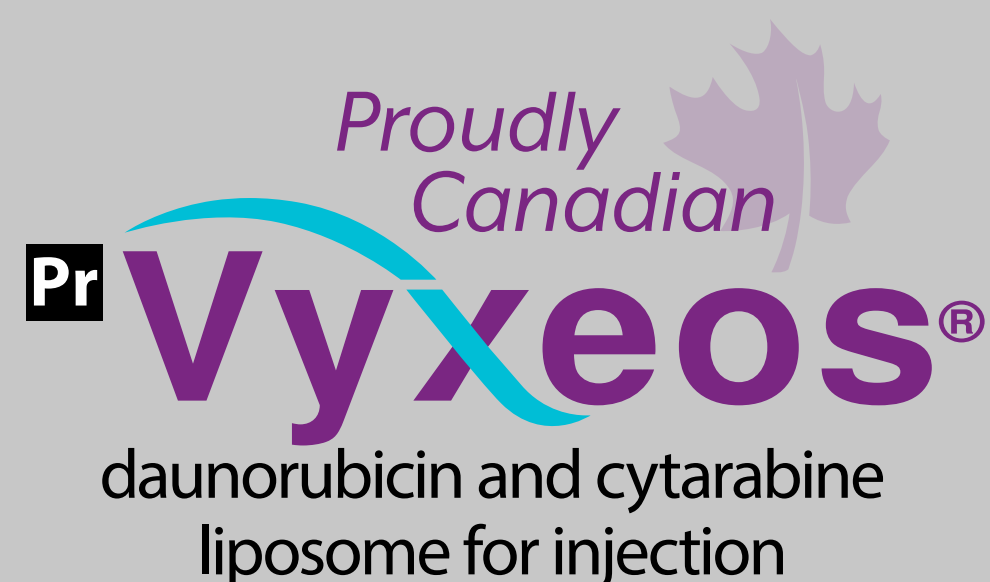
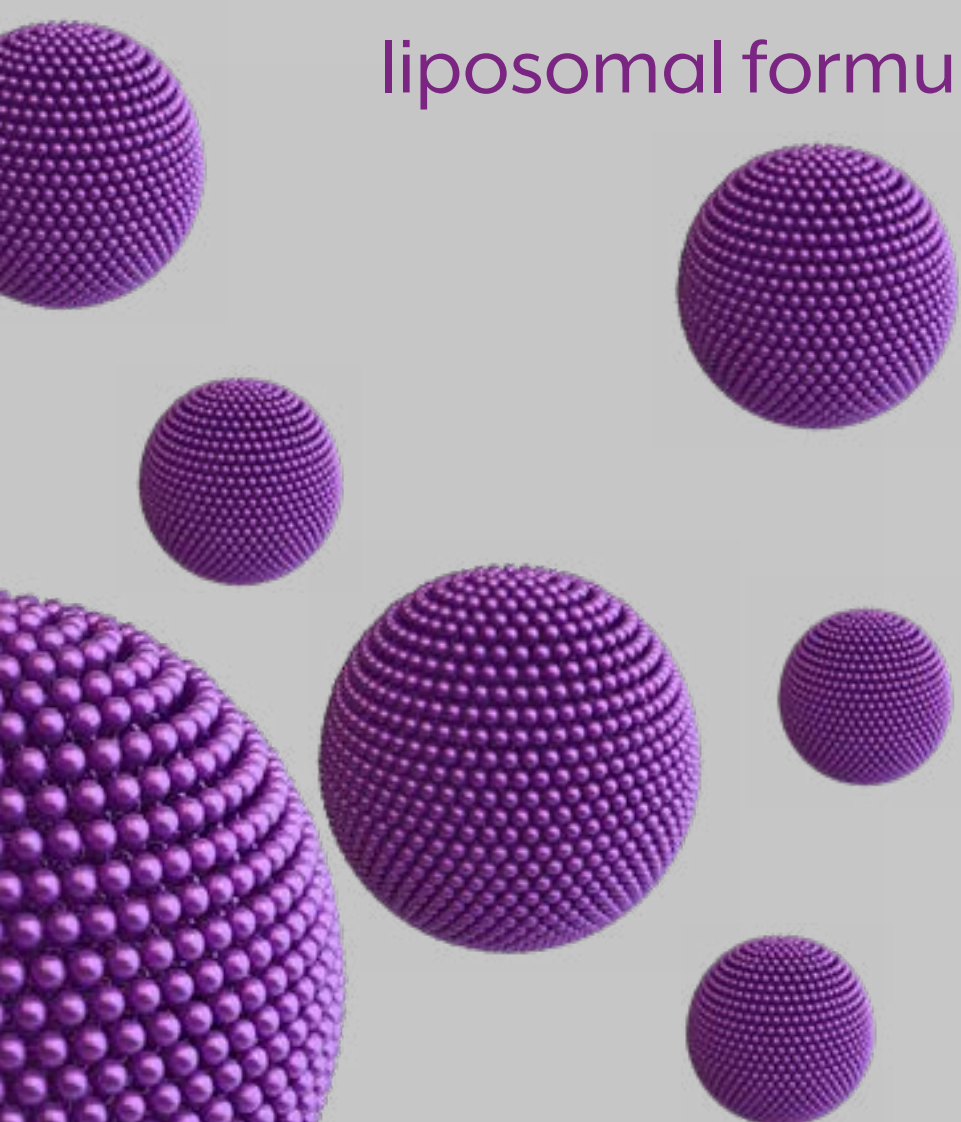




# GREATER THAN THE SUM OF ITS PARTS<sup>1,2</sup>

## TOGETHER

The first dual-drug advanced liposomal formulation<sup>1</sup>



## LONGER

Superior overall survival in patients with high-risk AML<sup>2\*</sup>

Median overall survival:  
9.6 months with VYXEOS vs 6 months  
with conventional chemotherapy<sup>†</sup>

(HR: 0.69, 95% CI: 0.52–0.90,  
 $p = 0.005$  (2-sided))

Events reported in  
104/153 patients with  
VYXEOS vs 132/156)<sup>‡</sup>

PrVYXEOS® (daunorubicin and cytarabine liposome for injection) is indicated for the treatment of adults with newly diagnosed therapy-related acute myeloid leukemia (t-AML) or AML with myelodysplasia-related changes (AML-MRC).<sup>3</sup>

\* High-risk AML defined as t-AML or AML-MRC.

† Conventional chemotherapy includes the 7+3/5+2 regimen for induction and consolidation, using cytarabine and daunorubicin.<sup>2</sup>

‡ Number of deaths reported from the Intent-to-treat (ITT) population with VYXEOS (n = 153) vs the conventional chemotherapy arm (n = 156) from the phase 3, randomized, multicentre, open-label study which evaluated the efficacy and safety of VYXEOS in adults with newly diagnosed high-risk sAML.<sup>2,3</sup>

1. Tolcher AW, Mayer LD. Improving combination cancer therapy: the CombiPlex® development platform. *Future Oncol* 2018;14:1317–1332.  
2. Lancet JE, Uy GL, Cortes JE, *et al.* CPX-351 (cytarabine and daunorubicin) liposome for injection versus conventional cytarabine plus daunorubicin in older patients with newly diagnosed secondary acute myeloid leukemia. *J Clin Oncol* 2018;36:2684–2692.  
3. Current VYXEOS® Product Monograph, Jazz Pharmaceuticals Canada, Inc.

