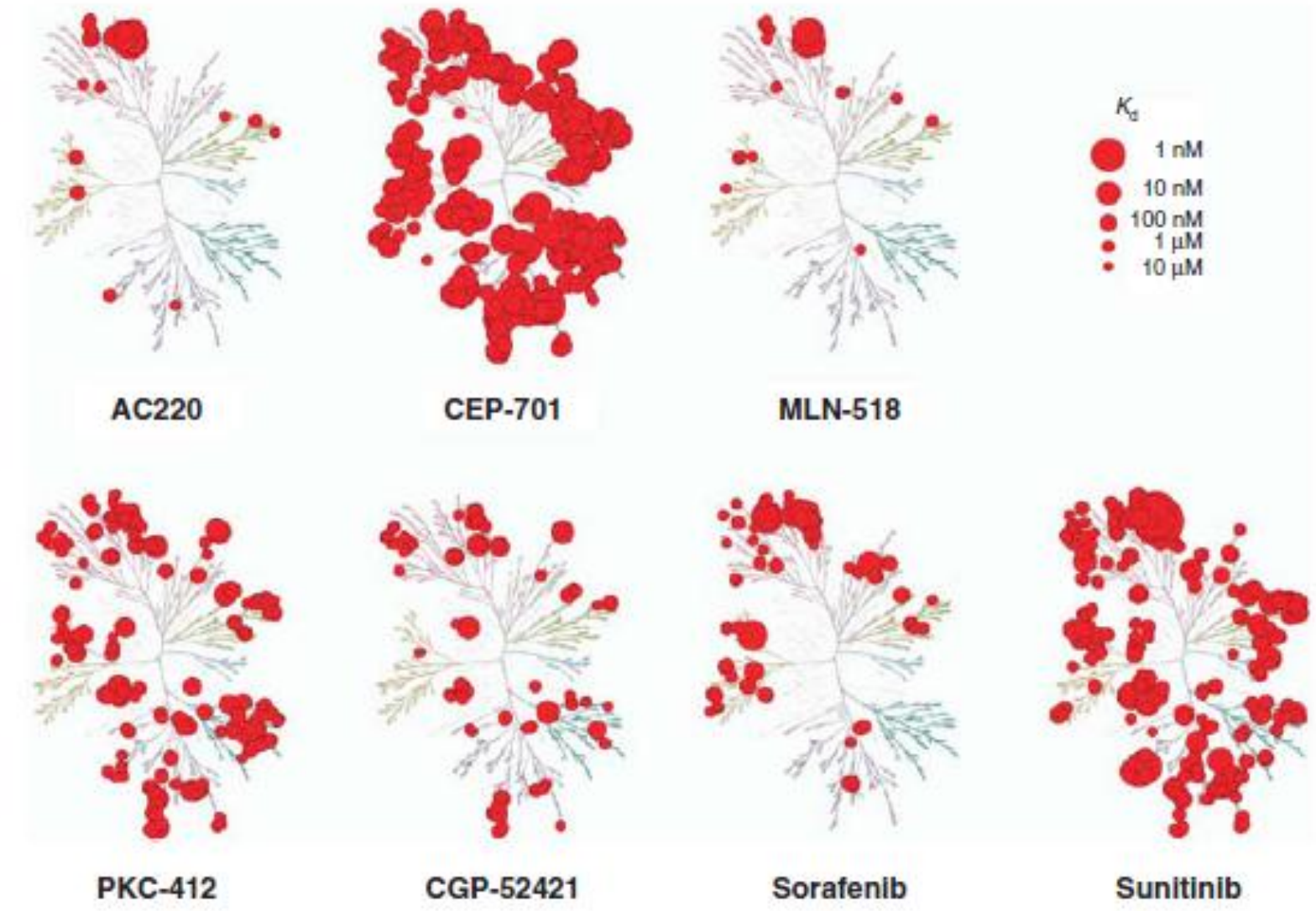
KW-2449



AC220

Source: Knapper, Expert Opin Investig Drugs (2011) 20:1377

Quizartinib Appears More Selective Than Other FLT3 inhibitors



Source: Knapper, Expert Opin Investig Drugs (2011) 20:1377

FLT3 Inhibitors In Development

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FLT3 inhibitor	Sponsor	Phase	AML Indication
Quizartinib monotherapy	AMBI	II	2nd and 3rd line AML
		III ready	2nd line AML
Midostaurin/chemo	NVS	III	ND AML
Crenolanib monotherapy	Arog	II	RR AML

**CALGB – Cancer and Leukemia Group B, NCI – National Cancer Center*

Source: Company Report, CLinicalTrial.gov; Note: RR - relapsed refractory, ND - newly diagnosed

Quizartinib Has Shown Superior Response Rate

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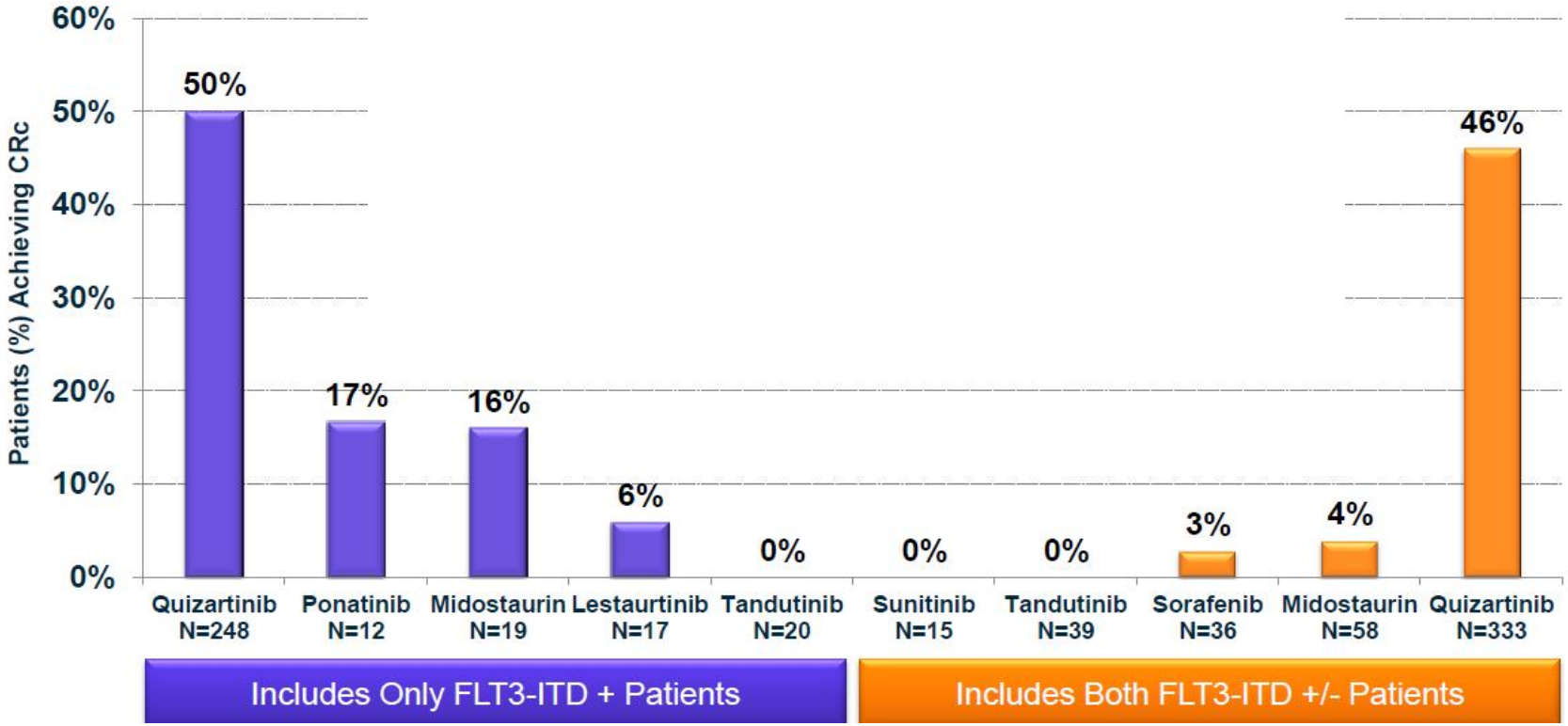
- Cross-study comparison showed ~46% patients on quizartinib reached bone marrow blast reduction to <5% in R/R AML, while other compounds were in the range of 0-17%
- Quizartinib is highly selective and potent against FLT3, while other compounds have broader spectrum of activity



