ASH Investor Reception

December 11, 2017

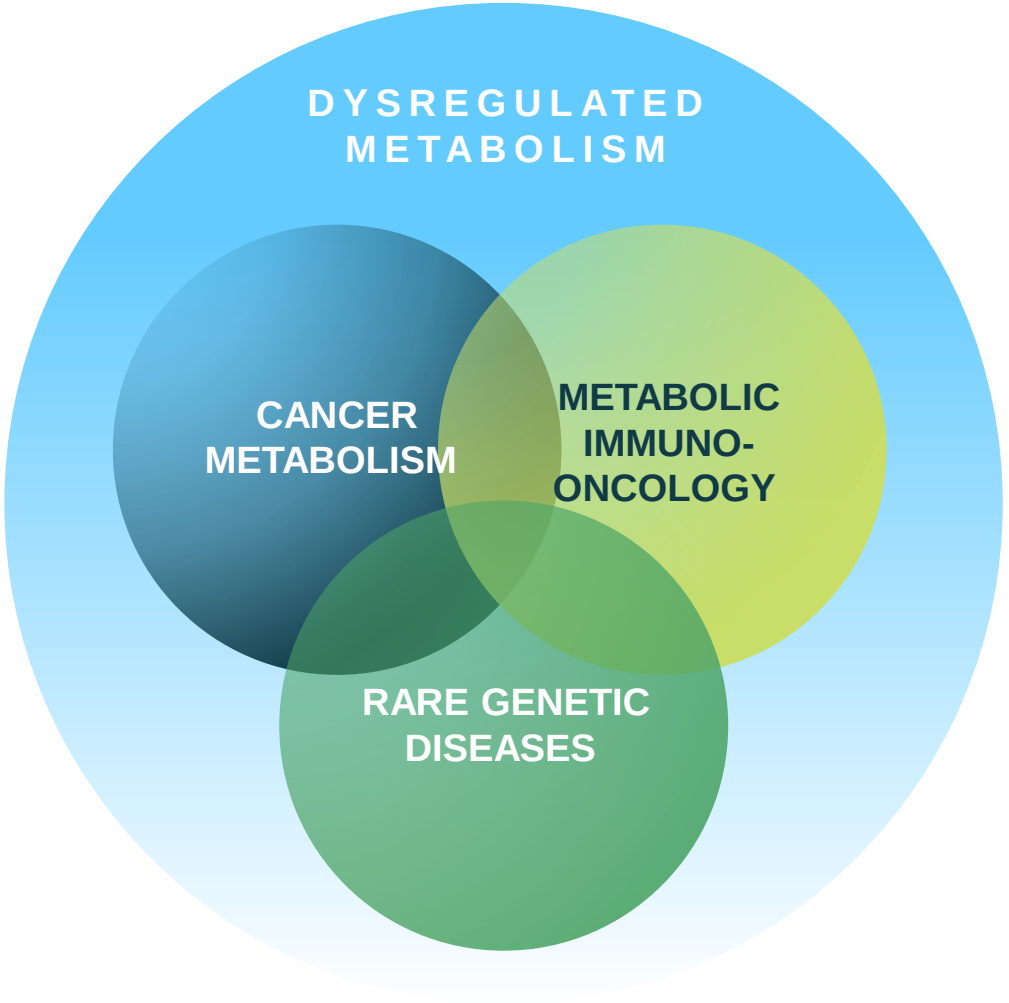
Forward Looking Statements

This presentation and various remarks we make during this presentation contain forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995. Such forward-looking statements include those regarding Agios' plans, strategies and expectations for its and its collaborator's preclinical, clinical and commercial advancement of its drug development programs including IDHIFA® (enasidenib), ivosidenib, AG-348 and AG-270; the potential benefits of Agios' product candidates; and the potential benefit of its strategic plans and focus. The words "anticipate," "expect," "intend," "potential," "milestone," "goal," "will," "on track," "upcoming," and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Such statements are subject to numerous important factors, risks and uncertainties that may cause actual events or results to differ materially from Agios' current expectations and beliefs. For example, there can be no guarantee that any product candidate Agios or its collaborator, Celgene, is developing will successfully commence or complete necessary preclinical and clinical development phases, or that development of any of Agios' product candidates will successfully continue. There can be no guarantee that any positive developments in Agios' business will result in stock price appreciation. Management's expectations and, therefore, any forward-looking statements in this presentation and various remarks we make during this presentation could also be affected by risks and uncertainties relating to a number of other important factors, including: Agios' results of clinical trials and preclinical studies, including subsequent analysis of existing data and new data received from ongoing and future studies; the content and timing of decisions made by the U.S. FDA and other regulatory authorities, investigational review boards at clinical trial sites and publication review bodies; Agios' ability to obtain and maintain requisite regulatory approvals and to enroll patients in its planned clinical trials; unplanned cash requirements and expenditures; competitive factors; Agios' ability to obtain, maintain and enforce patent and other intellectual property protection for any product candidates it is developing; Agios' ability to maintain key collaborations, such as its agreements with Celgene; and general economic and market conditions. These and other risks are described in greater detail under the caption "Risk Factors" included in Agios' public filings with the Securities and Exchange Commission. Any forward-looking statements contained in this presentation and various remarks we make during this presentation speak only as of the date hereof, and Agios expressly disclaims any obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law.

Today’s Agenda

- **Our Vision and Opening Remarks** – David Schenkein, M.D.
- **IDH Clinical Review** – Chris Bowden, M.D.
- **Q&A with KOLs**:
  - Richard M. Stone, M.D. (Dana-Farber Cancer Institute)
  - Martin S. Tallman, M.D. (Memorial Sloan Kettering Cancer Center)
- **Closing Remarks** – David Schenkein, M.D.

Driven By a Clear Vision and Values



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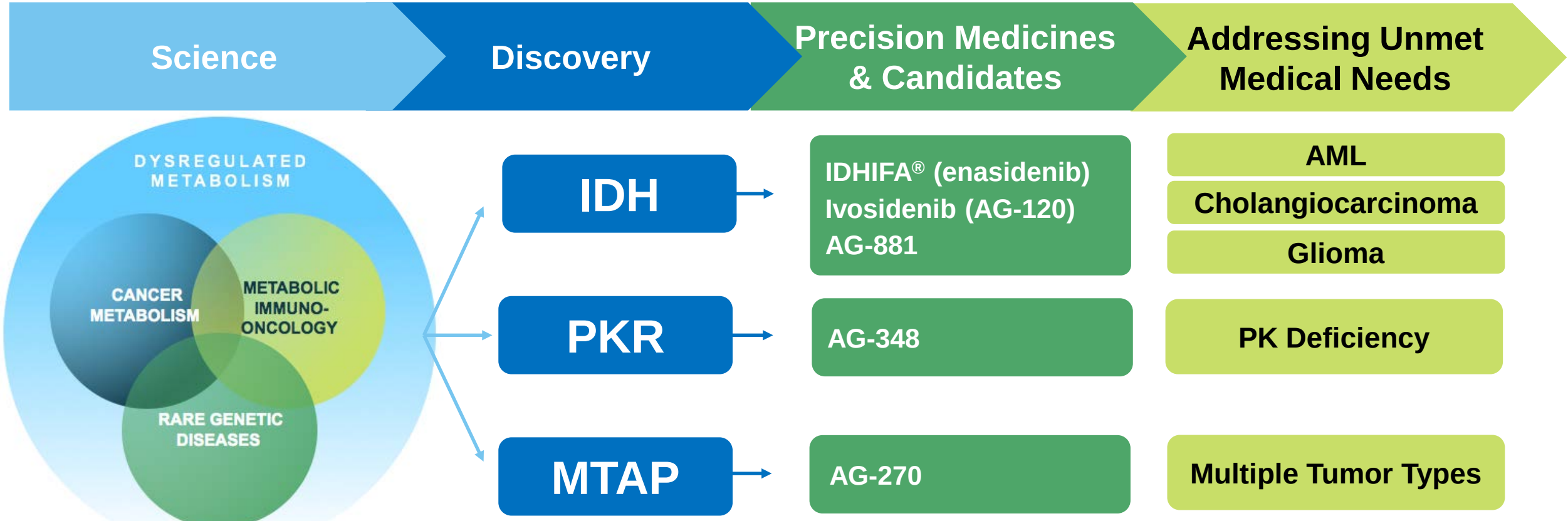
Agios is passionately committed to applying our scientific leadership in the field of cellular metabolism to transform the lives of patients with cancer and rare genetic diseases.

