abbvie

Request for Administration of VENCLEXTA® (venetoclax tablets) Be Added to ICD-10 Procedure Coding System (ICD-10-PCS)

ICD-10 Coordination and
Maintenance Committee Meeting

AbbVie

March 5, 2019

VENCLEXTA Overview

- VENCLEXTA is an oral BCL-2 inhibitor that targets the BCL-2 protein in order to help restore the process of apoptosis in cancer cells
- VENCLEXTA is jointly commercialized by AbbVie and Genentech, a member of the Roche Group, in the United States
- VENCLEXTA is indicated in combination with azacitidine, or decitabine, or low-dose cytarabine for the treatment of newly-diagnosed acute myeloid leukemia (AML) in adults who are age 75 or older, **or** who have comorbidities that preclude use of intensive induction chemotherapy
- On November 21st, FDA granted accelerated approval for VENCLEXTA for the treatment of AML

Request for Unique Code Identifying VENCLEXTA Be Included in ICD-10-PCS

FDA Approval	On November 21st, FDA granted accelerated approval for VENCLEXTA for the treatment of AML
Issue	Current ICD-10-PCS codes do not describe the administration of venetoclax tablets, otherwise known as VENCLEXTA

Acute Myeloid Leukemia

- Acute illness
- People frequently hospitalized quickly at diagnosis
- Current treatments for patients who can't receive intensive chemotherapy take a median of 3-4 or more months to achieve response

AML is a Rare and Life-Threatening form of Cancer

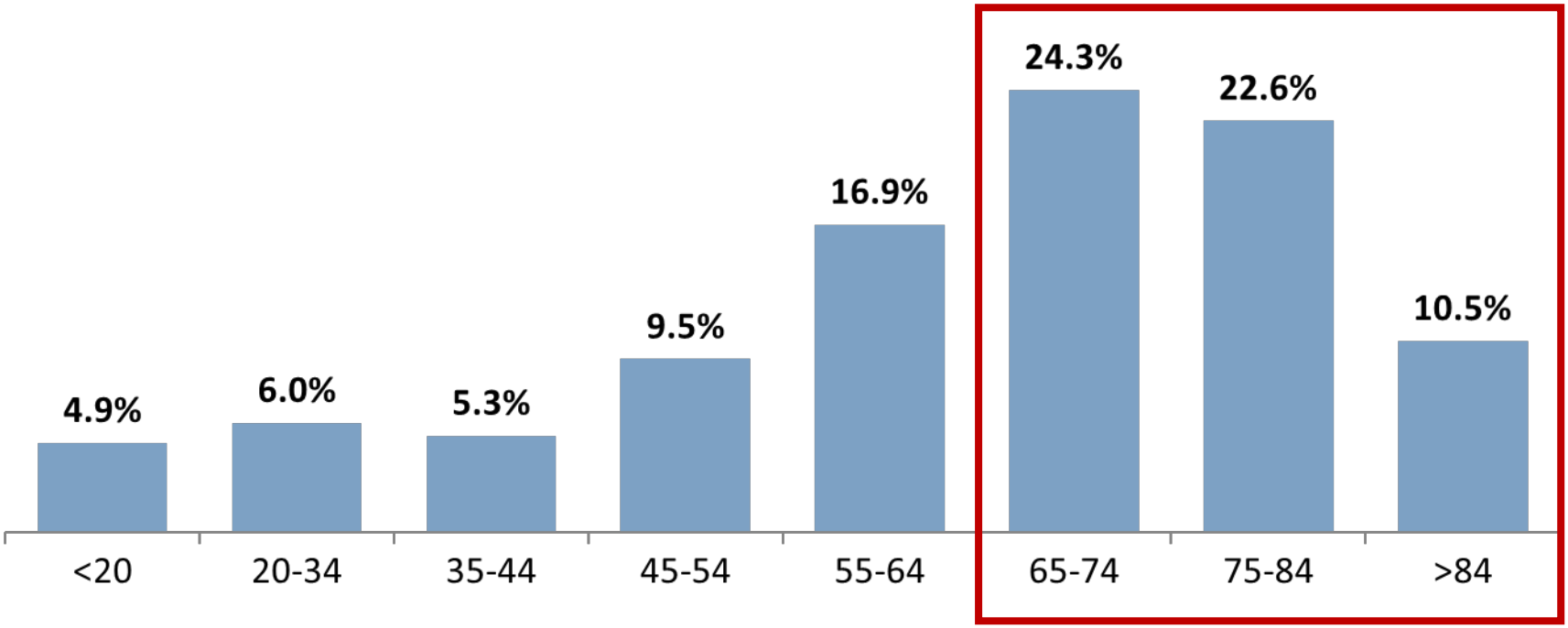
Incidence[1]	• Est. 19,520 new cases of AML in United States in 2018 • New AML cases per year: 4.3 in 100,000 • Median age at diagnosis: 68
Treatment[2]	• 66% receive intensive chemotherapy – Preferably followed by Allo SCT, if possible[3] • 12% receive non-intensive chemotherapy • 21% receive supportive care only
Mortality[1]	• Est. 10,670 deaths in the United States in 2018[1]