Source: Company Reports, Knapper et al, Expert Opin Investig Drugs 2011, 20:1377-1395, Talpaz et al, ASCO 2011

Quizartinib Has Superior Plasma Inhibitory Properties

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Drug	WT FLT3 IC_{50}, medium, nM	FLT3/ITD IC_{50}, medium, nM	FLT3/ITD IC_{50}, plasma, nM	In vivo $t_{1/2}$, h
Lestaurtinib	10	2	700	8[25]
Midostaurin	30	3	1700	24+[26]
Sorafenib	28	3	484	24+[27]
Sunitinib	2	1	ND	24+[28]
KW-2449	36	10	144	4[11]
AC220	5	1	18	24+[5]

SEMK2 cells (wild-type FLT3) and Molm-14 cells (FLT3/ITD) were incubated with increasing concentrations of inhibitor. *R* values for all experiments were greater than 0.98. Sunitinib was not analyzed in plasma, as there are no active FLT3 AML trials with this agent. The plasma half-lives (In vivo $t_{1/2}$) were obtained from early-phase clinical trial data (see references). ND indicates not determined.

Source: Pratz et al, Blood (2010) 115:1425

FLT3 Inhibitor Monotherapy in AML

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Drug	Trial Phase	Route and dose	Patient population	n (AML)	*FLT3* mutation	Clinical response	Adverse effects
Semaxinib (SU5416)	II	Intravenous 145 mg/m^2 twice-weekly	Relapsed/ refractory AML > 60 yrs and unfit for intensive treatment	42 (42)	7 ITD*	BM blasts < 5% without count recovery in 1 case > 50% reduction in BM blasts in 7 cases (no responses in ITD cases)	Nausea, headache, bone pain
Semaxinib (SU5416)	II	Intravenous 145 mg/m^2 twice-weekly	Relapsed/refractory AML High-risk MDS	55 (33)	Unknown	BM blasts < 5% without count recovery in 1 case > 50% reduction in BM blasts in 3 cases	Headache, dyspnea, fatigue, infusion reactions, thrombosis
Sunitinib (SU11248)	I	Oral 50 – 350 mg (single dose)	AML (unrestricted)	29 (29)	3 ITD 2 TKD	Not applicable	Nausea, diarrhea
Sunitinib (SU11248)	I	Oral 50 – 75 mg/day	Relapsed/refractory AML Unfit for intensive treatment	15 (15)	2 ITD 2 TKD	PB blast clearance or BM blast reduction in 4/4 *FLT3* mutant, 2/7 FLT3 WT cases	Fatigue, hypertension, edema
Lestaurtinib (CEP701)	I – II	Oral 40 – 80 mg twice-daily	Relapsed/refractory AML with FLT3-activating mutations	17 (17)	16 ITD 1 TKD	BM blasts < 5% without count recovery in 1 case PB blast clearance in 4 cases	Nausea, diarrhea, fatigue
Lestaurtinib (CEP701)	II	Oral 60 – 80 mg twice-daily	Newly-diagnosed AML > 70 yrs (or 60 – 70 yrs with co-morbidity)	29 (29)	2 ITD 3 TKD	PB blast clearance or > 50% BM blast reduction in 3/5 *FLT* mutant, 5/22 *FLT3* WT cases	Nausea, diarrhea, constipation, liver enzyme changes
Midostaurin (PKC412)	II	Oral 75 mg thrice-daily	Relapsed/refractory AML or high-risk MDS with FLT3-activating mutation	20 (19)	18 ITD 2 TKD	BM blasts < 5% without count recovery in 3 cases > 50% reduction in PB blasts in 14 cases, > 50% reduction in BM blasts in 6 cases	Nausea, diarrhea, fatigue, headache, edema ? pulmonary infiltrates
Midostaurin (PKC412)	IIb	Randomized Oral 50 or 100 mg twice-daily	Relapsed/refractory AML or newly diagnosed AML unfit for intensive chemotherapy High-risk MDS	95 (92)	26 ITD 9 TKD	> 50% reductions in PB or BM blast seen in 71% *FLT3* mutant, 42% *FLT3* WT patients. 1 PR No difference between 50 and 100 mg	Nausea, vomiting

Source: Knapper, Expert Opin Investig Drugs (2011) 20:1377

FLT3 Inhibitor Monotherapy in AML

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Drug	Trial Phase	Route and dose	Patient population	n (AML)	*FLT3* mutation	Clinical response	Adverse effects
Tandutinib (MLN-518)	I	Oral 50 – 700 mg twice-daily	Relapsed/refractory AML Unfit for intensive treatment High-risk MDS	40 (39)	8 ITD 1 TKD	PB blast clearance and reduction in BM blasts in 2 ITD cases (at doses above 525 mg)	Muscle weakness, fatigue, nausea, diarrhea, edema
Tandutinib (MLN-518)	II	Oral 525 mg twice-daily	Relapsed/refractory AML Unfit for intensive treatment *FLT3*-ITD mutation	20 (20)	20 ITD	18 evaluable patients. 6 showed decrease in PB or BM blasts	Muscle weakness (DLT), nausea
Sorafenib (BAY 43-9006)	I	Oral 200 mg twice-daily – 1200 mg once-daily	Relapsed/refractory AML	16 (16)	6 ITD 3 TKD	> 50% reduction in PB or BM blasts in 6/6 *FLT3* ITD, 0/3 FLT3-TKD, 3/7 *FLT3* WT patients	Pleural effusion, nausea, vomiting, rash
Sorafenib (BAY 43-9006)	I	Oral 200 mg twice-daily – 1200 mg once-daily	Relapsed/refractory AML High-risk MDS	21 (20)	11 ITD	> 50% reduction in PB or BM blasts in 11/20 patients (9/11 *FLT3* ITD patients) 1 transient CR (*FLT3*-ITD)	Pleural effusion, hyperbilirubinemia
KW-2449	I	Oral 12.5 – 250 mg twice-daily	Relapsed/refractory AML/ ALL. High-risk MDS Resistant/intolerant CML	37 (31)	Not stated	> 50% reduction in PB or BM blasts in 8/31 (26%) AML patients (5 *FLT3*-mutated, 3 *FLT3* WT)	Nausea, vomiting, fatigue, diarrhea
AC220	I	Oral 12 – 450 mg once-daily	Relapsed/refractory AML	76 (76)	18 ITD (11 not tested)	9 CRs (12%), 14 PRs (18%) FLT3-ITD: 22%CR, 33% PR FLT3 WT: 6% CR, 13% PR	GI events, edema QTc prolongation (DLT)

*Retrospective *FLT3* mutation screening in 35 patients only. No *FLT3*-TKD mutation analysis performed.