Highly Productive Drug Development Engine



Demonstrated ability to rapidly translate novel biology into precision medicines in areas of high unmet need

2017 ASH Presentations

Topic/Date	Title	Abstract No.
Ivosidenib R/R AML – Oral Monday, Dec. 11, 3:45p.m.	Ivosidenib (AG-120) in Mutant IDH1 AML and Advanced Hematologic Malignancies: Results of a Phase 1 Dose Escalation and Expansion Study	725
Ivosidenib or Enasidenib Frontline AZA Combo – Oral Monday, Dec. 11, 11:00a.m.	Mutant Isocitrate Dehydrogenase (mIDH) Inhibitors, Enasidenib or Ivosidenib, in Combination with Azacitidine (AZA): Preliminary Results of a Phase 1b/2 Study in Patients with Newly Diagnosed Acute Myeloid Leukemia (AML)	639
Ivosidenib or Enasidenib Frontline 7+3 Combo – Oral Monday, Dec. 11, 4:00p.m.	Ivosidenib or Enasidenib Combined with Standard Induction Chemotherapy Is Well Tolerated and Active in Patients with Newly Diagnosed AML with an IDH1 or IDH2 Mutation: Initial Results from a Phase 1 Trial	726
Ivosidenib Untreated AML – Poster Sunday, Dec. 10, 6p.m.	Genetic Profiling and Deep IDH1 Mutation Clearance to ≤0.04% in Ivosidenib (AG-120)-Treated Patients with Mutant IDH1 Relapsed or Refractory and Untreated AML	2684
Enasidenib Untreated AML – Oral Monday, Dec. 11, 10:45a.m.	Enasidenib Monotherapy Is Effective and Well-Tolerated in Patients with Previously Untreated Mutant-IDH2 (mIDH2) Acute Myeloid Leukemia (AML)	638
Enasidenib Stable Disease – Poster Saturday, Dec. 9, 5:30p.m.	Continuing Enasidenib Treatment for Patients with Mutant-IDH2 (mIDH2) Relapsed or Refractory Acute Myeloid Leukemia (R/R AML) with Stable Disease May Result in Improved Survival and Responses over Time	1299
AG-348 DRIVE PK – Poster Sunday, Dec. 10, 6:00p.m.	Results Update from the DRIVE PK Study: Effects of AG-348, a Pyruvate Kinase Activator, in Patients with Pyruvate Kinase Deficiency	2194
PKD Natural History Study – Poster Monday, Dec. 11, 6:00p.m.	Genotype-Phenotype Correlation and Molecular Heterogeneity in Pyruvate Kinase Deficiency: Data from the PKD Natural History Study	3479

Key Takeaways from our Data

Updated Ivosidenib Phase 1 R/R AML Data

- Data in IDH1m R/R AML support planned year-end NDA submission
- Ivosidenib well tolerated; most AEs were Grade 1–2 in severity
- Durable responses
  - CR+CRh rate of 30.4% with duration of 8.2 months
- Transfusion independence, decrease in febrile neutropenia and infections are additional measures of clinical benefit

First Ivosidenib & Enasidenib Frontline AML Combination Data

- IDHm combination with standard of care front-line therapy is safe and well tolerated
- Efficacy from both combination trials is early but encouraging
- Data support further investigation in the frontline setting (AGILE & planned 7+3 Phase 3)

Updated DRIVE PK Data

- AG-348 continues to be well tolerated
- Hemoglobin increases >1.0 g/dL in 26 of 52 patients overall; responses remain durable with completion of six month core treatment period

IDHm Inhibitors Data Overview

Chris Bowden, M.D.
Chief Medical Officer

Phase 1 Single-arm, Open-label, Multicenter Trial of Ivosidenib in IDH1m R/R AML

Dose escalation (n=78)
Enrollment complete

Patients with mIDH1+ advanced hematologic malignancies

Oral ivosidenib daily in continuous 28-day cycles

Doses included 100 mg BID, 300, 500, 800, 1200 mg QD

Dose expansion (n=180)
Enrollment complete: 500 mg QD in continuous 28-day cycles

1. R/R AML in 2nd+ relapse, relapse after SCT, refractory to induction or reinduction, or relapse within 1 year, **n=126**
2. Untreated AML not eligible for SOC, **n=25**
3. Other non-AML mIDH1 R/R advanced hematologic malignancies, **n=11**
4. Other R/R AML not eligible for Arm 1, **n=18**

Key analysis sets

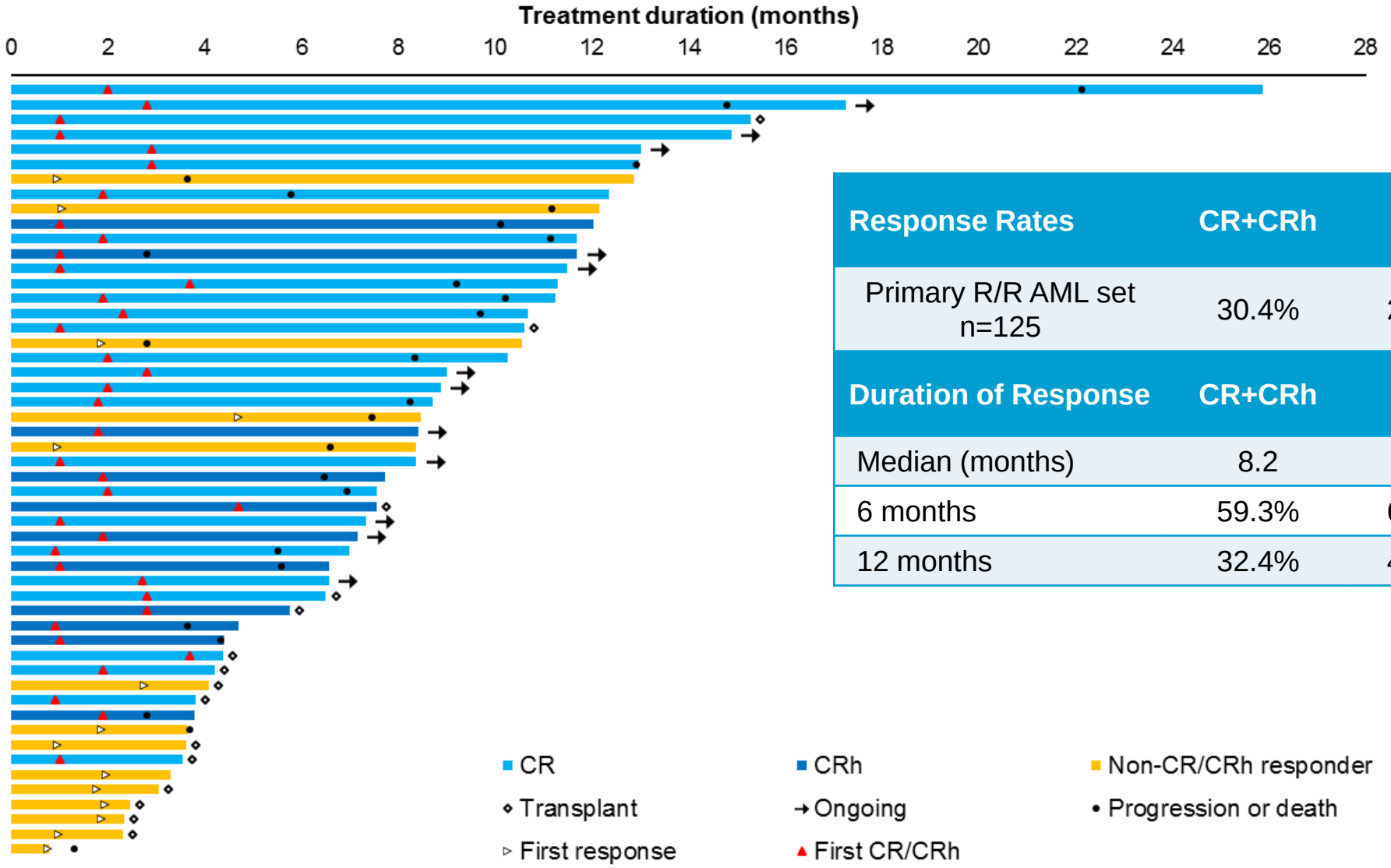
- Safety Analysis Set (N=258): All treated patients
- Primary R/R AML Analysis Set (N=125): 33 from dose escalation, 92 from dose expansion with at least 6 months of follow-up