## AML TREATMENT OVERVIEW

COMBINATION CHEMOTHERAPY HAS BEEN USED AS INTENSIVE THERAPY FOR HIGH-RISK AML IN ADULTS FOR DECADES<sup>1,2\*</sup>

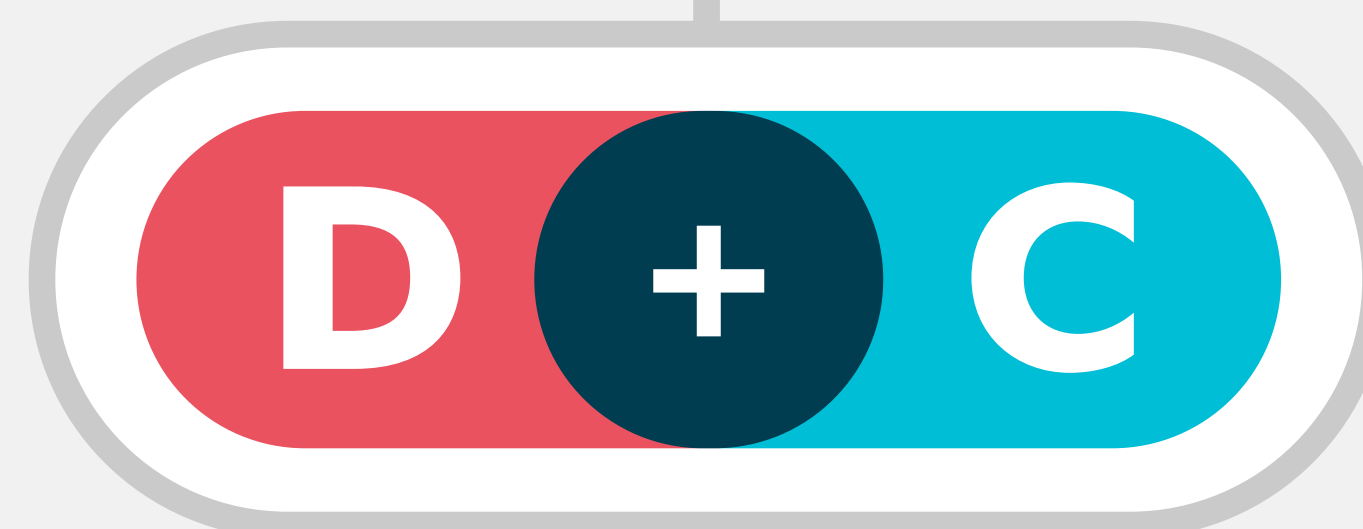
D

Daunorubicin and cytarabine

C

were originally administered individually, with comparable response rates

Combining daunorubicin (D) and cytarabine (C) was a rational approach due to their mechanisms of action<sup>1</sup>



The combination resulted in increased response rates with little increase in toxicity<sup>2</sup>

**HOWEVER, FOR OLDER PATIENTS AND THOSE WITH sAML<sup>3†</sup> CONVENTIONAL CHEMOTHERAPY\* IS ASSOCIATED WITH LOWER REMISSION RATES, EARLY MORTALITY AND HIGHER RELAPSE THAN IN YOUNG PATIENTS AND IN DE NOVO AML**

**In the early 2000s,**

VYXEOS began development in Canada – a liposomal formulation designed to optimize the synergistic ratio of daunorubicin and cytarabine<sup>1</sup>

**VYXEOS OFFERS AN INTENSIVE TREATMENT TO HIGH-RISK ADULT PATIENTS WITH sAML WHO, UP UNTIL NOW, HAD FEW OPTIONS AVAILABLE TO THEM<sup>4\*‡</sup>**

sAML: Secondary AML

\* High-risk AML defined as t-AML or AML-MRC.

† Conventional chemotherapy includes the 7+3/5+2 regimen for induction and consolidation, using cytarabine and daunorubicin.<sup>3</sup>‡ sAML defined as AML occurring after therapy and/or an antecedent myeloid disease, e.g., MDS or MPN, excluding chronic myeloid leukemia, regardless of prior cytotoxic therapy for these disorders. This includes the sub-types, t-AML, AML-MRC and CMMoL AML.<sup>5,6</sup>1. Tolcher AW, Mayer LD. Improving combination cancer therapy: the CombiPlex® development platform. *Future Oncol* 2018;14:1317–1332.2. Tardi P, Johnstone S, Harasym N, *et al.* In vivo maintenance of synergistic cytarabine:daunorubicin ratios greatly enhances therapeutic efficacy. *Leuk Res* 2009;33:129–139.3. Lancet JE, Uy GL, Cortes JE, *et al.* CPX-351 (cytarabine and daunorubicin) liposome for injection versus conventional cytarabine plus daunorubicin in older patients with newly diagnosed secondary acute myeloid leukemia. *J Clin Oncol* 2018;36:2684–2692.4. Talati C, Lancet JE. CPX-351: changing the landscape of treatment for patients with secondary acute myeloid leukemia. *Future Oncol* 2018;14:1147–1154.5. Granfeldt Østgård LS, Medeiros BC, Sengeløv H, *et al.* Epidemiology and clinical significance of secondary and therapy-related acute myeloid leukemia: A national population-based cohort study. *J Clin Oncol* 2015;33:3641–3649.

6. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Acute Myeloid Leukemia V.2.2021. © National Comprehensive Cancer Network, Inc. 2021. All rights reserved. Accessed January 2021. To view the most recent and complete version of the guideline, go online to NCCN.org.

**Pr Vyxeos®**  
daunorubicin and cytarabine  
liposome for injection

# VYXEOS DESIGNED FOR OPTIMAL SYNERGISTIC ACTIVITY<sup>1</sup>

A synergistic ratio of daunorubicin and cytarabine for anti-leukemia activity, as shown *in vitro*<sup>1</sup>

1:5

An advanced liposome to maintain 1:5 *in vivo*<sup>2\*</sup>

**SYNERGY.**  
GREATER THAN



Click to access the Tolcher, *et al.* publication to learn more

\* 1:5 ratio is 1 part daunorubicin to 5 parts cytarabine.

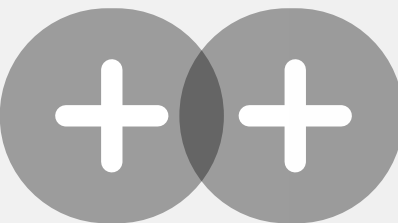
1. Tolcher AW, Mayer LD. Improving combination cancer therapy: the CombiPlex® development platform. *Future Oncol* 2018;14:1317–1332.
2. Dicko A, Mayer LD, Tardi PG. Use of nanoscale delivery systems to maintain synergistic drug ratios *in vivo*. *Expert Opin Drug Deliv* 2010;7:1329–1341.