Allo SCT= Allogeneic Stem Cell Transplant. AML=Acute Myeloid Leukemia.

1. NCI. Cancer Stat Facts: Acute Myeloid Leukemia (AML). https://seer.cancer.gov/statfacts/html/amyl.html. Accessed July 2018. 2. Finn L, et al. Cancer Epidemiol. 2015;39(6):1084-1092. 3. Larson RA. Post-remission therapy for acute myeloid leukemia in younger adults. Wolters Kluwer Health. https://www.uptodate.com/contents/post-remission-therapy-for-acute-myeloid-leukemia-in-younger-adults. Accessed November 2, 2018.

AML Is Generally a Disease of Older People and Is Burdensome to the Medicare Population[1,2]

Percent of new AML cases by age group[1]

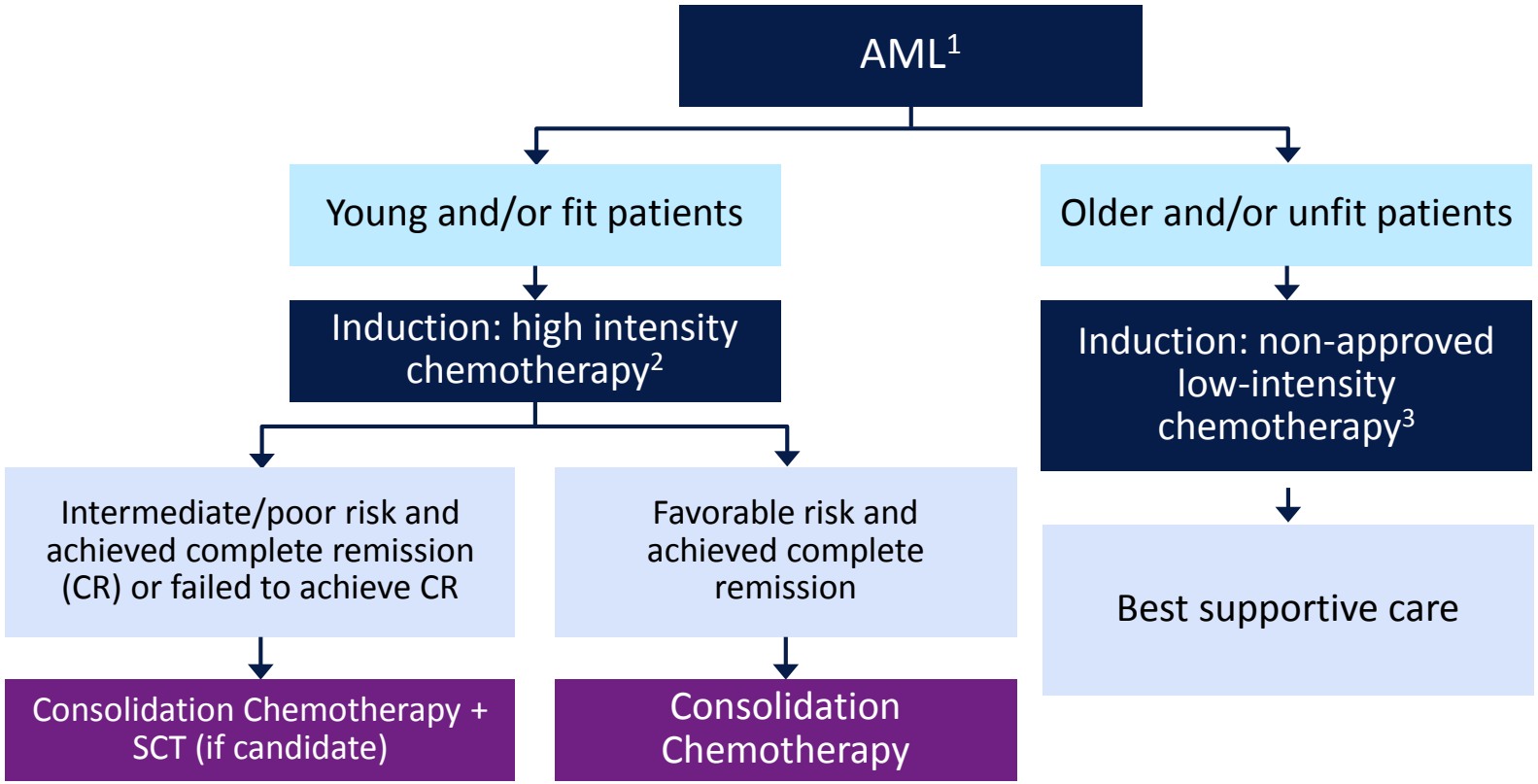


AML is the most common acute leukemia affecting adults and represents 1.1% of all new cancer cases in the United States[1]

AML=Acute Myeloid Leukemia

1. NCI. Cancer Stat Facts: Acute Myeloid Leukemia (AML). https://seer.cancer.gov/statfacts/html/amyl.html. Accessed February 5, 2019. 2. Meyers J et al. RTI Health Solutions. 2012; 15(4):A214.

Before Venetoclax, Highly Effective Therapy Was Only Available to Very Fit and Younger Patients



AML=Acute Myeloid Leukemia; CR=Complete Response; SCT=Stem Cell Transplant

1. Kolitz,JE. Overview of acute myeloid leukemia in adults. Wolters Kluwer Health. https://www.uptodate.com/contents/overview-of-acute-myeloid-leukemia-in-adults. Updated September 19, 2017. Accessed February 5, 2019. 