ClinicalTrials.gov NCT02074839. DLTs, dose limiting toxicities; MTD, maximum tolerated dose; RP2D, recommended phase 2 dose
The first 125 treated patients from Arm 1 of expansion (n=92) and eligible dose escalation patients (n=33) treated at 500 mg QD who were enrolled ≥ 6 months prior to the primary analysis cut-off date of 12 May 2017.

Ivosidenib R/R AML Safety Summary

- For all 258 patients: Ivosidenib was well tolerated; most AEs were Grade 1-2 in severity
  - Diarrhea, leukocytosis, nausea, fatigue and febrile neutropenia most common (≥25%)
- AEs of interest for 125 patient primary analysis set:
  - Leukocytosis: Grade ≥3 leukocytosis reported in 8% of patients and managed with hydroxyurea; none were fatal
  - ECG QT prolongation: Grade 3 QT prolongation reported 8% of patients; none were Grade 4 or fatal
  - IDH-differentiation syndrome (IDH-DS): All Grades reported 9.6%; none were Grade 4 or fatal

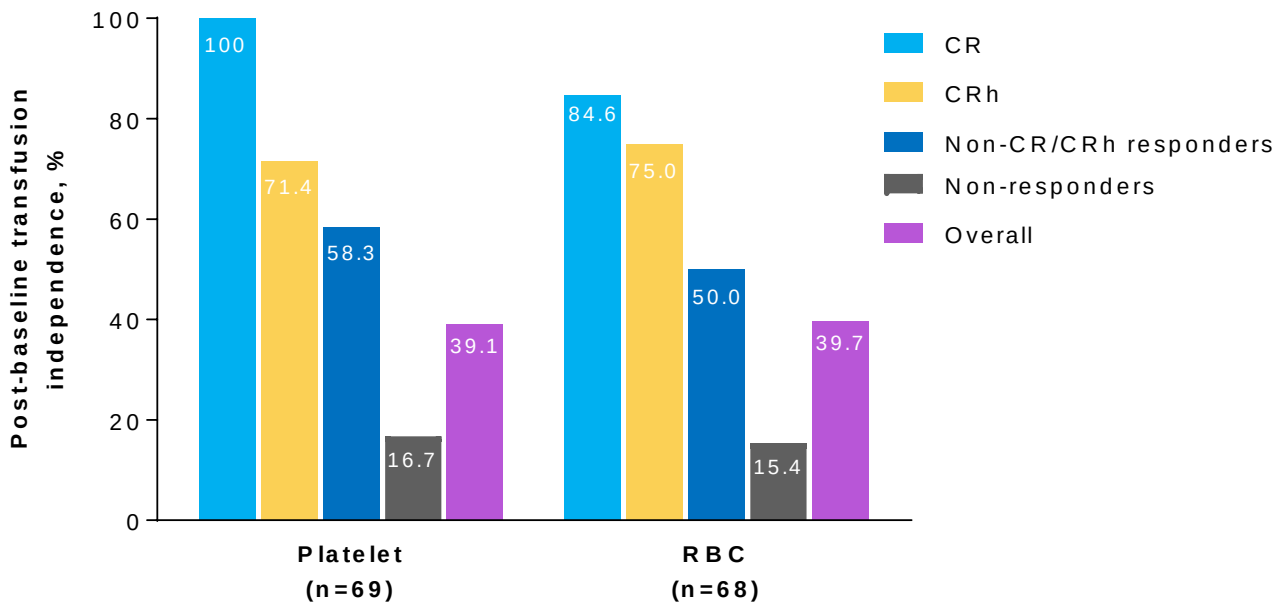
Duration of Treatment & Best Overall Response in Responders Primary R/R AML Set (N=52)



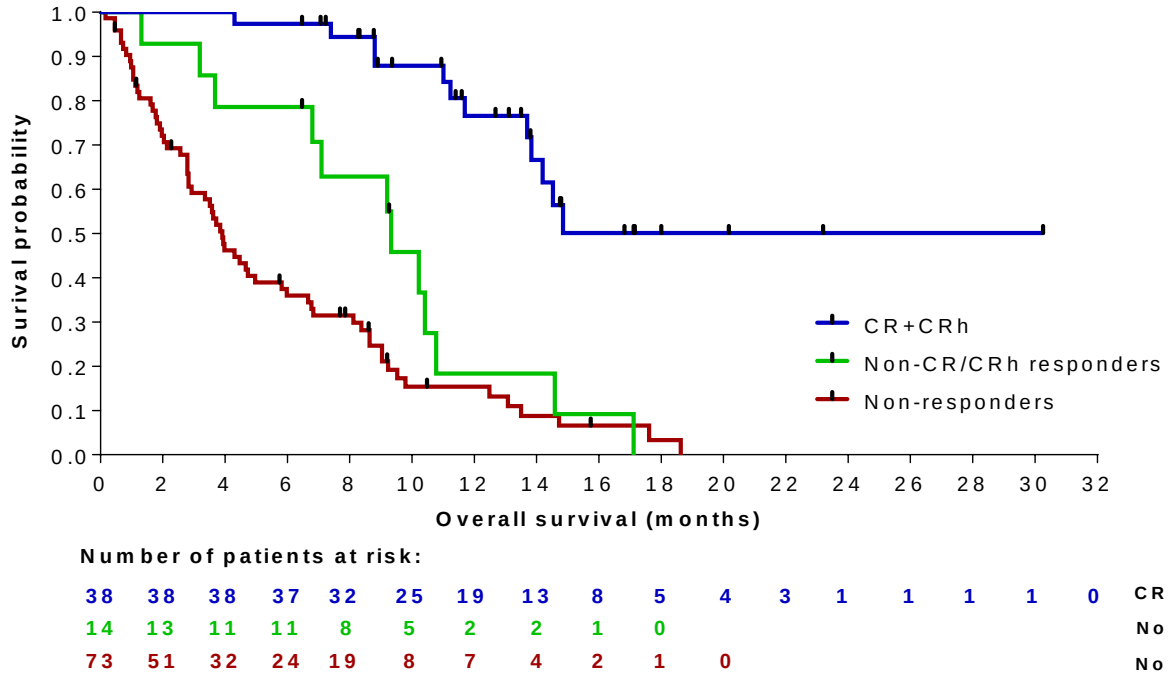
Response Rates	CR+CRh	CR	Overall Response
Primary R/R AML set n=125	30.4%	21.6%	41.6%
Duration of Response	**CR+CRh**	**CR**	**Overall Response**
Median (months)	8.2	9.3	6.5
6 months	59.3%	67.5%	55.0%
12 months	32.4%	41.2%	24.6%

Where first response and first CR/CRh are the same time point, only the first CR/CRh symbol is shown