ALL: Acute lymphoblastic leukemia; AML: Acute myeloid leukemia; BM: Bone marrow; CML: Chronic myeloid leukemia; CR: Complete remission; DLT: Does-limiting toxicity; FLT3: FMS-like tyrosine kinase 3; GI: Gastrointestinal; ITD: *FLT3* internal tandem duplication; MDS: Myelodysplastic syndrome; PB: Peripheral blood; PR: Partial remission; TKD: *FLT3* tyrosine kinase domain point mutation; WT: *FLT3* wild type.

Source: Knapper, Expert Opin Investig Drugs (2011) 20:1377

FLT3 Inhibitor Monotherapy in AML

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Drug	Trial Phase	TKI dosing	Chemotherapy	Population	n	*FLT3* mutation	Clinical response	Adverse effects
Sunitinib	I – II	Oral 25 mg once-daily Continuous *then* days 1 – 7 of each cycle of chemotherapy plus maintenance	Induction: AraC/daunorubicin ('7 + 3') Consolidation: AraC 3 g/m^2 (3 cycles)	Newly diagnosed *FLT3* mutated > 60 years	12*	8 ITD 4 TKD	10 evaluable patients 7/10 CR/Cri 1/10 PR	Aplasia, hand-leg syndrome (with continuous dosing schedule) Febrile neutropenia, diarrhea
Lestaurtinib	III	Randomized oral 80 mg twice-daily for up to 28 days after each cycle of chemotherapy	Either : mitoxantrone, etoposide, cytarabine 1 g/m^2 if 1st CR < 6 months or high-dose AraC if 1st CR 6 – 24 months	First relapse *FLT3* mutated	224	198 ITD 17 TKD 8 both	Chemo + lestaurtinib: 26% CR, 4.73 m OS Chemo only: 21% CR, 4.57 m OS	24% patients in lestarutinib arm discontinued therapy early in comparison to only 7% in control arm. Higher incidence of infection in lestaurtinib arm
Lestaurtinib	III	Randomized oral 80 mg twice-daily for up to 28 days after each cycle of chemotherapy	Induction: AraC/daunorubicin with or without etoposide/gemtuzumab ozogomicin (2 cycles) Consolidation: MACE/Midac or High-dose AraC (2 cycles)	Newly diagnosed *FLT3* mutated 18 – 60 years	88‡	66 ITD 22 TKD	CR/ CRi in 77/83 evaluable patients (93%)	Nausea, vomiting, diarrhea increased in lestaurtinib patients taking concomitant azole antifungal prophylaxis – better tolerated following adapted dosing
Midostaurin	Ib	Oral. 50 or 100 mg twice-daily either concomitantly (days 1 – 7, 15 – 21) or sequentially (days 8 – 21) with chemotherapy cycles	Induction: AraC/daunorubicin ('7 + 3') Consolidation: AraC 3 g/m^2 (3 cycles)	Newly diagnosed 20 – 65 years	40§	9 ITD 4 TKD	*FLT3* WT (n = 27): 74% CR, 81% 1 yr OS, 59% 2 yr OS *FLT3* mutated (n = 13): 92% CR, 85% 1 yr OS, 62% 2 yr OS	100 mg dose: poorly tolerated (nausea and vomiting) 50 mg dose better tolerated

*Interim data presented at ASH 2010.

‡Non-randomized interim data presented on lestaurtinib-treated patients only (not chemo only control arm) at ASH 2009 (enrolment continues).

§Patient recruitment and outcome data given for 50 mg twice-daily dose group only.

AraC: Cytarabine; ASH: American Society of Hematology; CR: Complete remission; CRi: Complete remission with incomplete marrow recovery; FLT3: FMS-like tyrosine kinase 3; ITD: *FLT3* internal tandem duplicatio OS: Overall survival; PR: Partial remission; TKD: *FLT3* tyrosine kinase domain point mutation; WT: *FLT3* wild type.

Source: Knapper, Expert Opin Investig Drugs (2011) 20:1377

FLT3 Inhibitor Monotherapy in AML

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Drug	Trial Phase	TKI dosing	Chemotherapy	Population	n	*FLT3* mutation	Clinical response	Adverse effects
Tandutinib	I – II	Oral. 200 mg or 500 mg twice-daily. Given continuously throughout therapy or on days 1 – 14 of each cycle of chemotherapy	Induction: AraC/daunorubicin ('7 + 3') Consolidation: AraC 3 g/m^2 (3 cycles)	Newly diagnosed 26 – 83 years	29	5 ITD	CRs in 11/15 patients in cohorts 1 and 2 Not subsequently reported	Diarrhea, nausea, vomiting
Sorafenib	I – II	Phase I: 400 mg alt days – 400 mg twice-daily (days 1 – 7) Phase II: 400 mg twice-daily (days 1 – 7) with each cycle of chemotherapy. Plus 12 months maintenance	Induction: AraC 1.5 g/m^2 (days 1 – 4), idarubicin 12 mg/m^2 (days 1 – 3) Consolidation: AraC 0.75 mg/m^2 (days 1 – 3), idarubicin 8 mg/m^2 (days 1 – 2)	Phase I: relapsed/ refractory Phase II: newly diagnosed	10 51	6 ITD 1 Both 13 ITD 2 TKD	Phase II: *FLT3* ITD 14/15 CR (93%) including 1 CRp *FLT3* wild type 24/ 36 CR (66%)	
Sorafenib	II	Randomized 400 mg twice-daily between cycles of chemotherapy Plus 12 months maintenance	Induction: AraC/daunorubicinc ('7 + 3') Consolidation: AraC 1 g/m^2 (2 cycles)	Newly diagnosed > 60 years	197	28 ITD	CR/CRi in 48%/9% with sorafenib, 60%/ 4% with placebo No difference seen in *FLT3* ITD group	Diarrhea, rash, mucositis, hypertension

*Interim data presented at ASH 2010.

‡Non-randomized interim data presented on lestaurtinib-treated patients only (not chemo only control arm) at ASH 2009 (enrolment continues).

§Patient recruitment and outcome data given for 50 mg twice-daily dose group only.

AraC: Cytarabine; ASH: American Society of Hematology; CR: Complete remission; CRi: Complete remission with incomplete marrow recovery; FLT3: FMS-like tyrosine kinase 3; ITD: *FLT3* internal tandem duplica
OS: Overall survival; PR: Partial remission; TKD: *FLT3* tyrosine kinase domain point mutation; WT: *FLT3* wild type.

Source: Knapper, Expert Opin Investig Drugs (2011) 20:1377

Sorafenib/Vidaza Combination Therapy Showed Promising Activity

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- Sorafenib in combination with chemo showed some inconclusive results
  - Sorafenib/cytarabine/idarubicin in younger patients (median age of 53) with FLT3 mutations achieved 100% (15) CR/CRp vs. 66% in WT (p=0.033) in front line*
  - However, a study of sorafenib/AraC in elderly patients (>60 y) did not show an improvement in CR rate, event free survival (EFS) or OS**
- Sorafenib in combination with azacitidine showed promising activity in relatively old patient population (median age of 64) in RR AML***
  - 16% (6) with CR, 27% (10) with CRi, and 3% (1) with PR
  - Median CR/CRi duration was 2.3 months
  - OS was 6.2 months

*Source: *Ravandi et al, J Clin Oncol (2010) 28:1856; **Serve et al, Blood (2010) 116:abstract 333; ***Ravandi et al, Blood (2013) doi:10.1182*

Quizartinib Monotherapy Showed Comparable Activity VS. Sorafenib/Vidaza

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- Quizartinib/Vidaza combination therapy is being evaluated in investigational sponsored studies