PREV 1 2 3 4 5 NEXT

**Pr Vyxeos®**  
daunorubicin and cytarabine  
liposome for injection

# THE FIRST DUAL-DRUG ADVANCED LIPOSOMAL FORMULATION<sup>1</sup>

Optimizing the delivery of  
daunorubicin and cytarabine<sup>2</sup>



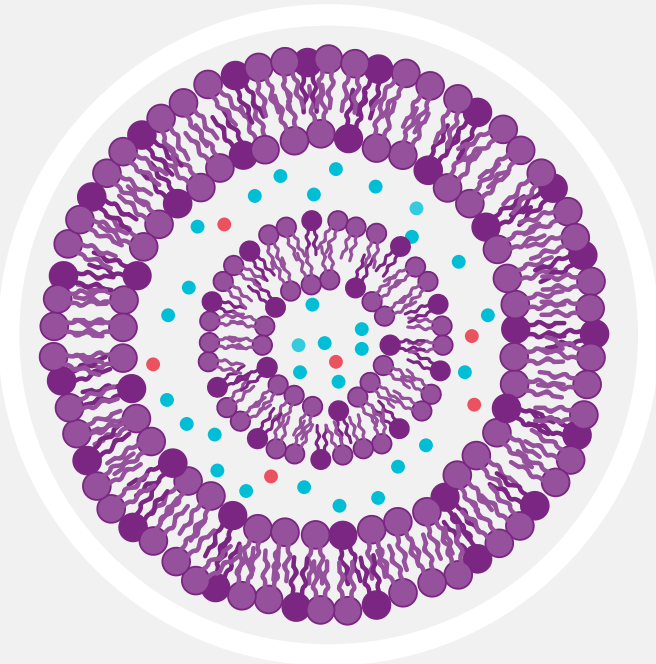
## SYNERGISTIC RATIO

Fixed 1:5 molar ratio  
of daunorubicin and  
cytarabine within an  
advanced liposomal  
formulation<sup>3</sup>



## PROLONGED

Synergistic molar ratio maintained for a  
prolonged period of time – over 24 hours  
after administration<sup>1,3</sup>



- Advanced liposomal formulation<sup>‡</sup>
- Daunorubicin
- Cytarabine

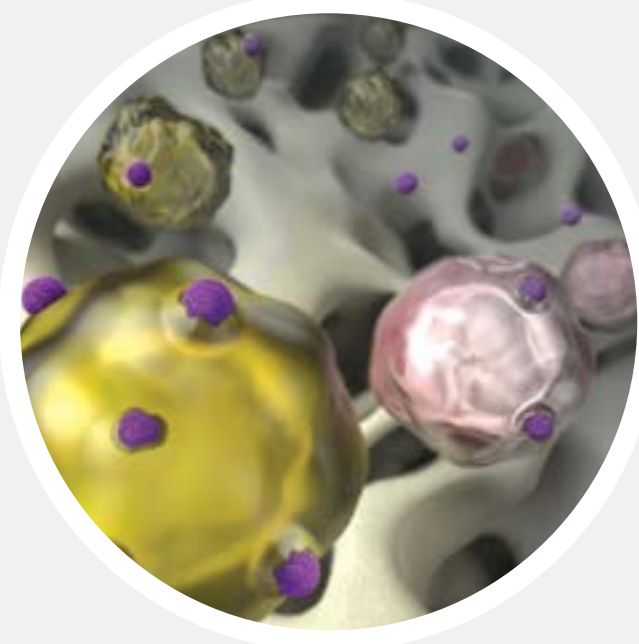
## HIGH CONCENTRATION

VYXEOS accumulates and persists  
in the bone marrow in high  
concentrations<sup>3\*</sup>



## PREFERENTIAL UPTAKE

VYXEOS is preferentially taken up by  
leukemia cells vs normal bone marrow cells<sup>3†</sup>



Click to watch  
VYXEOS  
in action

Adapted from the VYXEOS Product Monograph.

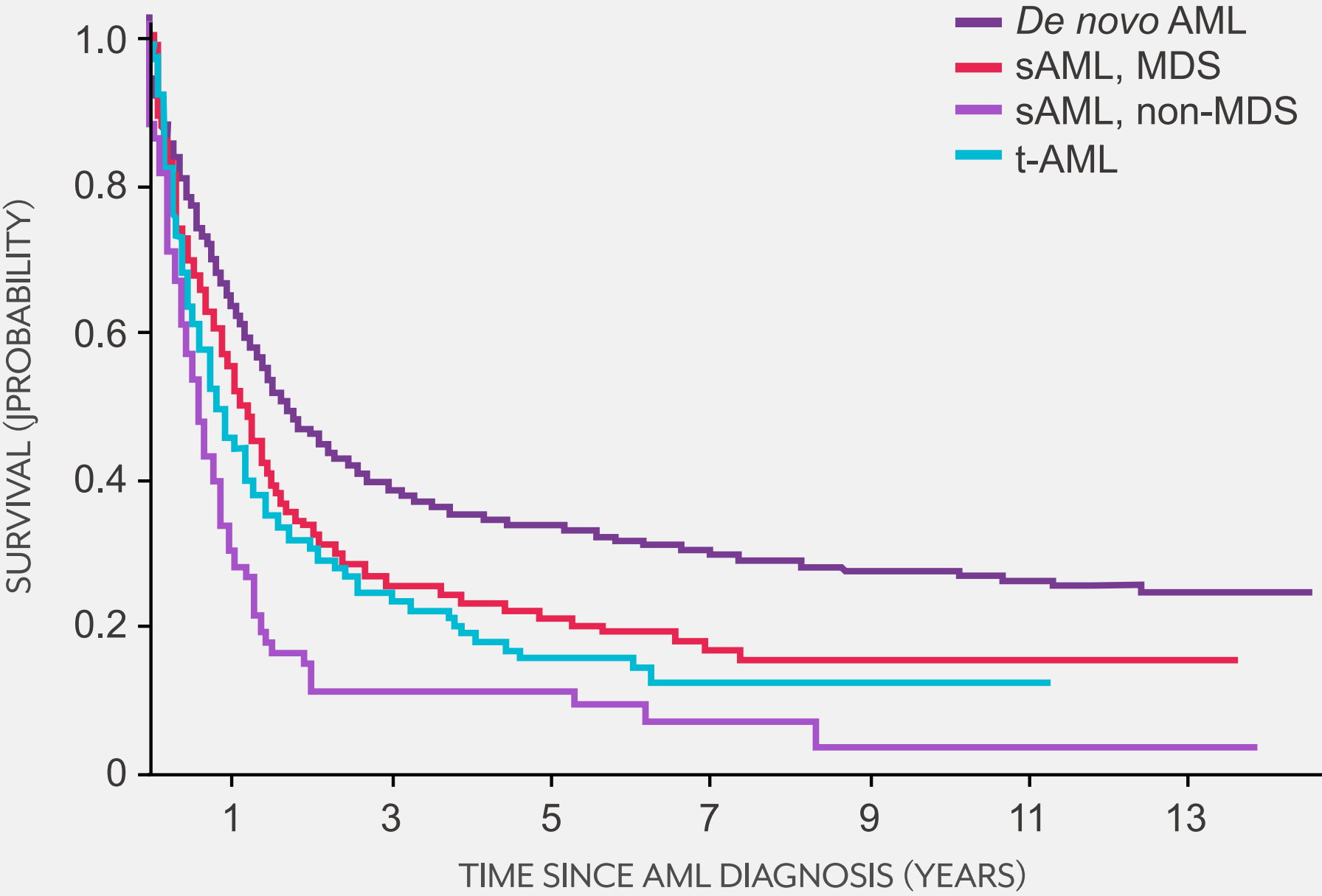
\* As shown in animal models.  
† As shown *in vitro*.  
‡ The advanced liposomal membrane is composed of distearoylphosphatidylcholine (DSPC), distearoylphosphatidylglycerol (DSPG) and cholesterol in a 7:2:1 ratio.<sup>3</sup>

1. Tolcher AW, Mayer LD. Improving combination cancer therapy: the CombiPlex<sup>®</sup> development platform. *Future Oncol* 2018;14:1317–1332.  
2. Lancet JE, Uy GL, Cortes JE, *et al*. CPX-351 (cytarabine and daunorubicin) liposome for injection versus conventional cytarabine plus daunorubicin in older patients with newly diagnosed secondary acute myeloid leukemia. *J Clin Oncol* 2018;36:2684–2692.  
3. Current VYXEOS<sup>®</sup> Product Monograph, Jazz Pharmaceuticals Canada, Inc.