2. Larson RA. Induction therapy for acute myeloid leukemia in younger adults. Wolters Kluwer Health. https://www.uptodate.com/contents/induction-therapy-for-acute-myeloid-leukemia-in-younger-adults. Updated September 7, 2017. Accessed February 5, 2019. 3. Larson RA. Acute myeloid leukemia: treatment and outcomes in older adults. Wolters Kluwer Health. https://www.uptodate.com/contents/acute-myeloid-leukemia-treatment-and-outcomes-in-older-adults. Updated January 9, 2019. Accessed February 5, 2019.

Older Patients Are Generally Ineligible for Intensive Chemotherapy, and, Prior to the Approval of Venetoclax, Outcomes Were Very Poor[1-5]

Eligible for Intensive Chemotherapy

- Younger patients
- Fewer co-morbidities

Intensive Chemotherapy

- Standard of care is "7+3"[1]
  - 7-day infusion of cytarabine
  - 3-day infusion of an anthracycline
- More recent option is VYXEOS™[2]
  - Liposomal combination of cytarabine and daunorubicin
- Subsequent post-remission therapies can be curative[3]

Complete Remission Rates: 70-80%[1]

Ineligible for Intensive Chemotherapy

- Older patients
- More co-morbidities

Lower Intensity Treatments

- Decitabine
  - CR+CRi rate: 26%[4]
- Azacitidine
  - CR+CRi rate: 18%[5]
- Low-dose cytarabine
  - CR+CRi rate: 11%[4]
- Best supportive care
  - Transfusions, antibiotics, etc.
  - CR rate: 0%

Outcomes for This Predominantly Medicare-aged Patient Population Are Very Poor

We believe VENCLEXTA will be the new standard of care for patients who are not eligible for intensive chemotherapy

CR=Complete Remission; CRi=Complete Remission with Incomplete Hematologic Recovery