Transfusion Independence & Overall Survival in Primary R/R AML Set



Transfusion independence achieved across multiple response categories



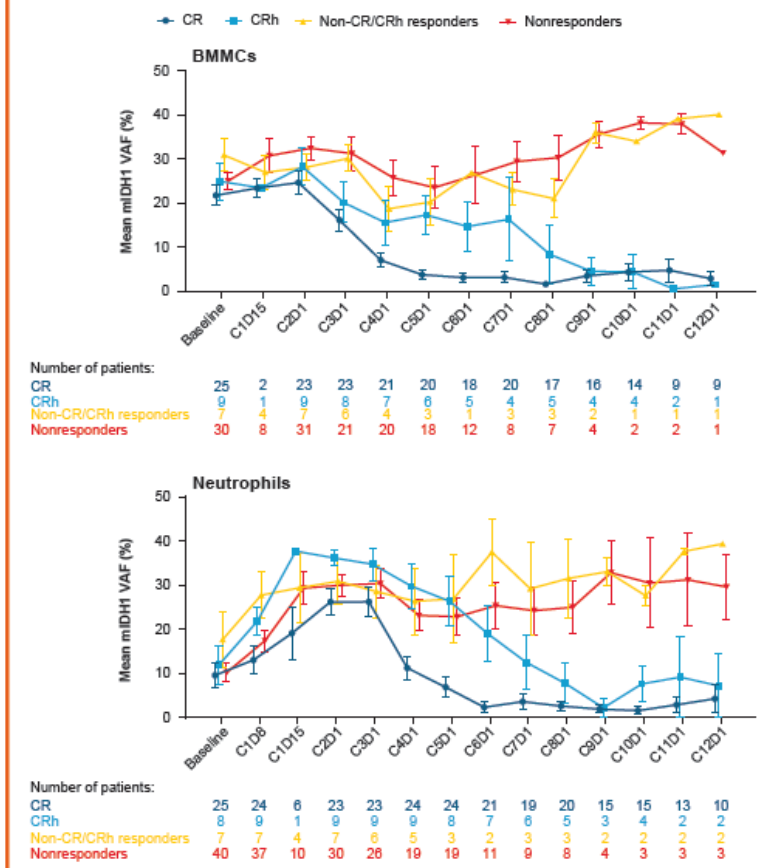
- Median OS for CR+CRh has not been reached
  - 9.3 months for non-CR+CRh responders
  - 3.9 months for non-responders
  - 8.8 months overall
- Median follow-up, 14.8 months

Data cutoff: 12May2017. CR, complete remission; CRh, CR with partial hematologic recovery; RBC, red blood cell

Ivosidenib Reduced *mIDH1* Allele Burden Patients Achieving CR or CRh

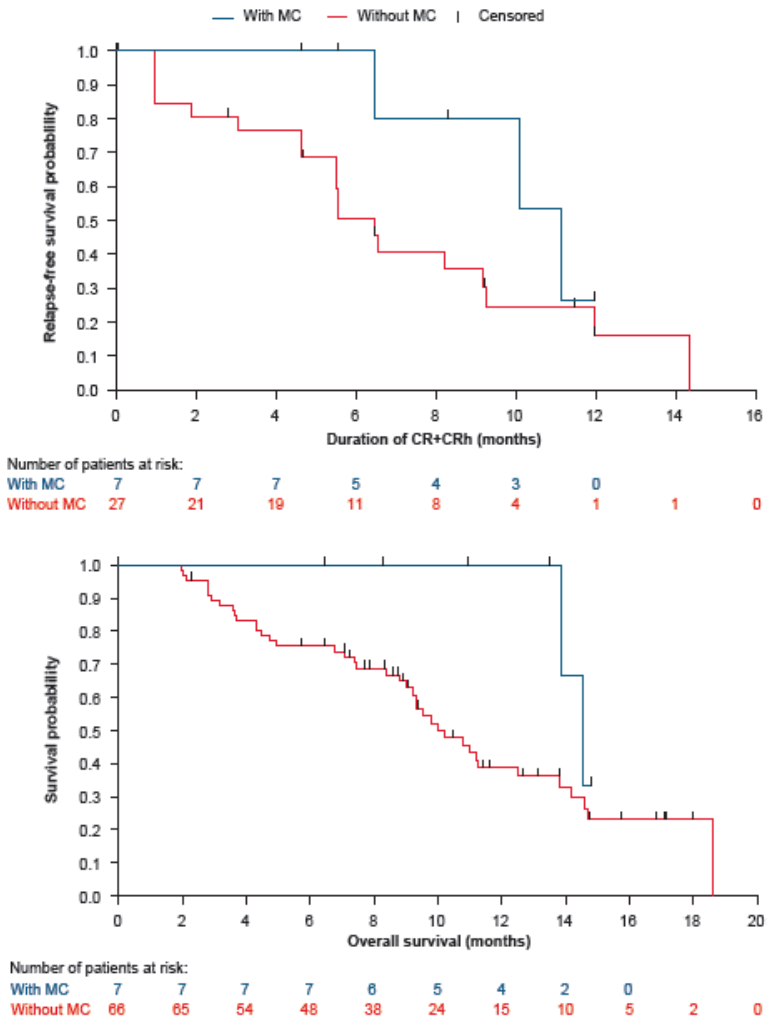
Longitudinal Mutant IDH1 Analysis: Poster 2684, Stone RM et al.

Figure 3. Ivosidenib treatment reduced *mIDH1* VAF in BMMCs and neutrophils from patients with best overall response of CR or CRh (R/R AML)



Mean ± standard error is presented
Clinical response was assessed by investigator according to the modified 2003 International Working Group criteria
CRh was derived by the sponsor and defined as CR except absolute neutrophil count >0.5×10⁹/L (500/μL) *and* platelet count >50×10⁹/L (50,000/μL)
Non-CR/CRh responders include CRi/CRp and MLFS not meeting criteria for CRh, and PR; nonresponders include SD and PD
Numbers below the graph represent number of subjects with mIDH1 VAF data at each visit
CRh = complete remission with partial hematologic recovery; CRi = complete remission with incomplete hematologic recovery; CRp = CR with incomplete platelet recovery; MLFS = morphologic leukemia-free state; PD = progressive disease; PR = partial response; SD = stable disease

Figure 4. Patients with IDH1 mutation clearance had improved duration of CR+CRh and OS (R/R AML, BMMCs)



Duration of CR+CRh = date of first documented CR/CRh to date of first documented confirmed relapse or death
Overall survival = time from first dose to the date of death due to any cause
Statistical testing not provided owing to small sample size and low event rate

- Patients with MRD-negative CR had improved duration of CR compared to patients with CR with persistent MRD in this limited dataset
- Patients with MRD-negative CR had improved overall survival compared to all other R/R AML patients with persistent MRD

Data cutoff: 12May2017

Key Takeaways – Ivosidenib in R/R AML

Updated Ivosidenib Phase 1 R/R AML Data

- IDH1m R/R AML data support planned year-end NDA submission
- Well tolerated; most AEs were Grade 1–2 in severity
- Durable responses, CR+CRh and ORR rates of 30.4% and 41.6%, respectively, and corresponding durations of 8.2 and 6.5 months
- Additional clinical benefits include:
  - Transfusion independence across best response categories
  - Decreased frequency of febrile neutropenia and infections in responders
- Median OS for CR+CRh has not been reached. OS was 9.3 months for non-CR+CRh responders and 8.8 months overall
- Ivosidenib reduced mIDH1 allele burden in patients who achieved CR or CRh

Ivosidenib & Enasidenib Single Agent Untreated AML Data

Ivosidenib & Enasidenib Phase 1 Single Agent Untreated AML

Ivosidenib: 34 AML patients not eligible for standard of care

- CR rate of 20.6% (7 patients), median duration not reached
- ORR rate of 55.9% (19 patients), median duration of 9.2 months

Enasidenib: 38 AML patients not eligible for standard of care

- CR rate of 18% (7 patients), median duration not reached
- ORR rate of 32% (12 patients), median duration of 12.2 months
- Median OS was 11.3 months and median EFS was 5.7 months