Drugs	Quizartinib		Vidaza/ Sorafenib	Standard Chemo	Chemo/ Lestaurtinib
Data	Phase II RR AML		Phase II RR AML	Phase II RR AML	
Mutation	FLT3-ITD(+)	FLT3-ITD(-)	Overall	FLT3 mutations	
Pts	136	40	43 (40 FLT3-ITD)	112	112
Median age	50	54	64	54	59
CR	4%	3%	16% (6)	12% (13)	17% (19)
CRp	1%	3%		9% (10)	9% (10)
CRi	40%	25%	27% (10)		
ORR	75%	45%	46%		
Median CR/CRi duration	10.6 wk	7.0 wk	2.3 mon		
OS	24 wk		6.2 mon	3.9 mon	3.9 mon
Reference	Cortez et al, ASCO 2013 #7012		Ravandi et al, Blood (2013) doi:10.1182	Levis et al, Blood (2011) 117:3294	

Midostaurin Appears to Have Limited Single Agent Activity

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Table 2. Clinical Response

	FLT3											
	Mutant						Wild-Type					
	50 mg Twice Daily		100 mg Twice Daily		Total		50 mg Twice Daily		100 mg Twice Daily		Total	
Response*	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
No.	18		17		35		30		27		57	
PR	0		1	6	1	3	0		0		0	
Hematologic improvement	9	50	7	41	16	46	13	43	7	26	20	35
Blast response												
Total	12	67	13	76	25	71	15	50	9	33	24	42
PB and bone marrow	5	42	1	8	6	24	4	27	2	22	6	25
Bone marrow only	0		4†	24	4	11	2	13	1	11	3	13
PB only	7	58	8	62	15	60	9	60	6	67	15	63
2-log PB blast reduction	8	44	9	53	17	49	11	37	8	30	19	33
Overall response (CR, PR, HI, BR)	12	67	13	76	25	71	20	67	12	44	32	56

Abbreviations: FLT3, FMS-like tyrosine kinase 3 receptor; PR, partial remission; PB, peripheral blood; CR, complete remission; HI, hematologic improvement; BR, blast response.
*Rows are not mutually exclusive.
†This group includes the patient with the PR.

- Midostaurin inhibits multiple targets including FLT3, c-KIT, VEGFR-2, PDGFR
- Majority of the effect was limited to blast reduction (BR, by ≥50%) in FLT3-mutant patients
- Ongoing Phase III trial is assessing midostaurin in combination with cytarabine/daunorubicin in newly diagnosed FLT3-mutated AML, data anticipated in mid-2014 (according to ClinicalTrial.gov)

Source: Fischer et al, J Clin Oncol (2010) 28:4339

Lestaurtinib/Chemo Combo Failed to Show Superiority vs. Chemo in 2nd Line AML

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- Lestaurtinib is an orally available indolocarbazole derivative targeting FLT3-ITD mutation
- Lestaurtinib failed to meet endpoints of CR/CRp and OS, and was associated with higher toxicity

Parameter	Chemotherapy only, n (%)	Chemotherapy + lestaurtinib, n (%)	*P*
No. of total patients	112	112	> .99
CR	13 (12)	19 (17)	.25
CRp	10 (9)	10 (9)	> .99
Total CR/CRp	23 (21)	29 (26)	.35
First remission 1-6 mo, CR/CRp	6 (11)	10 (19)	.42
First remission ≥ 6 mo, CR/CRp	17 (29)	19 (32)	.84
< 50 y of age, CR/CRp	4 (12)	9 (27)	.21
≥ 50 y of age, CR/CRp	19 (24)	20 (25)	> .99

Source: Levis et al, Blood (2011) 11:3294-3301

D835Y Mutation Confers Resistance to Tandutinib, Limiting Future Application

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- Tandutinib (MLN518), a piperazinyl quinazoline compound, showed some activity against FLT3, c-KIT and PDGFR
- Preclinical data suggested that D835Y, the most common FLT3-TKD mutation, has resistance to tandutinib*
- A Phase I dose escalating study showed elevated plasma concentration in some patients**
- In a follow-up Phase II monotherapy study, 6 out of 18 patients showed transient evidence of minor hematologic and bone marrow response***
- Although there is synergy between tandutinib and AraC/daunorubicin, tandutinib has not been advanced in AML

*Source: * Clark et al, Blood (2004) 104:2867; **DeAngelo et al, Blood (2006) 108:3674; ***DeAngelo et al, Blood (2004) 104::1792a*

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CURRENT DATA AND ONGOING TRIALS FOR QUIZARTINIB

Quizartinib – A FLT3 Inhibitor in Acute Myeloid Leukemia (AML)

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- AML standard of care is intensive chemo induction followed with transplant
- FLT3-ITD mutation causes constant, ligand-independent activation of FLT3, resulting in shorter remissions and higher relapse rate
- Single-arm Phase IIb trial in relapsed/refractory (R/R) AML with FLT3-ITD mutation showed substantial number of pts bridged to transplant as well as improved OS vs. historical data
- Phase III in R/R AML with FLT3-ITD in early 2014
- Evaluating additional opportunities in earlier lines in both FLT3-ITD positive and negative pts

Source: Company Reports

Quizartinib Clinical Experience in R/R AML

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	Phase 1	Phase 2	Phase 2b
N=	76	333	76
FLT3-ITD	Positive and Negative	Positive and Negative	Positive only
Patients	All comers	Cohort 1: ≥60 years old, 1st relapse within 1 year or refractory to 1st line treatment (N=157) Cohort 2: ≥18 years old, relapse after, or refractory to 2nd line treatment or HSCT (N=176)	≥18 years old, relapse after, or refractory to 2nd line treatment or HSCT
Dose	12 mg – 450 mg	200 mg, 135/90 mg	30/60 mg
Objectives	Safety, MTD	CR, CRc	CRc
Time	Mar 2007-Jan 2009	Nov 2009 – Nov 2011	May 2012 – Mar 2013
Outcomes	MTD Identified (200 mg)	High response rate, Bridge to transplant	Comparable efficacy, Improved safety
Data	ASH 2009	Exploratory: ASH 2011 Confirmatory: ASH 2012	Planned for ASH 2013