# PATIENTS WITH SECONDARY AML HAVE POOR OUTCOMES

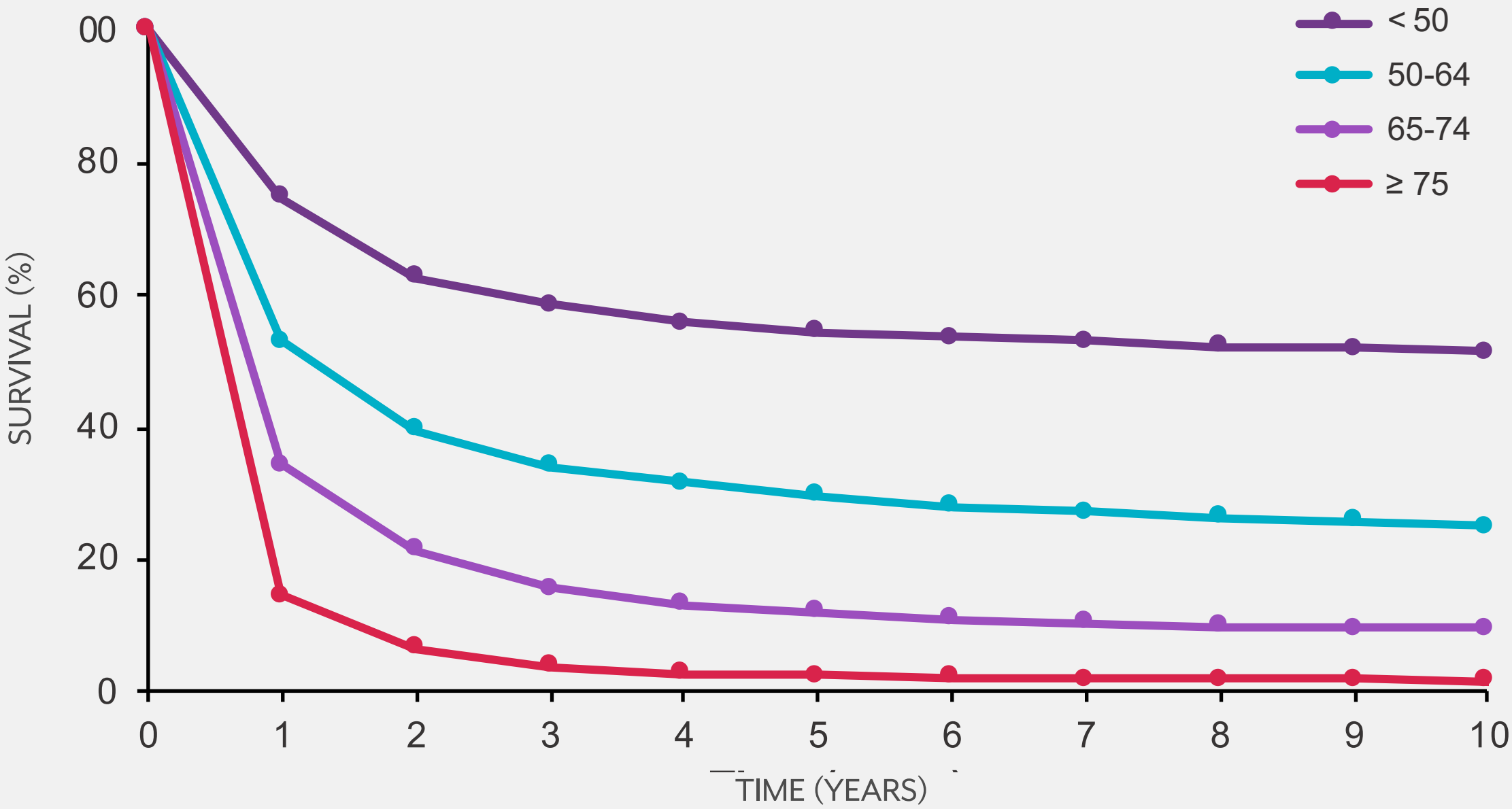
LOW SURVIVAL RATES ARE INDICATIVE OF AN UNMET TREATMENT NEED IN PATIENTS WITH SECONDARY AML

KAPLAN-MEIER CURVES OF SURVIVAL ACCORDING TO TYPE OF AML IN INTENSIVE THERAPY PATIENTS OVERALL<sup>1</sup>



Adapted from Granfeldt Østgård, *et al.*

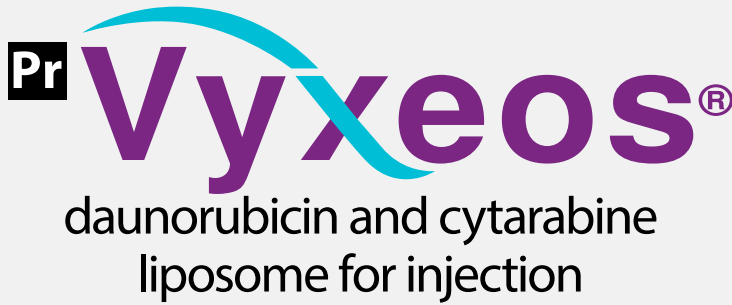
RELATIVE SURVIVAL STRATIFIED BY TIME AND AGE OF AML PATIENTS<sup>2</sup>



Adapted from National Cancer Institute (NCI) Surveillance, Epidemiology, and End Results Program (SEER) data from 2000–2016.

sAML: Secondary AML  
tAML: Therapy-related AML

1. Granfeldt Østgård LS, Medeiros BC, Sengeløv H, *et al.* Epidemiology and clinical significance of secondary and therapy-related acute myeloid leukemia: A national population-based cohort study. *J Clin Oncol* 2015;33:3641–3649.  
2. NCI. Surveillance Research Program. SEER Explorer. Available at: Accessed August 2023 at: <https://seer.cancer.gov/explorer>.



WHO 2016:

CLASSIFICATION OF HIGH-RISK AML SUBTYPES: t-AML AND AML-MRC

THERAPY-RELATED AML (t-AML)

According to WHO, t-AML is defined as previously untreated AML with a history of prior cytotoxic therapy<sup>1,2\*</sup>

Cytotoxic therapies associated with development of t-AML<sup>2</sup>:

1. Alkylating agents and radiation
2. Topoisomerase II inhibitors
3. Immunosuppressive therapies
- a. Latency period of 4–10 years
- a. Latency period of 2–3 years
- a. Latency period of 3–4 years

AML, WITH MYELOYDYSPLASIA-RELATED CHANGES (AML-MRC)

AML: ≥ 20% blasts in peripheral blood<sup>2</sup>

AML arising from a prior MDS or an MDS/MPN<sup>2</sup>

OR

AML with an MDS-related cytogenetic abnormality<sup>2</sup>

OR

AML with multilineage dysplasia<sup>2</sup>

Click for full details

A DIAGNOSIS OF AML-MRC MAY REQUIRE CYTOGENETIC TESTING OR A MORPHOLOGY EXAM FOR CONFIRMATION<sup>1</sup>



Meet Matthew



Meet Gordon



Meet Julia

MDS: Myelodysplastic syndrome  
MPN: Myeloproliferative neoplasm  
WHO: World Health Organization  
\* Antimetabolites, antimicrotubule agents, growth factors, and immunomodulators have also been implicated in t-AML.<sup>2</sup>

1. Arber DA, Orazi A, Hasserjian R, *et al.* The 2016 revision to the World Health Organization classification of myeloid neoplasms and acute leukemia. *Blood* 2016;127:2391– STRATIFIED 2405.  
2. Czader M, Orazi A. Therapy-related myeloid neoplasms. *Am J Clin Pathol* 2009;132(3):410–425.