Phase 1 Frontline AML Combination Trials

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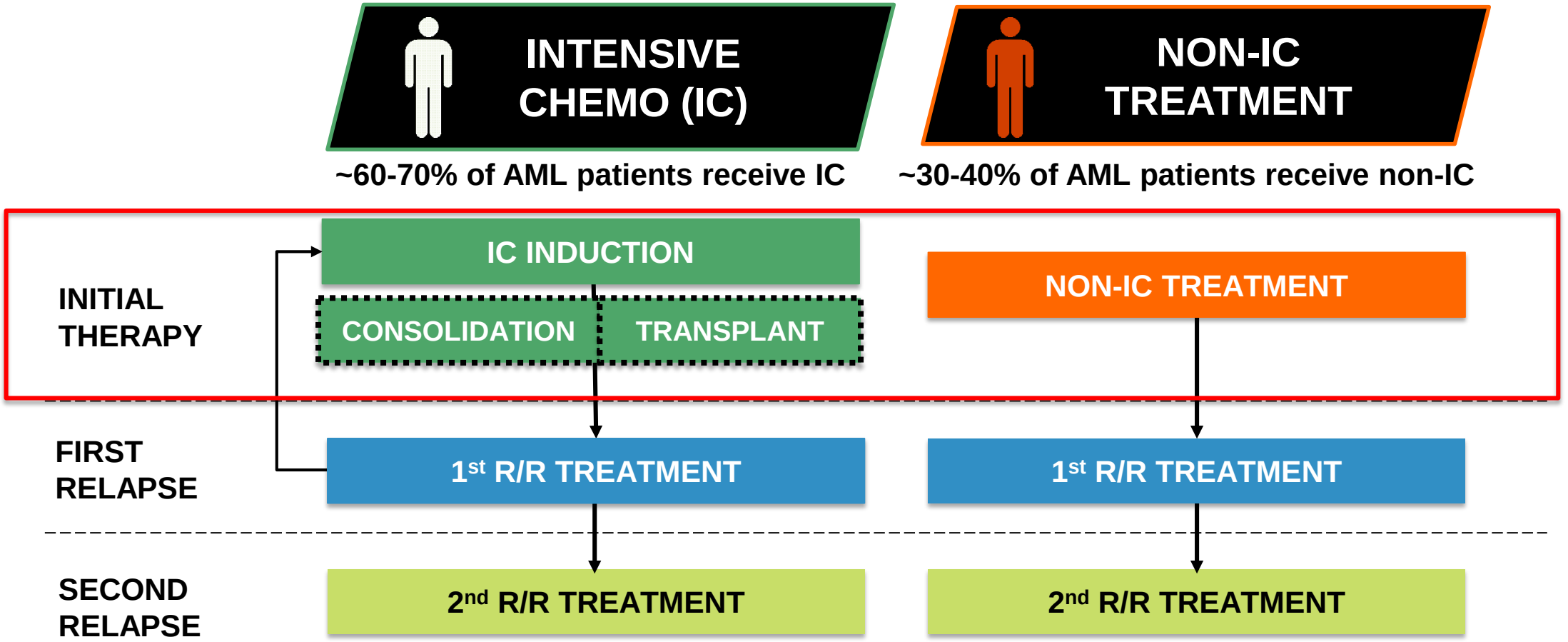
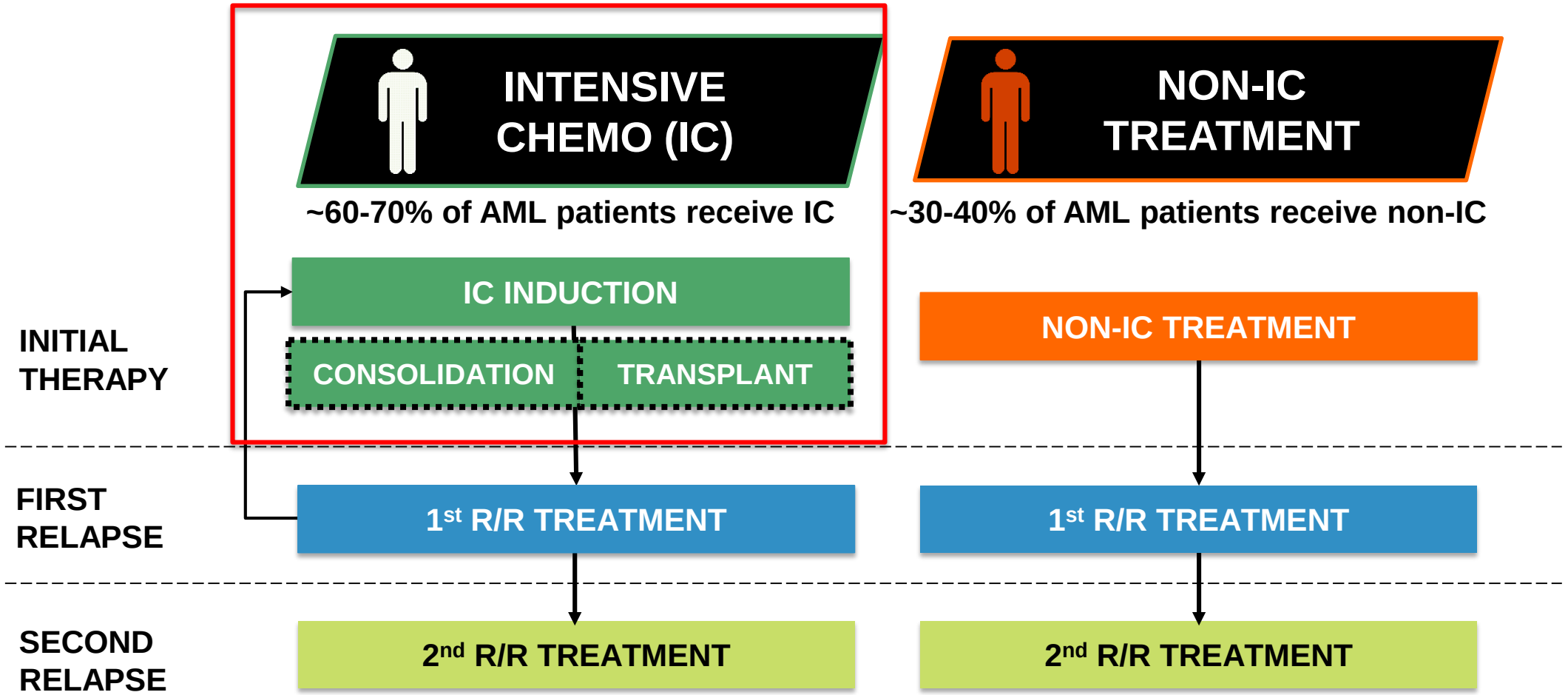
Current AML Treatment Landscape