11

Source: Company Reports; Note: MTD – maximum tolerated dose, FPI-LPI

Quizartinib Phase II Data – Rapid Reduction in Blasts

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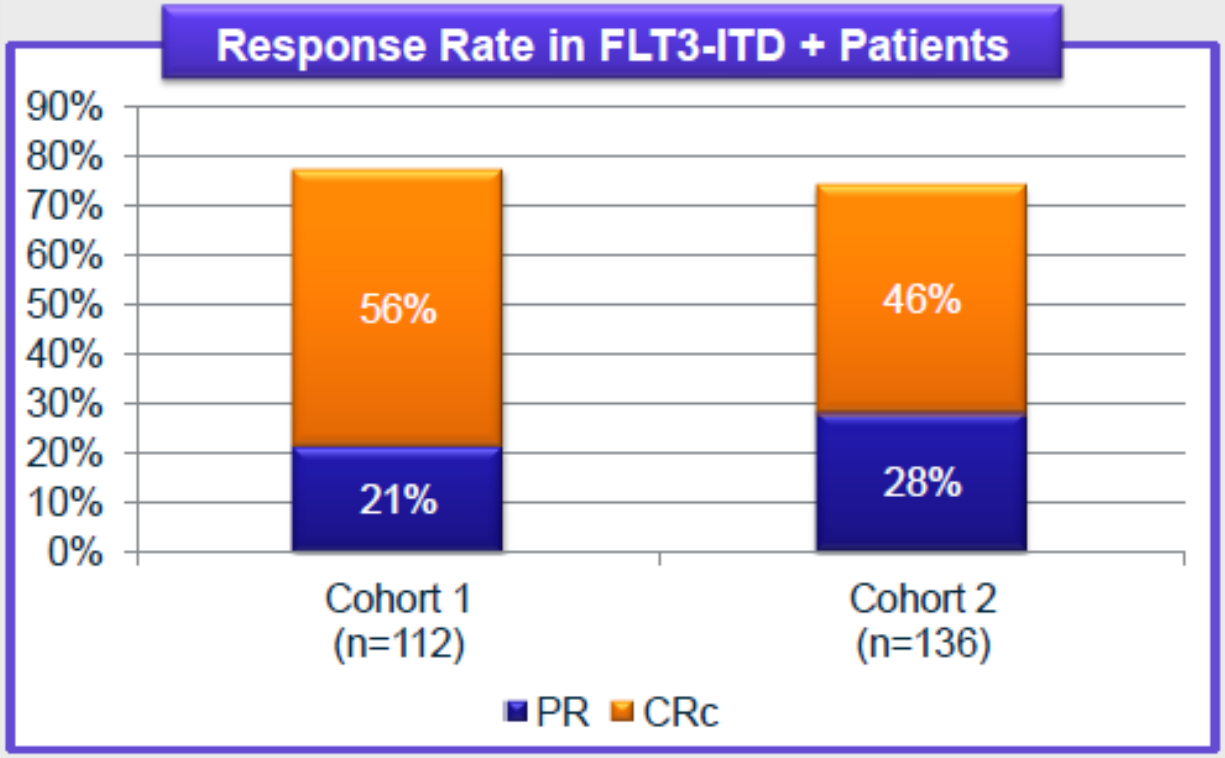
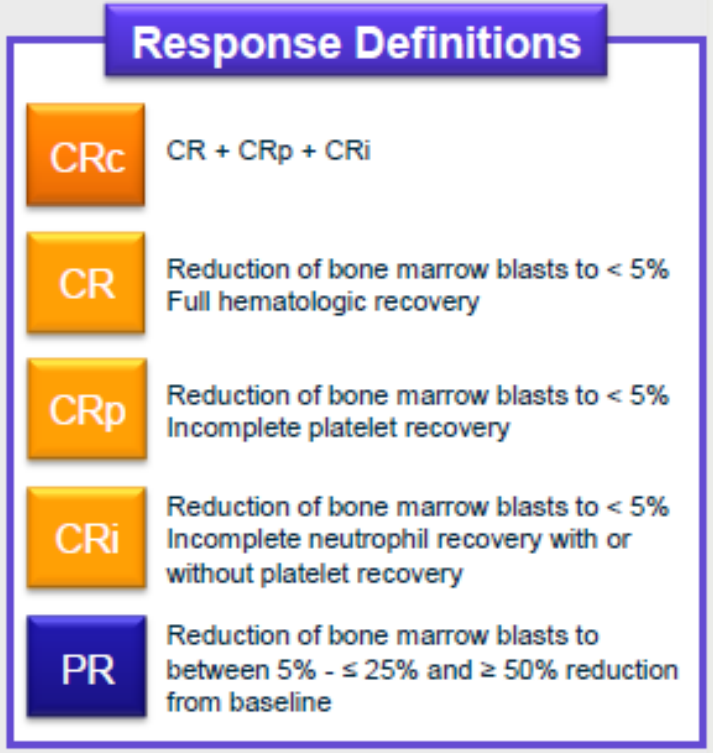
- ~50% of FLT-ITD+ patients achieved CRc from both Cohort 1&2
- Pts with CRc increased bridging to transplant as well as an improved OS
- Median time to CRc was 4.3 weeks





Source: Company Reports

Quizartinib Phase II Data – Increased Treatment Duration and OS in FLT3-ITD+ Pts

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Treatment Duration

	Cohort 1 N = 112 Treatment Time in Weeks				Cohort 2 N = 136 Treatment Time in Weeks			
	Mean	Median	Min	Max	Mean	Median	Min	Max
Responders (CRc or PR)	21.8	17.5	2.0	70.6+	15.9	10.0	2.7	108.1+
Non-responders	5.0	4.4	0.1	12.4	6.9	5.0	0.3	23.3

+ indicates that a patient is still receiving treatment with quizartinib

Overall Survival

	Cohort 1 N = 112 n (%)	Cohort 2 N = 136 n (%)
# (%) Bridged to an HSCT	11 (9.8)	47 (34.6)
Median Overall Survival (OS) (weeks), [range] (n=248)	25.4 [0.4-96.0+]	24.0 [0.7-109.1+]
Median OS if bridged to an HSCT (weeks), [range] (n=58)	32.7 [12.7-93.0+]	34.1 [13.6-109.1+]
Median OS if not bridged to an HSCT (weeks), [range] (n=190)	24.9 [0.4-96.0+]	18.4 [0.7-108.3+]

+ indicates that subjects are still alive

Source: Company Reports

Quizartinib Phase II Data – Improved OS for Pts Achieved CRc or PR in Cohort 1

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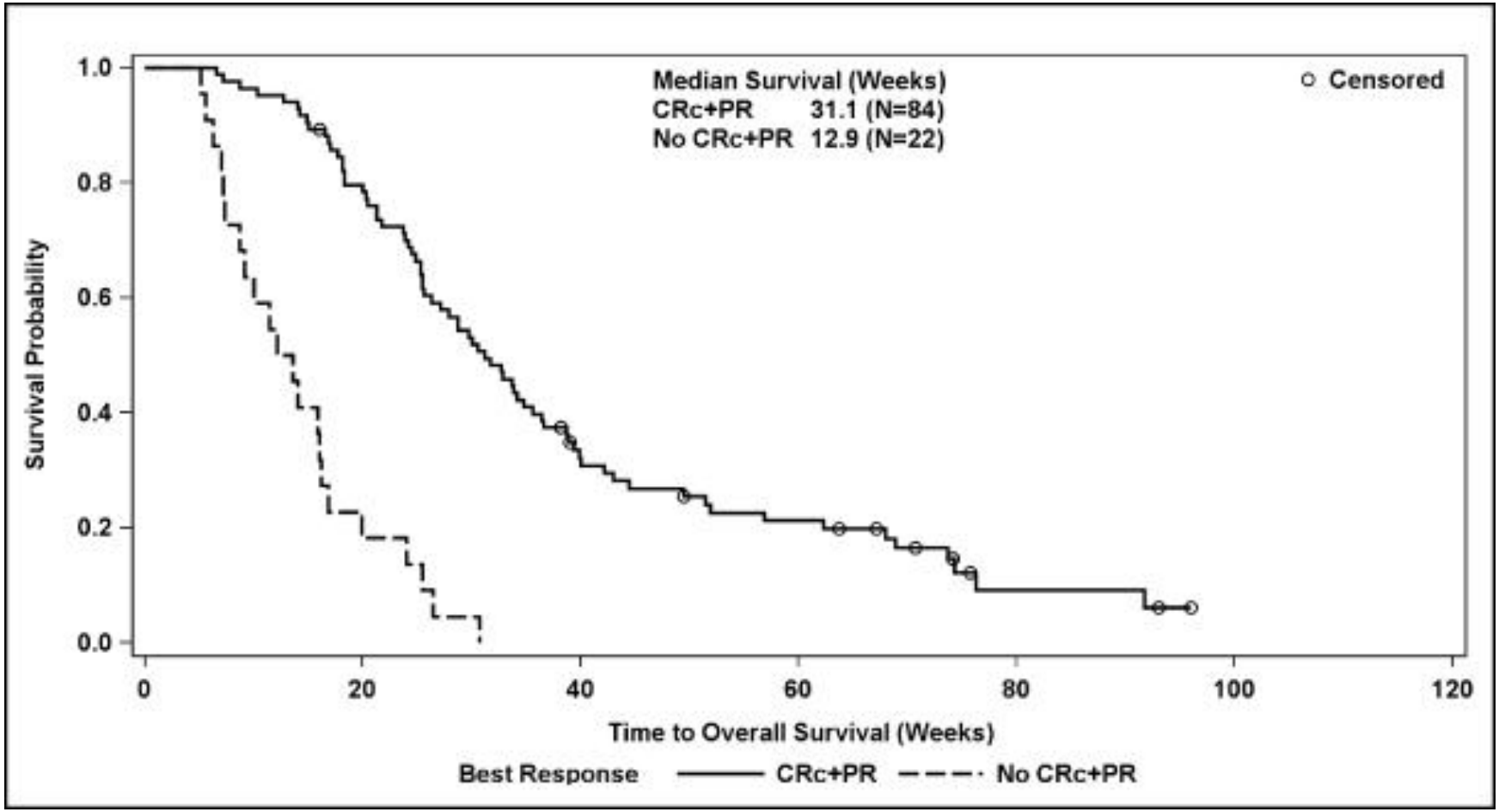
- Median OS – 25.4 wks vs. 13 wks of historical controls
- 10% pts in Cohort 1 bridged to an HSCT