# MATTHEW



## Matthew\*

Male, 72 years old  
Enjoys gardening and spending time  
with his grandchildren



## Symptoms

Presented via his GP:  
Fatigue, dyspnea and bone pain



## Clinical history

No prior hematologic disease or  
cytotoxic therapy



## Blood work

WBC:  $1.4 \times 10^9/L$   
Hgb: 97 g/L  
Platelets:  $34 \times 10^9/L$

**What tests would  
you order?**





# MATTHEW



## Matthew\*

Male, 72 years old  
Enjoys gardening and spending time  
with his grandchildren



## Symptoms

Presented via his GP:  
Fatigue, dyspnea and bone pain



## Clinical history

No prior hematologic disease or  
cytotoxic therapy



## Blood work

WBC:  $1.4 \times 10^9/L$   
Hgb: 97 g/L  
Platelets:  $34 \times 10^9/L$



## Morphology

Bone marrow: Myeloid blasts 22%



## Cytogenetics

Complex karyotype  
41, XY, del(5q), -8, -10, -12, -17, -21

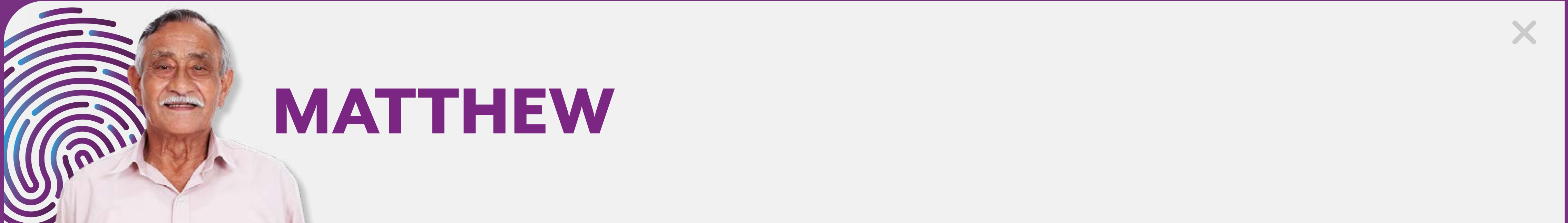


## Gene mutations

Wildtype: *NPM1*, *CEBPA*, *RUNX1*, *FLT3*, *TP53*, *ASXL1*,  
*IDH1/2*, *DDX41*, *BCOR*, *EZH2*, *SF3B1*, *SRSF2*, *ZRSR2*  
Mutation: *STAG2* and *U2AF1*

How would you  
classify this patient?





**Matthew\***  
Male, 72 years old  
Enjoys gardening and spending time with his grandchildren



**Symptoms**  
Presented via his GP:  
Fatigue, dyspnea and bone pain



**Clinical history**  
No prior hematologic disease or cytotoxic therapy



**Blood work**  
WBC:  $1.4 \times 10^9/L$   
Hgb: 97 g/L  
Platelets:  $34 \times 10^9/L$



**Morphology**  
Bone marrow: Myeloid blasts 22%



**Cytogenetics**  
Complex karyotype  
41, XY, del(5q), -8, -10, -12, -17, -21



**Gene mutations**  
Wildtype: *NPM1*, *CEBPA*, *RUNX1*, *FLT3*, *TP53*, *ASXL1*, *IDH1/2*, *DDX41*, *BCOR*, *EZH2*, *SF3B1*, *SRSF2*, *ZRSR2*  
Mutation: STAG2 and U2AF1



**Diagnosis according to AML classification:**  
WHO 2016: AML-MRC (AML with an MDS-related cytogenetic abnormality)  
WHO 2022: AML-MR  
ICC 2022: AML with MR gene mutations

Approximately 23% of *de novo* AML patients present with cytogenetically defined AML-MRC<sup>†</sup>

WHAT WOULD YOUR TREATMENT STRATEGY BE?

AML-MR: AML myelodysplasia related  
AML-MRC: AML with myelodysplasia-related changes  
GP: General practitioner  
Hgb: Hemoglobin  
ICC: International Consensus Classification  
WHO: World Health Organization

\* This case is not a real patient and may not be representative of all patients.  
† As defined by WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues. Revised 4th edition 2017.  
Fuhrmann I, Lenk M, Haferlach T, et al. AML, NOS and AML-MRC as defined by multilineage dysplasia share a common mutation pattern which is distinct from AML-MRC as defined by MDS-related cytogenetics. *Leukemia* 2022;36:1939–1942.



## GORDON



### Gordon\*

Male, 68 years old  
Married, no children  
Likes spending time with his dogs  
on the beach



### Symptoms

Presented via his GP:  
Dyspnea, weight loss and petechiae



### Clinical history

No prior history of MDS or  
cytotoxic therapy



### Blood work

WBC:  $3.1 \times 10^9/L$   
Hgb: 92 g/L  
Platelets:  $92 \times 10^9/L$

What tests would  
you order?





# GORDON



## Gordon\*

Male, 68 years old  
Married, no children  
Likes spending time with his dogs  
on the beach



## Symptoms

Presented via his GP:  
Dyspnea, weight loss and petechiae



## Clinical history

No prior history of MDS or  
cytotoxic therapy



## Blood work

WBC:  $3.1 \times 10^9/L$   
Hgb: 92 g/L  
Platelets:  $92 \times 10^9/L$



## Morphology

Bone marrow: Myeloid blasts 36%  
Confirmed multilineage dysplasia



## Cytogenetics

46, XY, normal karyotype



## Gene mutations

Wildtype: *NPM1*, *CEBPA*, *FLT3*, *TP53*, *IDH1/2*,  
*DDX41*, *BCOR*, *EZH2*, *SF3B1*, *SRSF2*, *ZRSR2*  
Mutation: *ASXL1*

**How would you  
classify this patient?**





# GORDON



## Gordon\*

Male, 68 years old  
Married, no children  
Likes spending time with his dogs on the beach



## Symptoms

Presented via his GP:  
Dyspnea, weight loss and petechiae



## Clinical history

No prior history of MDS or cytotoxic therapy



## Blood work

WBC:  $3.1 \times 10^9/L$   
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Platelets:  $92 \times 10^9/L$



## Morphology

Bone marrow: Myeloid blasts 36%  
Confirmed multilineage dysplasia



## Cytogenetics

46, XY, normal karyotype



## Gene mutations

Wildtype: *NPM1*, *CEBPA*, *FLT3*, *TP53*, *IDH1/2*,  
*DDX41*, *BCOR*, *EZH2*, *SF3B1*, *SRSF2*, *ZRSR2*  
Mutation: *ASXL1*



## Diagnosis according to AML classification:

WHO 2016: AML-MRC (AML with multilineage dysplasia)  
WHO 2022: AML-MR  
ICC 2022: AML with MR gene mutations

## Up to 80% of patients diagnosed with AML-MRC may have multilineage dysplasia<sup>1,2</sup>

In a retrospective study of *de novo* AML cases without recurrent genetic rearrangements, *NPM1* or *biCEBPA* mutation, only 6% had multilineage dysplasia in the absence of AML-MRC cytogenetics.<sup>3</sup>