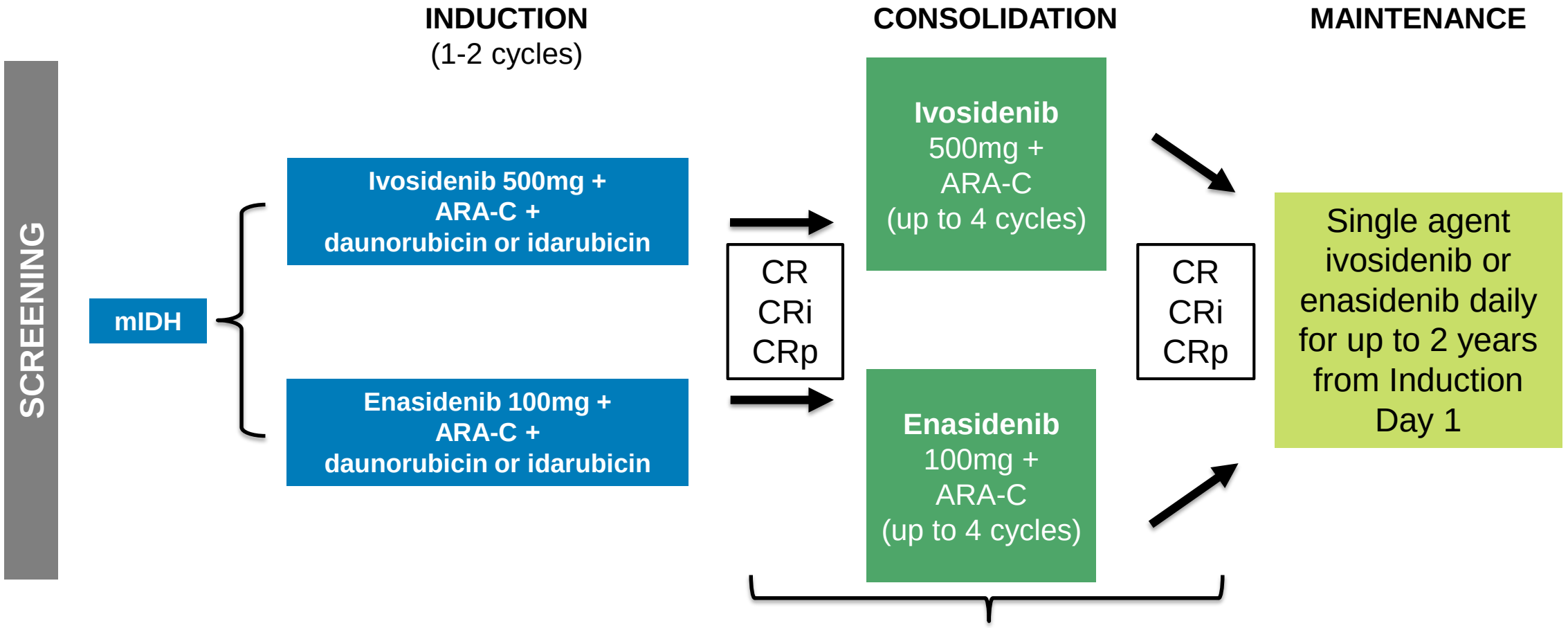
Advancing IDHm Inhibitors into Frontline Setting

	Trials Including both Ivosidenib & Enasidenib	Ivosidenib Only
IC ELIGIBLE (7+3)	**Phase 1** **Primary objective:** Safety and tolerability of ivosidenib or enasidenib with standard induction & consolidation chemo **ASH 2017:** n=88 IDHm patients with newly diagnosed (de novo or secondary) AML	**Phase 3** *(planned for 2018)* Ivosidenib or enasidenib with standard induction & consolidation chemo
IC-INELIGIBLE (VIDAZA®)	**Phase 1/2** **Primary objective:** Safety and tolerability of ivosidenib or enasidenib with VIDAZA® **ASH 2017:** n=17 IDHm patients with newly diagnosed AML who are not candidates for intensive chemo	**AGILE** **Global Phase 3** *(ongoing)* ~400 patients randomized to Ivosidenib + VIDAZA® or placebo; primary endpoint O/S

Current AML Treatment Landscape



Ivosidenib or Enasidenib with Standard Induction Chemotherapy in Patients with Newly Diagnosed AML



Demographics & Safety Summary

- Median age
  - Ivosidenib: 60.5 yrs, 53% (n=17) 60 yrs or over
  - Enasidenib: 63 yrs, 62% (n=35) 60 yrs or over
- AML type:
  - De novo: 69% of ivosidenib arm (n=22); 57% of enasidenib arm (n=32)
  - Secondary: 31% of ivosidenib arm (n=10); 43% of enasidenib arm (n=24)
- Combination of ivosidenib or enasidenib with standard AML induction therapy is safe and well tolerated
  - Some secondary AML patients treated with enasidenib exhibited prolonged time to platelet recovery, may reflect the reduced hematopoietic reserve of these patients
  - One dose-limiting toxicity in the enasidenib arm of persistent Grade 4 thrombocytopenia in the absence of residual leukemia
  - No dose-limiting toxicities in the ivosidenib arm

Most common Grade ≥3 non-hematologic AEs for ivosidenib and enasidenib combo arms:

	Ivosidenib (AG-120) + CT (n=32)	Enasidenib (AG-221) + CT (n=56)
Patients with >1 grade 3 or higher TEAE, n (%)	**30 (94)**	**51 (91)**
Febrile neutropenia	**19 (60)**	**35 (63)**
Blood bilirubin increased	**3 (9)**	**5 (9)**
Hypertension	**3 (9)**	**5 (9)**
Colitis	**3 (9)**	**3 (5)**
Alanine aminotransferase increased	**3 (9)**	**1 (2)**
Aspartate aminotransferase increased	**3 (9)**	**-**
Lung infection	**2 (6)**	**3 (5)**
Bacteremia	**1 (3)**	**5 (9)**
Diarrhea	**1 (3)**	**4 (7)**

Data cut 01AUG2017

Best Overall Response Summary

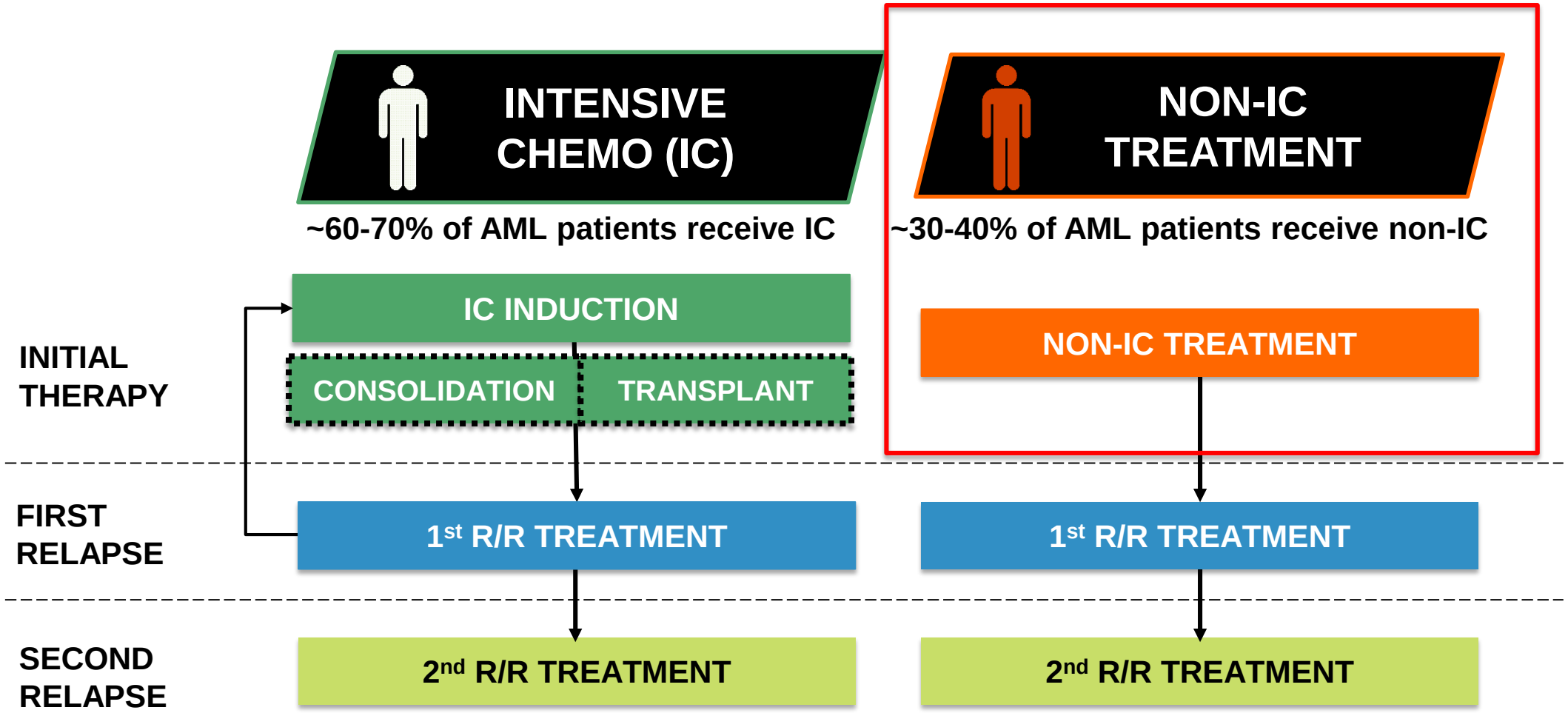
	Ivosidenib (AG-120) + CT			Enasidenib (AG-221) + CT		
Response, n (%)	All (n=30)	*De novo* (n=21)	sAML (n=9)	All (n=50)	*De novo* (n=27)	sAML (n=23)
CR+CRi/CRp	23 (77)	19 (91)	4 (44)	31 (62)	18 (67)	13 (57)
CR	19 (63)	15 (71)	4 (44)	25 (50)	16 (59)	9 (39)
CRi/CRp	4 (13)	4 (19)	-	6 (12)	2 (7)	4 (17)
MLFS	1 (3)	-	1 (11)	10 (20)	4 (15)	6 (26)
PR	2 (7)	1 (5)	1 (11)	-	-	-
Persistent disease	2 (7)	1 (5)	1 (11)	5 (10)	2 (7)	3 (13)
NE	2 (7)	-	2 (22)	4 (8)	3 (11)	1 (4)