Source: Company Reports

Quizartinib Phase II Cohort 2 Data – Improve OS in FLT3-ITD (+) Pts

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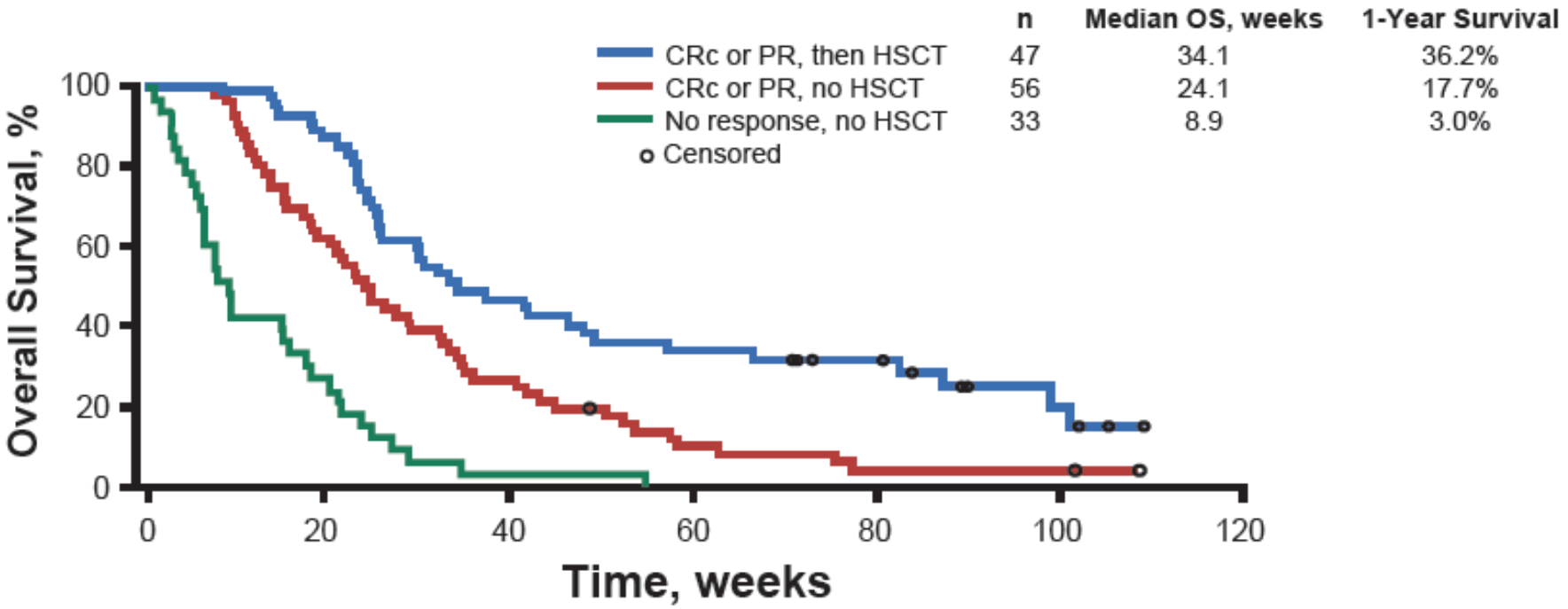
- Median OS was 24 wks vs. 6 wks of historical controls
- 35% pts in Cohort 2 bridged to an HSCT



CRc=composite complete remission (CR + CRp + CRi); FLT3-ITD=FMS-like tyrosine kinase 3 internal tandem duplication; HSCT=hematopoietic stem cell transplantation; OS=overall survival; PR=partial remission.

Source: Cortes et al, ASCO 2013, #7012

Quizartinib Phase II Safety Profile Manageable

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Adverse Event	Grade 1/2 n (% of N)	Grade3/4 n (% of N)	Total Patients (1) n (% of N)
Nausea	169 (51)	9 (3)	178 (53)
Febrile neutropenia (2)	NA	137 (41)	139 (42)
Diarrhea	122 (37)	14 (4)	136 (41)
Vomiting	120 (36)	11 (3)	131 (39)
Fatigue	95 (29)	18 (5)	113 (34)
Pyrexia (3)	89 (27)	12 (4)	103 (31)
Anemia	11(3)	87 (26)	98 (29)
Electrocardiogram QT prolonged (4)	63 (19)	35 (11)	98 (29)
Edema peripheral	88 (26)	3 (1)	91 (27)
Decreased appetite	81 (24)	9 (3)	90 (27)
Dysgeusia	78 (23)	0	78 (23)
Constipation	68 (20)	2 (1)	71 (21)

Note: Patients are counted once only for each adverse event based on the maximum grade experienced for that event.

(1) Totals may exceed sums of columns due to reporting of adverse events without an associated Grade.

(2) Febrile neutropenia cannot be reported as Grade 1 or 2.

(3) One case of Grade 5 pyrexia and pancytopenia (abnormally low reduction in all blood cells produced by bone marrow) was reported.

(4) All but one case of Grade 3/4 electrocardiogram QT prolongation was Grade 3.

Source: Company Reports

Quizartinib Phase IIb Preliminary Efficacy

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- As of Jan 28, 2013, total 34 pts were on drug for >28 days
- CRc rate was 38% (6/16) in 30mg cohort and 39% (7/18) in 60mg cohort
- 25% (4/16) in the 30mg cohort and 33% (6/18) in the 60mg cohort were bridged to transplant

Response To Quizartinib	30mg Cohort N = 16 n (%)	60 mg Cohort N = 18 n (%)
CRc (CR + CRp + CRi)	**6 (37.5)**	**7 (38.9)**
CR	0	1 (5.6)
CRp	0	1 (5.6)
CRi	6 (37.5)	5 (27.8)
PR	1 (6.3)	7 (38.9)