1. Larson RA. Induction therapy for acute myeloid leukemia in younger adults. Wolters Kluwer Health. https://www.uptodate.com/contents/induction-therapy-for-acute-myeloid-leukemia-in-younger-adults. Accessed February 5, 2019. 2. Jazz Pharmaceuticals. VYXEOS™ Prescribing Information. http://pp.jazzpharma.com/pi/vyxeos.en.USPI.pdf. Accessed February 5, 2019. 3. Larson RA. Post-remission therapy for acute myeloid leukemia in younger adults. Wolters Kluwer Health. https://www.uptodate.com/contents/post-remission-therapy-for-acute-myeloid-leukemia-in-younger-adults. Accessed November 2, 2018. 4. Kantarjian HM et al. J Clin Oncol. 2012;30(21):2670-2677. 5. Al-Ali HK et al. Journal of Geriatric Oncology. 2014;5(1):89-105.

VENCLEXTA Received Two Breakthrough Therapy Designations in AML from the Food and Drug Administration[1-3]

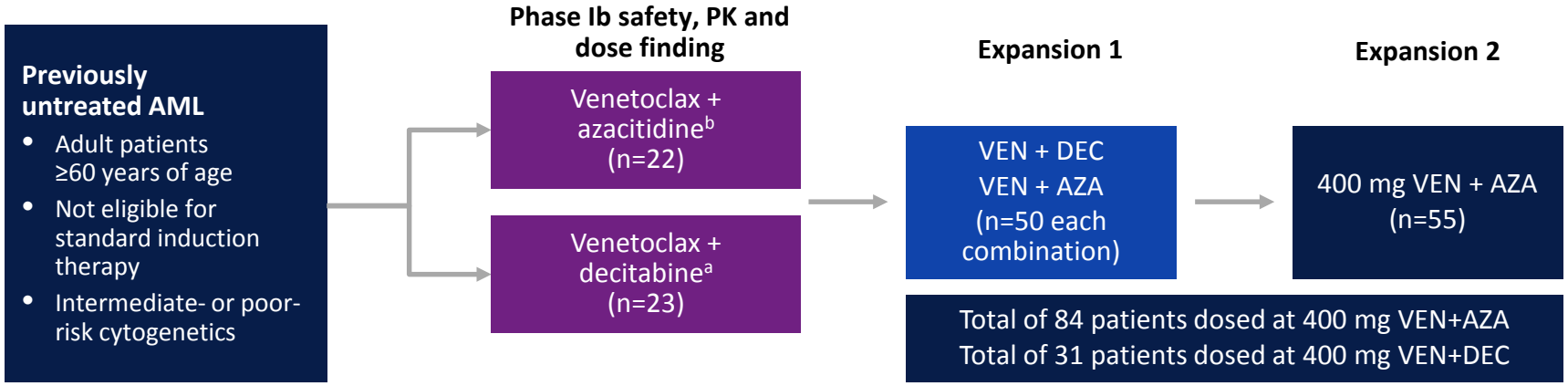
A breakthrough therapy[1] is granted to a drug:

- Intended alone or in combination with one or more other drugs to treat a serious or life threatening disease or condition; and
- Clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development

VENCLEXTA + Azacitidine or Decitabine	VENCLEXTA + Low-dose cytarabine
Breakthrough Therapy Designation Awarded in January 2016[2]	Breakthrough Therapy Designation Awarded in July 2017[3]