## WHAT WOULD YOUR TREATMENT STRATEGY BE?

AML-MR: AML myelodysplasia related

AML-MRC: AML with myelodysplasia-related changes

GP: General practitioner

Hgb: Hemoglobin

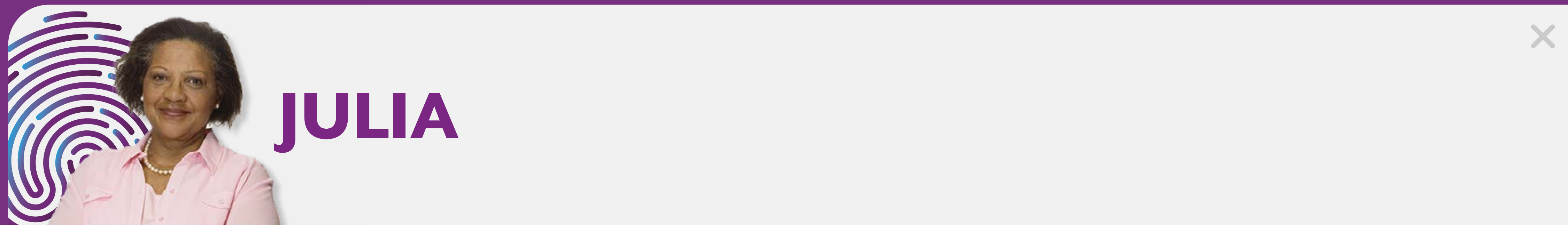
ICC: International Consensus Classification

MDS: Myelodysplastic syndromes

WHO: World Health Organization

\* This case is not a real patient and may not be representative of all patients.

1. Miesner M, Haferlach C, Bacher U, *et al.* Multilineage dysplasia (MLD) in acute myeloid leukemia (AML) correlates with MDS-related cytogenetic abnormalities and a prior history of MDS or MDS/MPN but has no independent prognostic relevance: a comparison of 408 cases classified as “AML not otherwise specified” (AML-NOS) or “AML with myelodysplasia-related changes” (AML-MRC). *Blood* 2010;116:2742–2751.
2. Montalban-Bravo G, Kanagal-Shamanna R, Class CA, *et al.* Outcomes of acute myeloid leukemia with myelodysplasia related changes depend on diagnostic criteria and therapy. *Am J Hepatol* 2020;95:612–622.
3. Fuhrmann I, Lenk M, Haferlach T, *et al.* AML, NOS and AML-MRC as defined by multilineage dysplasia share a common mutation pattern which is distinct from AML-MRC as defined by MDS-related cytogenetics. *Leukemia* 2022;36:1939–1942.



**Julia\***

Female, 52 years old  
Married and has 2 children who provide support



**Symptoms**

Presented via the emergency room:  
Fatigue, general weakness, fever and pallor



**Clinical history**

Diagnosed with MDS 2 years prior,  
but refused treatment

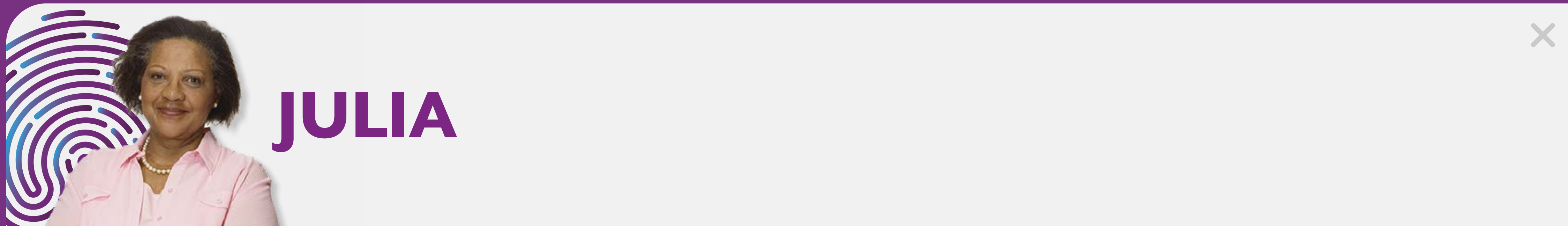


**Blood work**

WBC:  $2.9 \times 10^9/L$   
Hgb: 95 g/L  
Platelets:  $95 \times 10^9/L$

**What tests would  
you order?**





**Julia\***

Female, 52 years old  
Married and has 2 children who provide support



**Symptoms**

Presented via the emergency room:  
Fatigue, general weakness, fever and pallor



**Clinical history**

Diagnosed with MDS two years prior,  
but refused treatment



**Blood work**

WBC:  $2.9 \times 10^9/L$   
Hgb: 95 g/L  
Platelets:  $95 \times 10^9/L$



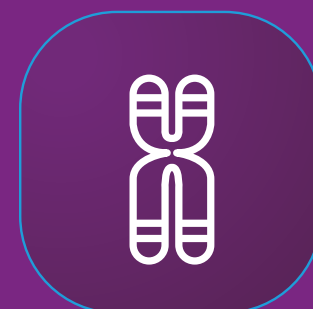
**Morphology**

Bone marrow: Myeloid blasts 40%



**Cytogenetics**

46, XX, del(5q)

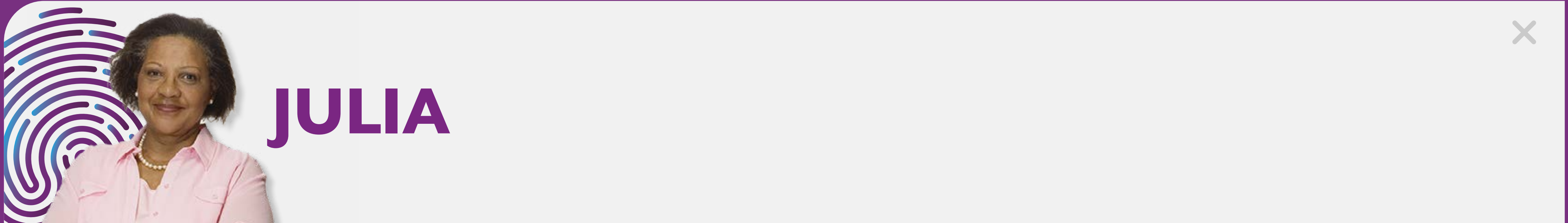


**Gene mutations**

Wildtype: *NPM1*, *CEBPA*, *FLT3*, *TP53*, *IDH1/2*  
Mutation: None

**How would you  
classify this patient?**





**Julia\***  
Female, 52 years old  
Married and has 2 children who provide support



**Morphology**  
Bone marrow: Myeloid blasts 40%



**Symptoms**  
Presented via the emergency room:  
Fatigue, general weakness, fever and pallor



**Cytogenetics**  
46, XX, del(5q)



**Clinical history**  
Diagnosed with MDS two years prior, but refused treatment



**Gene mutations**  
Wildtype: *NPM1*, *CEBPA*, *FLT3*, *TP53*, *IDH1/2*  
Mutation: None



**Blood work**  
WBC:  $2.9 \times 10^9/L$   
Hgb: 95 g/L  
Platelets:  $95 \times 10^9/L$



**Diagnosis according to AML classification:**  
WHO 2016: AML-MRC (AML arising from prior MDS)  
WHO 2022: AML-MR  
ICC 2022: AML with MR cytogenetic abnormality

**Almost 1 in 4 cases of AML is diagnosed in a patient under the age of 55 years**  
Whilst the prognosis of younger patients is better, this demographic still accounts for approximately 10% of AML deaths.