Source: Company Reports

Quizartinib Phase IIb Lower Dose Efficacy Comparable to Phase II Data

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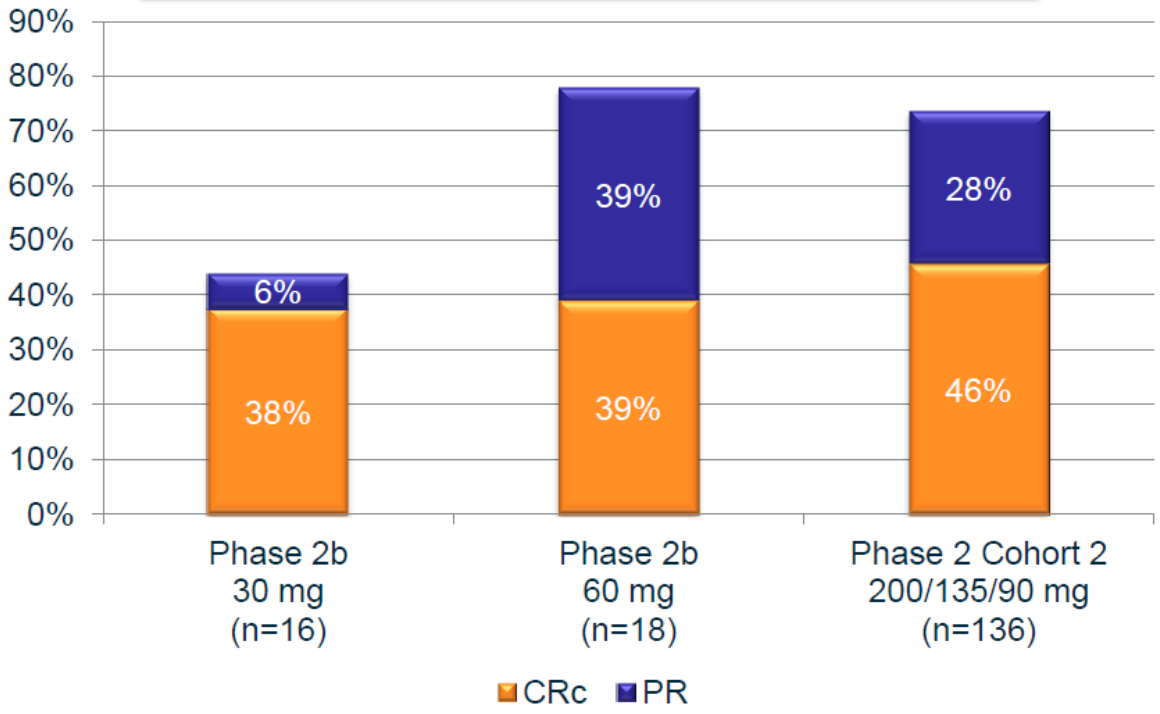
Response Rates in FLT3-ITD + Patients



Phase 2 Comparison

Response	Phase 2b 30 mg Cohort	Phase 2b 60 mg Cohort	Phase 2 Cohort 2
CRc+PR	44%	78%	74%
CRc	38%	39%	46%
CR+CRp	0%	11%	5%
Bridge to Transplant	25%	33%	35%

Source: Company Reports

Quizartinib Phase IIb Lower Dose Safety Improved vs. Phase II Data

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Comparing Grade 3 QT Prolongation in Phase 2b Versus Phase 2				
	Phase 2b*		Phase 2	
	30 mg	60 mg	90/135 mg	200 mg
	N=20	N=19	N=316	N=17
Adverse Event	n (%)	n (%)	n (%)	n (%)
QT Prolongation	0 (0%)	1 (5%)	50 (16%)	6 (35%)

Source: Company Reports

Quizartinib Development Strategy

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- Ongoing Phase IIb dose range finding trial
  - Phase IIb trial initiated in April 2012 to evaluate two lower doses (30 and 60mg/day). After termination of collaboration with Astellas in Sept. 2013, AMBI will assume all responsibility to complete the trial
  - It is a randomized, open-label trial of quizartinib monotherapy in FLT3-ITD+ patients with R/R AML after two prior lines of therapy
- Planned Phase III trial to be initiated in 2014
- Opportunities in additional AML indications
  - Combo with chemo for frontline therapy
  - Maintenance therapy post-HSCT
  - Monotherapy for R/R AML pts with FLT3-ITD

Source: Company Reports

Quizartinib Ongoing Trials

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Summary	Title	Arms	Sites	Primary Endpoint	Key 2nd Endpoint	Pts	Start	Completion	NCT
Phase II in RR AML	A Phase 2, Randomized, Open-Label Study of the Safety and Efficacy of Two Doses of Quizartinib (AC220; ASP2689) in Subjects With FLT3-ITD Positive Relapsed or Refractory Acute Myeloid Leukemia (AML)	1) Dose level 1 2) Dose level 2	US, EU	CRc, QTcF	CR, OS, EFS, LFS, duration of remission	76	Apr, 2012	May, 2013	NCT01565668
Phase I in frontline AML	A Phase 1 Study of AC220 (ASP2689) in Combination With Induction and Consolidation Chemotherapy in Patients With Newly Diagnosed Acute Myeloid Leukemia	quizartinib (oral liquid) / daunorubicin (IV) / cytarabine (IV) dose escalation	US	Safety, DLT	PK	58	Oct, 2011	Mar, 2014	NCT01390337
Phase I in maintenance AML post transplant	A Phase 1 Study of AC220 (ASP2689) as Maintenance Therapy in Subjects With Acute Myeloid Leukemia Who Have Been Treated With an Allogeneic Hematopoietic Stem Cell Transplant	quizartinib dose escalation	US	Safety, DLT	CR, duration of remission, OS	30	Apr, 2012	Mar, 2015	NCT01468467

Source: ClinicalTrial.gov

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ACUTE MYELOID LEUKEMIA (AML)

AML Is Aggressive and Deadly

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- AML is the uncontrolled growth of abnormal white blood cells (blasts) accumulated in the bone marrow
- Intensive chemo is the standard of care and few recent treatment advances with no targeted therapies; stem cell transplant is the only “cure”
- FLT3-ITD mutation occurs in 35% of AML patients; it causes constant, ligand-independent activation of FLT3, resulting in shorter remissions and higher relapse rate

Region	AML Incidence	Annual Deaths	FLT3-ITD Incidence
United States	13,780	10,200	4,823
Europe	15,150		5,300
Japan	5,230		1,830

Source: Company Reports

AML Standard of Care

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- AML is the uncontrolled growth of abnormal white blood cells (blasts) accumulated in the bone marrow
- Standard therapy for AML is a combination of cytarabine and an anthracycline, with a CR rate of 60-70% and a cure rate of 15-25% in front line
- Patients with t(8;21), inversion 16 or t(15;17) have CR rate of 90% and cure rates of 50-80%; for patients (<65 years old) without these chromosome markers, CR rate is 70-80% and cure rate is 30-35% in front line
- Patients (>65 years old) with adverse karyotypes have CR rate of 35-50% and cure rate of <10% in front line
- Median PFS is ~7months and most patients will still relapse and require salvage therapy

Source: MD Anderson

AML Salvage Therapy

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- Treatment options are categorized based on cytogenetic and molecular markers at relapse
- Foremost marker is FLT3 (FMS-like tyrosine kinase)
- Further stratification is based on duration of initial remission and whether therapy is for first or subsequent relapses
- Acute promyelocytic leukemia is treated as a separate entity due to its varied clinical course and treatment regimens

Source: MD Anderson

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OTHER PIPELINE CANDIDATES

AC410 – A Selective JAK2 Inhibitor in Inflammatory and Autoimmune Diseases

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- Janus kinase (JAK) family is a validated target in inflammation
- JAK2 cytokines include IL-3, 5, 12, 13, 23, GM-CSF, and IFNγ
- AC410 is a small molecule, orally available JAK2 inhibitor
- Safety/efficacy was shown in preclinical studies
- Pharmacodynamic and biomarker activity compelling in Phase I study
- No evidence of cytopenias
- Advance development in autoimmune and inflammatory disease, seeking partnership