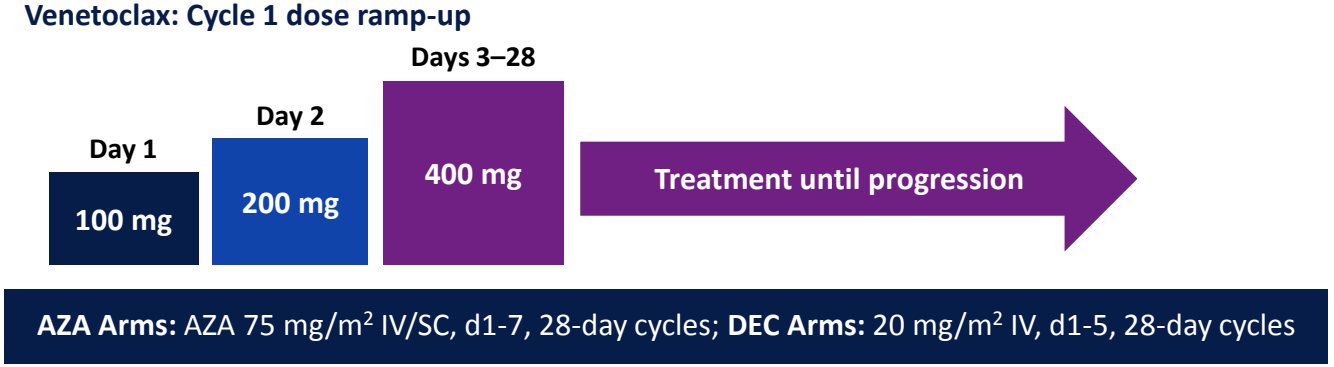
1. Breakthrough Therapy. US FDA. https://www.fda.gov/forpatients/approvals/fast/ucm405397.htm. Accessed September 14, 2018. 2. Abbvie. Venetoclax Receives 3rd Breakthrough Therapy Designation from the FDA for the Combination Treatment of Patients with Untreated Acute Myeloid Leukemia not Eligible for Standard Induction Chemotherapy. https://news.abbvie.com/news/venetoclax-receives-3rd-breakthrough-therapy-designation-from-fda-for-combination-treatment-patients-with-untreated-acute-myeloid-leukemia-not-eligible-for-standard-induction-chemotherapy.htm. Published January 28, 2016. Accessed February 5, 2019. 3. Roche. Investor Update: FDA grants breakthrough therapy designation for Venclexta in acute myeloid leukemia. https://www.roche.com/investors/updates/inv-update-2017-07-28.htm. Published July 28, 2017. Accessed February 5, 2019.

M14-358: Phase Ib Trial Studied Venetoclax + Decitabine or Azacitidine in 1L AML



Study endpoints:

- Primary (dose escalation): Safety, PK, dose-finding
- Primary (expansion): CR, CRh, CRi, OS
- Secondary (expansion): DOR, EFS
- Exploratory: Transfusion Independence, MRD, Safety (Infection/hemorrhage), Hospitalization

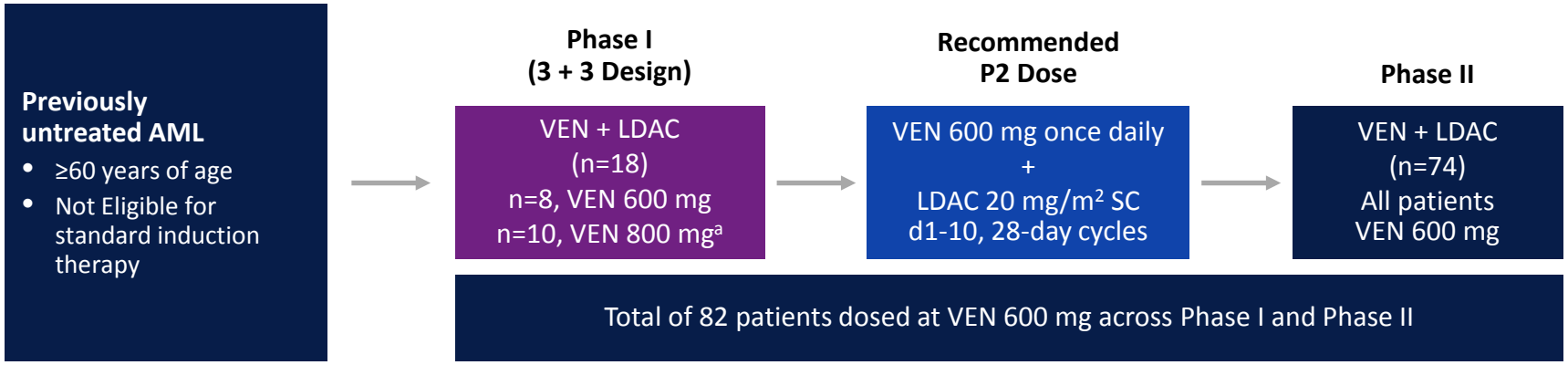


[a]20 mg/m² IV, d1-5, 28-day cycles; [b]75 mg/m² IV/SC, d1-7, 28-day cycles

1L=First Line; VEN=Venetoclax; DEC=Decitabine; AZA=azacitidine; PK=Pharmacokinetics; CR=Complete Response; CRh=Partial Recovery of Blood Cells; CRi=Complete Response with Incomplete Bone Marrow Recovery; OS=Overall Survival; DOR=Duration of Response; EFS=Event-free Survival; MRD=Minimal Residual Disease

Pollyea DA et al. Venetoclax in Combination with Hypomethylating Agents Induces Rapid, Deep, and Durable Responses in Patients with AML Ineligible for Intensive Therapy. In: American Society of Hematology (ASH) – 60th Annual Meeting; December 1-4, 2018; San Diego, CA, USA.