Best response from any time on study is shown

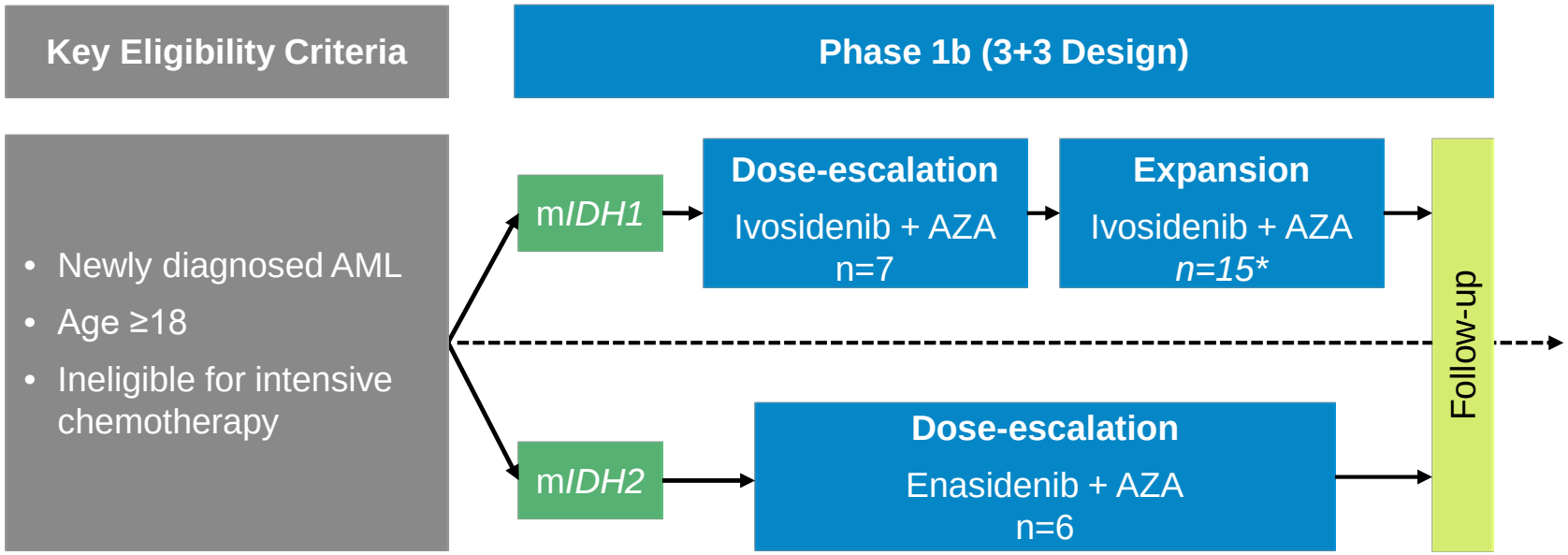
CR=complete response; CRi=CR with incomplete hematologic recovery; CRp=CR with incomplete platelet recovery; MLFS=morphologic leukemic-free state for patients with AML; PR=partial response; Persistent Disease = Stable Disease + Disease Progression ; NE=not evaluable

Data cut 01AUG2017

Current AML Treatment Landscape



Enasidenib or Ivosidenib in Combination with Azacitidine (VIDAZA®)



PHASE 2 DESIGN

2:1 randomization of enasidenib + AZA vs. AZA alone

PRIMARY ENDPOINT:

Overall response rate

KEY SECONDARY ENDPOINTS:

Safety
Event-free survival
Overall survival

Primary Endpoints:

- Recommended combination dose (RCD); safety

Key Secondary Endpoints:

- Overall response rate
- PK/PD
- QOL outcomes

*Expected final enrollment; 4 pts had enrolled in expansion as of data cutoff (1 Sep 2017)
ClinicalTrials.gov NCT02677922
AML, acute myeloid leukemia; AZA, azacitidine; IC, induction chemotherapy; ORR, overall response rate; QOL, quality of life; RCD, recommended combination dose