**WHAT WOULD YOUR TREATMENT STRATEGY BE?**

AML-MR: AML myelodysplasia related  
AML-MRC: AML with myelodysplasia-related changes  
Hgb: Hemoglobin  
ICC: International Consensus Classification  
WHO: World Health Organization  
\* This case is not a real patient and may not be representative of all patients.  
National Cancer Institute. Cancer stat facts: AML. Accessed May 2023 at: <https://seer.cancer.gov/statfacts/html/amyl.html>.

| History of MDS or MDS MPN             | Documented history of prior MDS or MDS/MPN                                                                                                               |                                                                                                                                                                                                                                         |                                                                                                                                                                                                                                                                                                                                                  |
|---------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| OR                                    |                                                                                                                                                          |                                                                                                                                                                                                                                         |                                                                                                                                                                                                                                                                                                                                                  |
| MDS-related cytogenetic abnormalities | <b>Complex karyotype</b><br>3 or more unrelated clonal abnormalities                                                                                     | <b>Unbalanced abnormalities</b> <ul style="list-style-type: none"><li>• -7/del(7q)</li><li>• del(5q)/t(5q)</li><li>• i(17q)/t(17p)</li><li>• -13/del(13q)</li><li>• del(11q)</li><li>• del(12p)/t(12p)</li><li>• idic(X)(q13)</li></ul> | <b>Balanced abnormalities</b> <ul style="list-style-type: none"><li>• t(11;16)(q23.3;p13.3)</li><li>• t(3;21)(q26.2;q22.1)</li><li>• t(1;3)(p36.3;q21.2)</li><li>• t(2;11)(p21;q23.3)</li><li>• t(5;12)(q32;p13.2)</li><li>• t(5;7)(q32;q11.2)</li><li>• t(5;17)(q32;p13.2)</li><li>• t(5;10)(q32;q21.2)</li><li>• t(3;5)(q25.3;q35.1)</li></ul> |
| OR                                    |                                                                                                                                                          |                                                                                                                                                                                                                                         |                                                                                                                                                                                                                                                                                                                                                  |
| Multilineage dysplasia                | Dysplasia present in at least 50% of the cells in at least 2 cell lines, unless an <i>NPM1</i> mutation or biallelic mutation of <i>CEBPA</i> is present |                                                                                                                                                                                                                                         |                                                                                                                                                                                                                                                                                                                                                  |

Arber DA, Orazi A, Hasserjian R, et al. The 2016 revision to the World Health Organization classification of myeloid neoplasms and acute leukemia. *Blood* 2016;127: 2391–2405.

# THE CLASSIFICATION OF AML HAS BEEN UPDATED TO REFLECT BREAKTHROUGHS IN DISEASE UNDERSTANDING<sup>1-3</sup>

- The VYXEOS indication is based on the WHO 2016 classification of AML<sup>1</sup>
- The 2022 WHO and ICC classifications have revised the definition of AML-MRC and t-AML<sup>2,3</sup>

WHO 2022<sup>2</sup>

AML: ≥ 20% blasts in peripheral blood

AML-MR

De novo AML with ≥ 1 MDS-related cytogenetic abnormality

OR

De novo AML with an MDS-related somatic mutation in ≥ 1 of 8 genes: **ASXL1**, **BCOR**, **EZH2**, **SF3B1**, **SRSF2**, **STAG2**, **U2AF1**, or **ZRSR2**

OR

AML with a history of MDS or MDS/MPN with or without cytogenetic or somatic abnormalities

ICC 2022<sup>3</sup>

AML: ≥ 20% blasts in BM or peripheral blood  
MDS/AML: 10–19% blasts in BM or peripheral blood

AML with MR cytogenetic abnormalities

OR

AML with MR gene mutations  
AML with a mutation in ≥ 1 of 9 genes: **ASXL1**, **BCOR**, **EZH2**, **RUNX1**, **SF3B1**, **SRSF2**, **STAG2**, **U2AF1**, or **ZRSR2**

OR

AML, progressed from MDS  
A qualifier that can be applied to any subgroup or category to denote: AML arising from a prior MDS

Click for more details

AML-pCT

A qualifier that can be applied to any subgroup or category to denote: AML with a history of prior chemotherapy, radiation therapy, or exposure to PARP1 inhibitors

AML, therapy-related

A qualifier that can be applied to any subgroup or category to denote: AML with a history of prior chemotherapy, radiation, or immune intervention

BM: Bone marrow  
ICC: International Consensus Classification  
MDS: Myelodysplastic syndrome  
MPN: Myeloproliferative neoplasm  
pCT: Post cytotoxic therapy  
WHO: World Health Organization

1. Arber DA, Orazi A, Hasserjian R, *et al.* The 2016 revision to the World Health Organization classification of myeloid neoplasms and acute leukemia. *Blood* 2016;127:2391–2405.

2. Khoury JD, Solary E, Abla O, *et al.* The 5th edition of the World Health Organization Classification of Haematolymphoid Tumours: Myeloid and Histiocytic/Dendritic Neoplasms. *Leukemia* 2022;36:1703–1719.

3. Arber DA, Orazi A, Hasserjian RP, *et al.* International Consensus Classification of Myeloid Neoplasms and Acute Leukemias: Integrating morphologic, clinical, and genomic data. *Blood* 2022;140:1200–1228.



# MYELODYSPLASIA-RELATED CYTOGENETIC ABNORMALITIES AS DESCRIBED IN THE WHO 2022 AND ICC 2022 GUIDELINES

THE WHO 2022 AND ICC CLASSIFICATIONS SHARE OVERLAPPING CYTOGENETIC ABNORMALITIES

## WHO 2022<sup>1</sup>

### AML-MR–defining cytogenetic abnormalities

- Complex karyotype ( $\geq 3$  abnormalities)
- 5q deletion or loss of 5q due to unbalanced translocation
- Monosomy 7, 7q deletion, or loss of 7q due to unbalanced translocation
- 11q deletion
- 12p deletion or loss of 12p due to unbalanced translocation
- Monosomy 13 or 13q deletion
- 17p deletion or loss of 17p due to unbalanced translocation
- Isochromosome 17q
- idic(X)(q13)