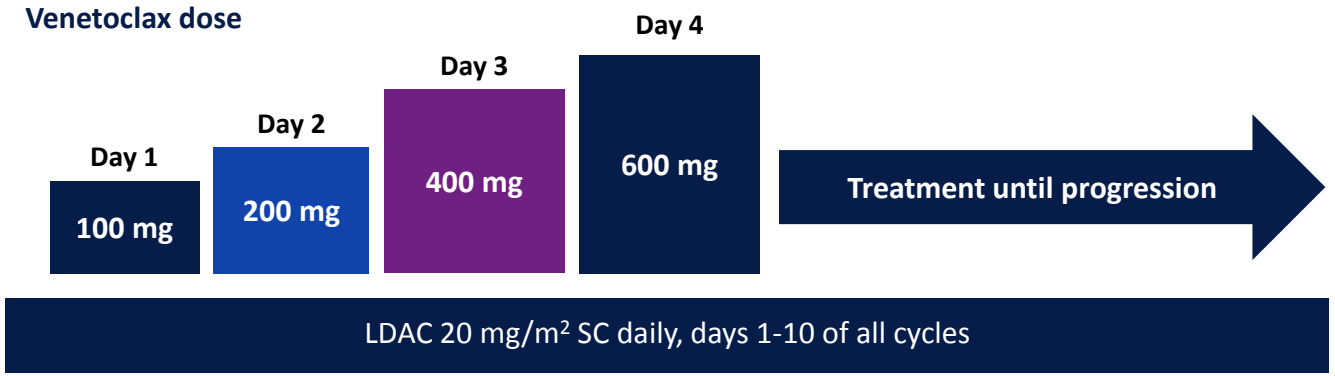
M14-387: Phase I/II Trial Studied Combination of Venetoclax + Low-Dose Cytarabine in 1L AML



Study endpoints:

Primary: safety, PK, MTD, ORR, TTP, and RP2D

Secondary: response rates (including CR, CRi, CRh, PR, and MLFS), DOR, OS



[a]Two patients had dose-limiting toxicity of thrombocytopenia at 800-mg dose

1L=First Line; VEN=Venetoclax; LDAC=Low-dose Cytarabine; PK=Pharmacokinetics; MTD=Maximum Tolerated Dose; ORR=Overall Response Rate; TTP=Time To Progression; RP2D=Recommended Phase II Dose; CR=Complete Response; CRi=Complete Response with Incomplete Bone Marrow Recovery; CRh=Partial Recovery of Blood Cells; PR=Partial Response; MLFS=Morphological Leukaemia-free State; DOR=Duration of Response; OS=Overall Survival

Wei, AH et al. Venetoclax with low-dose cytarabine induces rapid, deep, and durable responses in previously untreated older adults with AML ineligible for intensive chemotherapy. In: American Society of Hematology (ASH) – 60th Annual Meeting; December 1-4, 2018; San Diego, CA, USA.

With VENCLEXTA, Rates of Complete Remission Are Better than Historical Control Data with HMAs or LDAC Alone*,**,1-4

Efficacy Endpoints	Venetoclax + HMAs		Venetoclax + LDAC
	Venetoclax 400 mg + azacitidine, N=84*	Venetoclax 400 mg + decitabine, N=31*	Venetoclax 600 mg + LDAC, N=82*
CR + CRi	**71%**	**74%**	**54%**
CR	44%	55%	26%

	Azacitidine	Decitabine	LDAC
CR + CRi	**28%[3]**	**26%[4]**	**11%[4]**

***The data referenced in this slide is updated data from August 31, 2018 including the entire study populations treated with the labeled doses of venetoclax (400 mg venetoclax with azacitidine and decitabine and 600 mg venetoclax with LDAC). Results are compiled from separate trials and are not meant to draw comparative conclusions across treatment regimens.**

**Study numbers include patients that were classified as ≥75 years of age, or had comorbidities that precluded the use of intensive induction chemotherapy based on at least one of the following criteria: baseline Eastern Cooperative Oncology Group (ECOG) performance status of 2-3, severe cardiac or pulmonary comorbidity, moderate hepatic impairment, or CLcr ≥30 to <45 mL/min or other comorbidity.