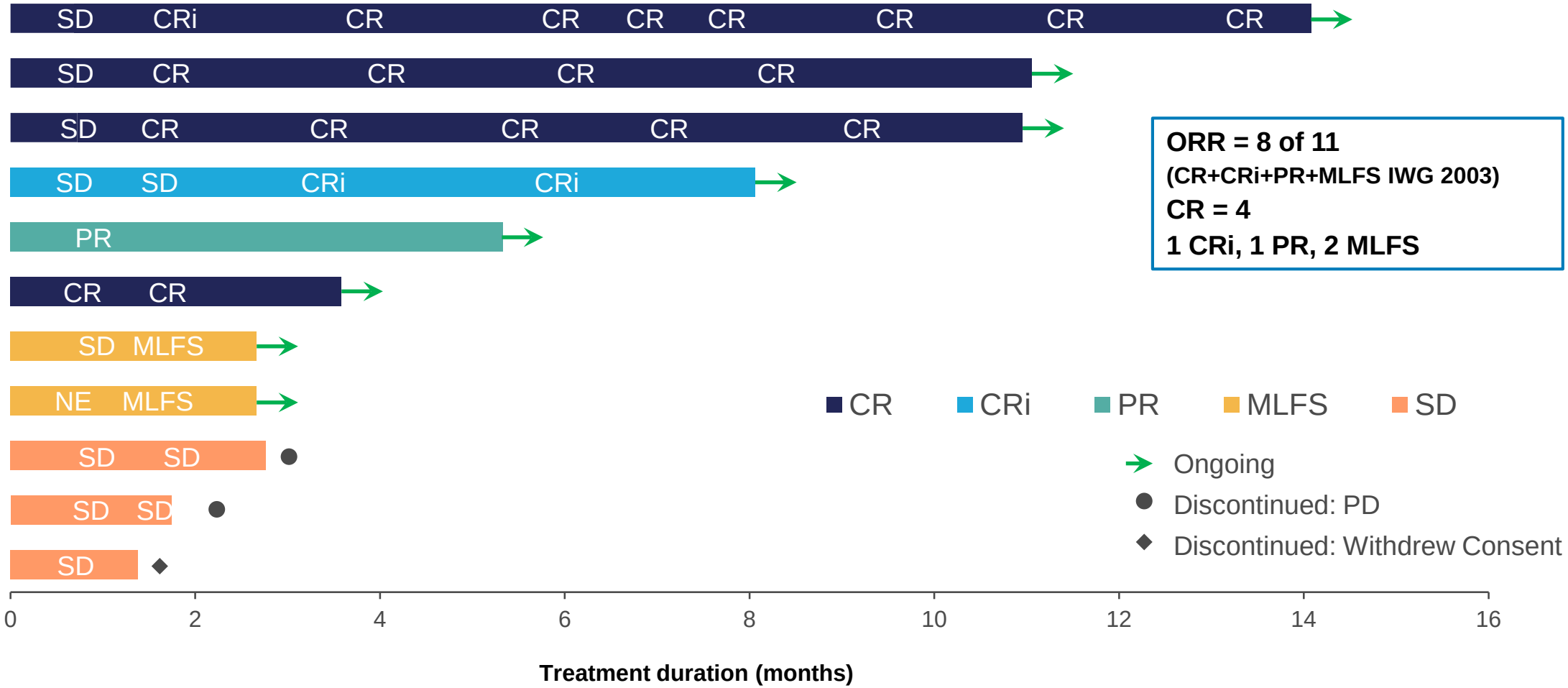
Demographics & Safety Summary

- **Median age:** 76 yrs for ivosidenib (all 65 or over); 68 yrs for enasidenib (5/6 patients 65 or over)
- **Ivosidenib combination: Grade 3-4 treatment-emergent events**
  - Most common hematologic adverse events were anemia (18%, 2/11) and febrile neutropenia (18%, 2/11) with neutropenia and thrombocytopenia each with one event (9% each)
  - Most common non-hematologic adverse event was pneumonia (18%, 2/11)
  - IDH differentiation syndrome reported in one patient
- **Enasidenib combination: Grade 3-4 treatment-emergent events**
  - Most common hematologic adverse event was neutropenia (33%, 2/6), with thrombocytopenia, febrile neutropenia, anemia, lymphocyte count decreased and white blood cell count decreased all with one event (17% each)
  - Most common non-hematologic adverse events were pneumonia (33%, 2/6) and hyperbilirubinemia (33%, 2/6)
  - IDH differentiation syndrome reported in one patient

Data cut 01AUG2017

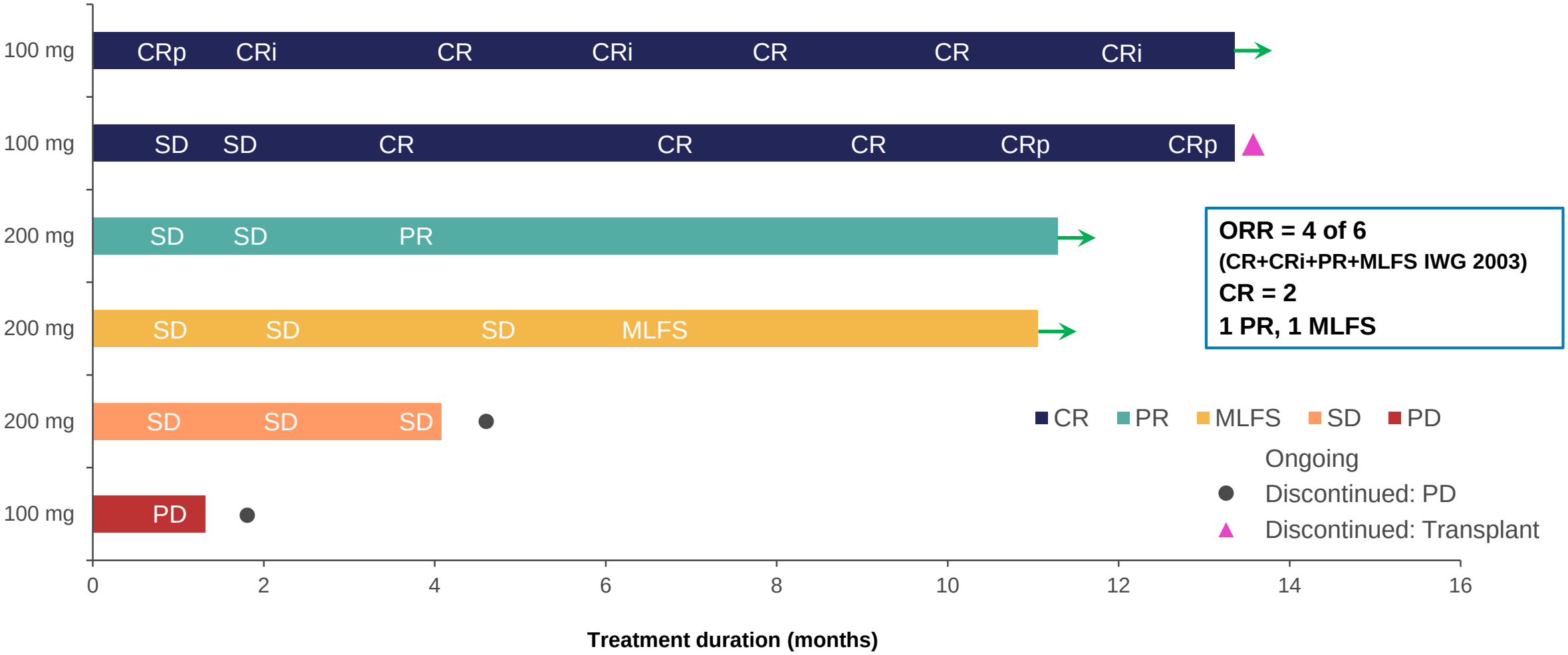
CR=complete response; CRi=CR with incomplete hematologic recovery; CRp=CR with incomplete platelet recovery; MLFS=morphologic leukemic-free state for patients with AML; PR=partial response; Persistent Disease = Stable Disease + Disease Progression ; NE=not evaluable

Ivosidenib + Aza: Treatment Duration, Response and Disposition



One additional patient was enrolled but did not have response data available at data cutoff
Data cutoff: Sep 1, 2017
CR = morphologic complete remission; CRi = morphologic complete remission with incomplete neutrophil recovery; CRp = morphologic complete remission with incomplete platelet recovery; PR = partial remission; MLFS = morphologic leukemia-free state; SD = stable disease; PD = progressive disease; MR = morphologic relapse after CR/CRi/CRp; NE = not evaluable

Enasidenib + Aza: Treatment Duration, Response and Disposition



Data cutoff: Sep 1, 2017

CR, complete remission; CRi, CR with incomplete hematologic recovery; CRp, CR with incomplete platelet recovery; MLFS, morphologic leukemia-free state; PD, progressive disease; PR, partial remission; SD, stable disease

AG-221-AML-005 Study: Case Presentation

- 77-year-old female with atrial fibrillation / atrial flutter and pulmonary emboli at diagnosis
  - WBC 16K, Hgb 8.4 g/dl, platelets 186K, 14% peripheral blasts
- July 2016 BM Biopsy:
  - Hypercellular with MDS-related changes and 27% blasts
  - Cytogenetics with t(7;11)(p15;p15); *IDH2*-R140Q, *NRAS* G12D, *DNMT3A* N797I, and *FLT3*-ITD 0.016
- Enasidenib 100 mg/ day - Cycle 1 - Day 28 marrow:
  - Hypercellular marrow with 2% blasts
  - Persistent cytogenetics; *IDH2*, *NRAS*, *DNMT3A* and *FLT3*-ITD abnormalities detected
- Cycle 2 - Day 28 marrow:
  - Normocellular, diploid, only *DNMT3A* and *IDH2* remain. Flow with 2% blasts
- Cycle 4 - Day 28 marrow:
  - *IDH2* no longer detected. MRD negative by flow cytometry
- After Cycle 8:
  - AZA dose reduced by 50% for progressive cytopenias
- **Cycle 11:**
  - **Ongoing CR; MRD-negative by cytogenetics, molecular analysis, and flow cytometry**

Key Takeaways – Phase 1 Frontline Combination Data

First Ivosidenib & Enasidenib Frontline AML Combination Data

- IDH inhibitors + standard of care frontline therapies well-tolerated in patients with newly diagnosed AML
- Preliminary clinical activity encouraging
- Data support ongoing and planned Phase 3 trials in newly diagnosed AML patients
  - Phase 3 AGILE study of ivosidenib + VIDAZA® enrolling
  - Phase 3 with ivosidenib or enasidenib plus 7+3 intensive chemo planned for 2018

Q&A

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