Source: Company Reports

AC708 and AC855 – Selective CSF1R Inhibitors for Cancer and Inflammation

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- The colony-stimulating factor-1 receptor (CSF1R) is part of a signaling pathway promoting proliferation and survival of macrophages. Over activation of macrophages is associated with tumor growth and inflammatory diseases
- AC708 and AC855 are small molecule compounds with *in vitro* and *in vivo* activity against CSF1R, and significantly reduced activity for FLT3, cKIT, and PDGFR
- Well tolerated in preclinical toxicology
- Plan to initiate IND-enabling studies for AC708 (and potentially AC855) in 2013
- Advance at least one compound in oncology or inflammation, seeking partnership

Source: Company Reports; Note: cKIT – v-kit Hardy-Zuckerman 4 feline sarcoma viral oncogene homolog, PDGFR – platelet-derived growth factor receptor

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PARTNERSHIPS

Partnership – Astellas

- Formed in Dec. 2009 to co-develop FLT3 kinase inhibitors including quizartinib
- Astellas has an exclusive w/w license, pays 50% development costs in North America and Europe and solely responsible for ROW
- Upfront $40M to AMBI
- AMBI retains U.S. co-promote option and 50/50 profit share, tiered double-digit royalties plus sales milestones

Source: Company Reports

Termination of Astellas Partnership Results in Full Ownership of Quizartinib by Ambit

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- On Mar 7th, 2013, Astellas exercised the right to terminate the partnership agreement after Sept 2, 2013.
- The termination appears to be due to Astellas' corporate restructuring, cost reduction initiatives, and lack of synergy with existing assets
- KOLs believe the termination of Astellas partnership does not reflect negatively on quizartinib as an asset
- Quizartinib becomes wholly owned asset and recent capital raise from IPO is sufficient to carry through the Phase III trial

Source: Company Reports

Partnership – Cephalon (Teva)

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- Formed in Nov. 2006 to co-develop BRAF kinase and a second targeted kinase
- Teva is solely responsible for W/W clinical development and commercialization
- Upfront $15.5M to AMBI
- AMBI obligation ended in 2009
- AMBI may receive royalties ranging from mid-single digits to the low-double digits as % of net sales from collaboration, including CEP-32496

Source: Company Reports

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INTELLECTUAL PROPERTY

Intellectual Property

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- Quizartinib
  - U.S. Patent 7,820,657, covers composition of matter
  - Expires in 2028
  - Pending applications ranging from 2028 to 2030 to cover crystalline forms of quizartinib, metabolites, and formulations of quizartinib, methods of manufacturing
- AC 430, AC409, AC410
  - U.S. Patent 8,349,851, covers composition of matter
  - Expires in 2030
- AC708
  - U.S. Patent pending

Source: Company Reports

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MANAGEMENT

Management	Title	Prior Experience
Michael Martino	President and CEO	CareFusion, Sonus, Arzeda, Mallinckrodt
Athena Countouriotis, MD	CMO	Pfizer, BMS, Cell Therapeutics
Alan Fuhrman	CFO	Naviscan, Sonus, Integrex, Capital Stream
Bob Armstrong, PhD	VP, Discovery and Preclinical Development	Chiron, Idun

Source: Company Reports

AMBI Income Statement	2011A	2012A	Mar-13A	Jun-13E	Sep-13E	Dec-13E	2013E	2014E	2015E	2016E	2017E	2018E
Collaboration agreements	23,843	17,633	6,592	6,500	5,000	3,000	21,092	15,000	12,000			
Quizartinib sales										2,020	17,752	41,045
Total revenue	23,843	17,633	6,592	6,500	5,000	3,000	21,092	15,000	12,000	2,020	17,752	41,045
COGS										162	1,420	3,284
% of revenue										*8%*	*8%*	*8%*
R&D	50,705	36,731	9,005	9,455	9,928	10,424	38,813	39,977	41,176	42,412	43,684	44,995
G&A	8,905	6,550	1,776	1,865	1,958	2,056	7,655	8,420	9,262	25,000	30,179	32,836
% of revenue											*170%*	*80%*
gain on sale of kinase profiling services	(2,108)	(2,497)	0	0	0	0	0	0	0	0	0	
Total operating expenses	57,502	40,784	10,781	11,320	11,886	12,480	46,467	48,397	50,439	67,573	75,283	81,114
Net income (loss) from operations	(33,659)	(23,151)	(4,189)	(4,820)	(6,886)	(9,480)	(25,375)	(33,397)	(38,439)	(65,553)	(57,531)	(40,069)
Interest expenses	(4,502)	(1,737)	(162)	0	0	0	(162)	0	0			
Other income	1,538	29	7	0	0	0	7	0	0			
Change in fair value of derivative liabilies	(795)	(2,291)	(3,957)	0	0	0	(3,957)	0	0			
Total other income (expenses)	(3,759)	(3,999)	(4,112)	0	0	0	(4,112)	0	0	0	0	0
Net income (loss) before income taxes	(37,418)	(27,150)	(8,301)	(4,820)	(6,886)	(9,480)	(29,487)	(33,397)	(38,439)	(65,553)	(57,531)	(40,069)
Provision (benefit) for income taxes	0	(121)	1	0	0	0	1	0	0			
Tax rate												
Net income (loss)	(37,418)	(27,029)	(8,302)	(4,820)	(6,886)	(9,480)	(29,488)	(33,397)	(38,439)	(65,553)	(57,531)	(40,069)
Non-controlling interest	(213)	382	73	50	50	50	223	200	200			
Net income (loss) attributable to AMBI	(37,631)	(26,647)	(8,229)	(4,770)	(6,836)	(9,430)	(29,265)	(33,197)	(38,239)	(65,553)	(57,531)	(40,069)
Accretion to redemption value of reddemable convertible preferred stock	(2,000)	(3,161)	(2,319)	0	0	0	(2,319)	0	0			
Change in fair value of redeemable non-controlling interest	4,477	(854)	(1,499)	0	0	0	(1,499)	0	0			
Net loss to common stockholders	(35,154)	(30,662)	(12,047)	(4,770)	(6,836)	(9,430)	(33,083)	(33,197)	(38,239)	(65,553)	(57,531)	(40,069)
Net loss per share	**(25,886.60)**	**(16,591.99)**	**(3,019.30)**	**(0.27)**	**(0.38)**	**(0.52)**	**(1.85)**	**(1.77)**	**(1.55)**	**(2.12)**	**(1.77)**	**(1.08)**
Basic shares	1	2	4	17,713	17,890	18,069	17,891	18,785	24,725	30,961	32,509	37,134
Dilutive shares				21,478	21,693	21,910	21,694	22,128	28,234	34,646	36,378	41,197

Source: Company Reports and Leerink Swann

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Disclosures Appendix

Analyst Certification

I, Howard Liang, Ph.D., certify that the views expressed in this report accurately reflect my views and that no part of my compensation was, is, or will be directly related to the specific recommendation or views contained in this report.

Distribution of Ratings/Investment Banking Services (IB) as of 03/31/13				
			IB Serv./Past 12 Mos.	
Rating	Count	Percent	Count	Percent
BUY [OP]	107	61.14	32	29.91
HOLD [MP]	68	38.86	0	0.00
SELL [UP]	0	0.00	0	0.00

Explanation of Ratings

Outperform (Buy): We expect this stock to outperform its benchmark over the next 12 months.

Market Perform (Hold/Neutral): We expect this stock to perform in line with its benchmark over the next 12 months.

Underperform (Sell): We expect this stock to underperform its benchmark over the next 12 months.The degree of outperformance or underperformance required to warrant an Outperform or an Underperform rating should be commensurate with the risk profile of the company.

For the purposes of these definitions the relevant benchmark will be the S&P 600® Health Care Index for issuers with a market capitalization of less than $2 billion and the S&P 500® Health Care Index for issuers with a market capitalization over $2 billion.

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