HMAs=Hypomethylating Agents; LDAC=Low-dose Cytarabine; CR=Complete Response; CRh=Partial Recovery of Blood Cells; CRi=Complete Response with Incomplete Bone Marrow Recovery

1. Pollyea DA et al. Venetoclax in Combination with Hypomethylating Agents Induces Rapid, Deep, and Durable Responses in Patients with AML Ineligible for Intensive Therapy. In: American Society of Hematology (ASH) – 60th Annual Meeting; December 1-4, 2018; San Diego, CA, USA. 2. Wei, AH et al. Venetoclax with low-dose cytarabine induces rapid, deep, and durable responses in previously untreated older adults with AML ineligible for intensive chemotherapy. In: American Society of Hematology (ASH) – 60th Annual Meeting; December 1-4, 2018; San Diego, CA, USA. 3. Dombret, H., et al. Blood. 2015;126(3):291-299. 4. Kantarjian HM et al. J Clin Oncol. 2012;30(21):2670-2677.

With VENCLEXTA, Rates of Complete Remission Are Better than Historical Control Data with HMAs or LDAC Alone*,[1]

Efficacy Endpoints	Venetoclax + HMAs		Venetoclax + LDAC
	Venetoclax 400 mg + azacitidine, N=67*	Venetoclax 400 mg + decitabine, N=13*	Venetoclax 600 mg + LDAC, N=61*
CR + CRh	**61%**	**62%**	**43%**
CR	37%	54%	21%
CRh	24%	8%	21%

*Study numbers include patients that were classified as ≥75 years of age, or had comorbidities that precluded the use of intensive induction chemotherapy based on at least one of the following criteria: baseline Eastern Cooperative Oncology Group (ECOG) performance status of 2-3, severe cardiac or pulmonary comorbidity, moderate hepatic impairment, or CLcr ≥30 to <45 mL/min or other comorbidity.

HMAs=Hypomethylating Agents; LDAC=Low-dose Cytarabine; CR=Complete Response; CRh=Partial Recovery of Blood Cells

1. AbbVie, Inc. VENCLEXTA Prescribing Information. https://www.rxabbvie.com/pdf/venclexta.pdf. Accessed February 5, 2019.

Venetoclax + HMA/LDAC Has a Tolerable Safety Profile Consistent with Known Adverse Events[1]

Safety: Grade ≥3 (%) subjects	Venetoclax + HMAs Venetoclax 400 mg + azacitidine N=67	Venetoclax + HMAs Venetoclax 400 mg + decitabine N=13	Venetoclax + LDAC Venetoclax 600 mg + LDAC N=61
Anemia	30	15	26
Febrile neutropenia	36	69	44
Neutropenia	49	38	46
Pneumonia	25	31	16
Thrombocytopenia	45	54	59

3% (2/61) patients reported laboratory results consistent with TLS on VEN+LDAC (Lab TLS)
No patients experienced Clinical TLS in these studies

HMAs=Hypomethylating Agents; LDAC=Low-dose cytarabine; VEN=Venetoclax; TLS=Tumor Lysis Syndrome

1. AbbVie, Inc. VENCLEXTA Prescribing Information. https://www.rxabbvie.com/pdf/venclexta.pdf. Accessed February 5, 2019.

A Unique Code for VENCLEXTA Should Be Included in ICD-10-PCS

VENCLEXTA addresses an unmet need for patients with AML who are ineligible for intensive chemotherapy

On November 21st, FDA granted accelerated approval for VENCLEXTA for AML

Current codes do not describe VENCLEXTA administration

Inclusion of unique codes will assist in treatment, billing, and reporting purposes

Unique codes accurately identifying VENCLEXTA in the ICD-10-PCS will facilitate claims for providers