## ICC 2022<sup>2</sup>

### AML with MR cytogenetic abnormalities

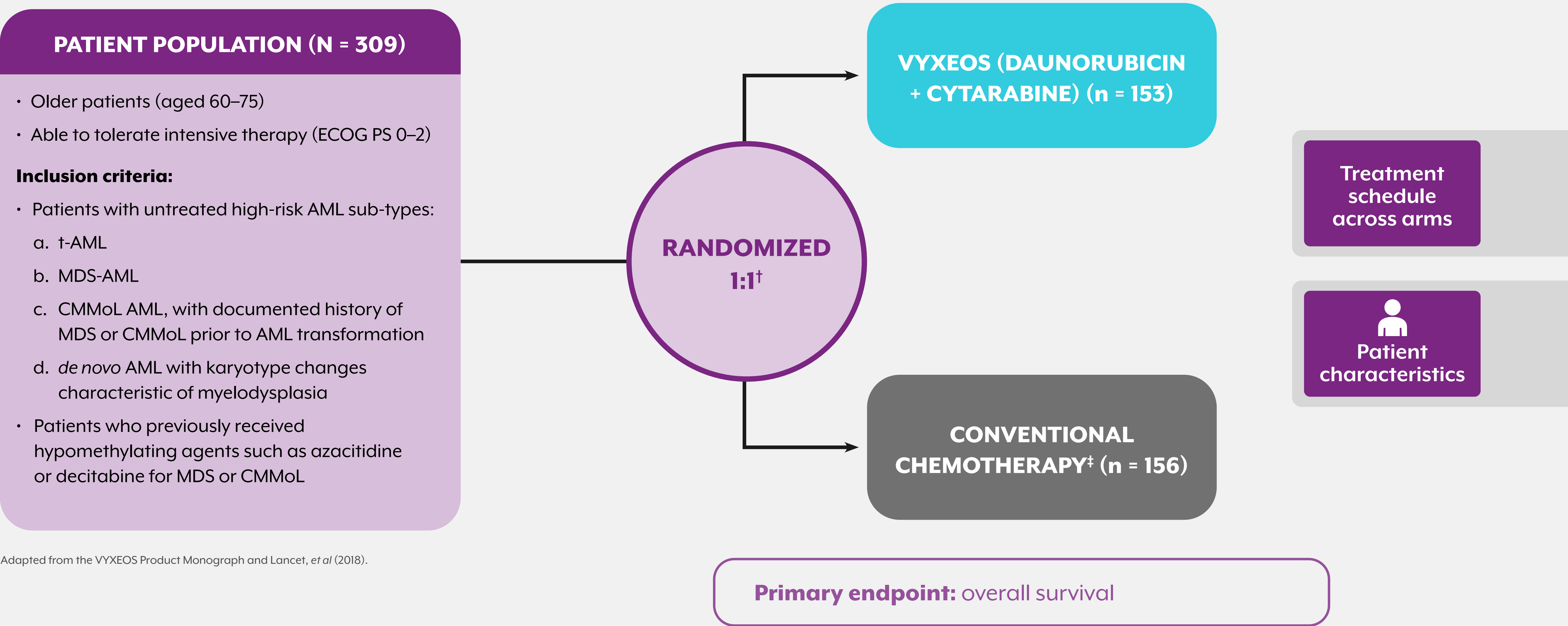
- Complex karyotype ( $\geq 3$  abnormalities in the absence of other class-defining recurring genetic abnormalities)
- del(5q)/t(5q)/add(5q)
- -7/del(7q)
- +8
- del(12p)/t(12p)/add(12p)
- i(17q)
- -17/add(17p) or del(17p)
- del(20q)
- idic(X)(q13) clonal abnormalities

ICC: International Consensus Classification  
WHO: World Health Organization

1. Khoury JD, Solary E, Abela O, et al. The 5th edition of the World Health Organization Classification of Haematolymphoid Tumours: Myeloid and Histiocytic/Dendritic Neoplasms. *Leukemia* 2022;36:1703–1719.
2. Arber DA, Orazi A, Hasserjian RP, et al. International Consensus Classification of Myeloid Neoplasms and Acute Leukemias: integrating morphologic, clinical, and genomic data. *Blood* 2022;140:1200–1228.

PHASE 3 STUDY DESIGN

A PHASE 3, RANDOMIZED, MULTICENTRE, OPEN-LABEL STUDY  
EVALUATED THE EFFICACY AND SAFETY OF VYXEOS IN ADULTS WITH  
NEWLY DIAGNOSED HIGH-RISK sAML<sup>1,2\*</sup>



# INDUCTION AND CONSOLIDATION SCHEDULE ACROSS TREATMENT ARMS<sup>1</sup>

## VYXEOS (DAUNORUBICIN + CYTARABINE)

(n = 153)



### FIRST INDUCTION

of daunorubicin 44 mg/m<sup>2</sup> and cytarabine 100 mg/m<sup>2</sup> administered on

Days **1** **3** **5**



### SECOND INDUCTION + CONSOLIDATION

- Induction: Daunorubicin 44 mg/m<sup>2</sup> and cytarabine 100 mg/m<sup>2</sup> administered on
- Consolidation: Daunorubicin 29 mg/m<sup>2</sup> and cytarabine 65 mg/m<sup>2</sup> administered on

Days **1** **3**

Adapted from the VYXEOS Product Monograph.

## CONVENTIONAL CHEMOTHERAPY\*

(n = 156)



### FIRST INDUCTION

Cytarabine 100 mg/m<sup>2</sup> administered on

Days **1** **2** **3** **4** **5** **6** **7**

Daunorubicin 60 mg/m<sup>2</sup> administered on

Days **1** **2** **3**



### SECOND INDUCTION + CONSOLIDATION

Cytarabine 100 mg/m<sup>2</sup> administered on

Days **1** **2** **3** **4** **5**

Daunorubicin 60 mg/m<sup>2</sup> administered on

Days **1** **2**

\* Conventional chemotherapy includes the 7+3/5+2 regimen for induction and consolidation, using cytarabine and daunorubicin.<sup>2</sup>

1. Current VYXEOS® Product Monograph, Jazz Pharmaceuticals Canada, Inc.

2. Lancet JE, Uy GL, Cortes JE, *et al.* CPX-351 (cytarabine and daunorubicin) liposome for injection versus conventional cytarabine plus daunorubicin in older patients with newly diagnosed secondary acute myeloid leukemia. *J Clin Oncol* 2018;36:2684–2692.



# PATIENT CHARACTERISTICS WERE SIMILAR ACROSS THE TREATMENT ARMS<sup>1,2</sup>



## PATIENT AND DISEASE CHARACTERISTICS

|                   |                                             | VYXEOS<br>n = 153<br>n (%) | CONVENTIONAL<br>CHEMOTHERAPY*<br>n = 156<br>n (%) |
|-------------------|---------------------------------------------|----------------------------|---------------------------------------------------|
| SEX               | Male                                        | 94 (61)                    | 96 (62)                                           |
|                   | Female                                      | 59 (39)                    | 60 (38)                                           |
|                   | Median age (range)                          | 68 (60–75)                 | 68 (60–75)                                        |
| ECOG PERFORMANCE  | PS 0–1                                      | 138 (90)                   | 134 (86)                                          |
|                   | PS 2                                        | 15 (10)                    | 22 (14)                                           |
| CYTOGENETIC RISK† | Favourable                                  | 7 (5)                      | 5 (3)                                             |
|                   | Intermediate                                | 64 (42)                    | 58 (38)                                           |
|                   | Poor                                        | 72 (47)                    | 83 (53)                                           |
|                   | Prior anthracycline exposure, n (%)         | 6 (3.9)                    | 5 (3.2)                                           |
|                   | All patients with prior HMA exposure, n (%) | 62 (40.5)                  | 71 (45.5)                                         |
| AML SUBTYPES      | t-AML                                       | 30 (20)                    | 33 (21)                                           |
|                   | AML with antecedent MDS                     | 71 (46)                    | 74 (47)                                           |
|                   | CMMoL                                       | 11 (7)                     | 12 (8)                                            |
|                   | de novo with MDS karyotype                  | 41 (27)                    | 37 (24)                                           |



FOR PATIENTS > 60 YEARS OLD WITH AML, THE NCCN GUIDELINES<sup>®</sup> RECOMMEND SELECTING A TREATMENT OPTION BASED ON PATIENT PERFORMANCE STATUS, COMORBID CONDITIONS, AND ADVERSE FEATURES SUCH AS SUBTYPE RATHER THAN CHRONOLOGIC AGE ALONE<sup>3</sup>

CMMoL: Chronic myelomonocytic leukemia  
ECOG: Eastern Cooperative Oncology Group  
MDS: Myelodysplastic syndromes  
NCCN: National Comprehensive Cancer Network  
PS: Performance status

\* Conventional chemotherapy includes the 7+3/5+2 regimen for induction and consolidation, using cytarabine and daunorubicin.<sup>2</sup>  
† As determined by the NCCN criteria.

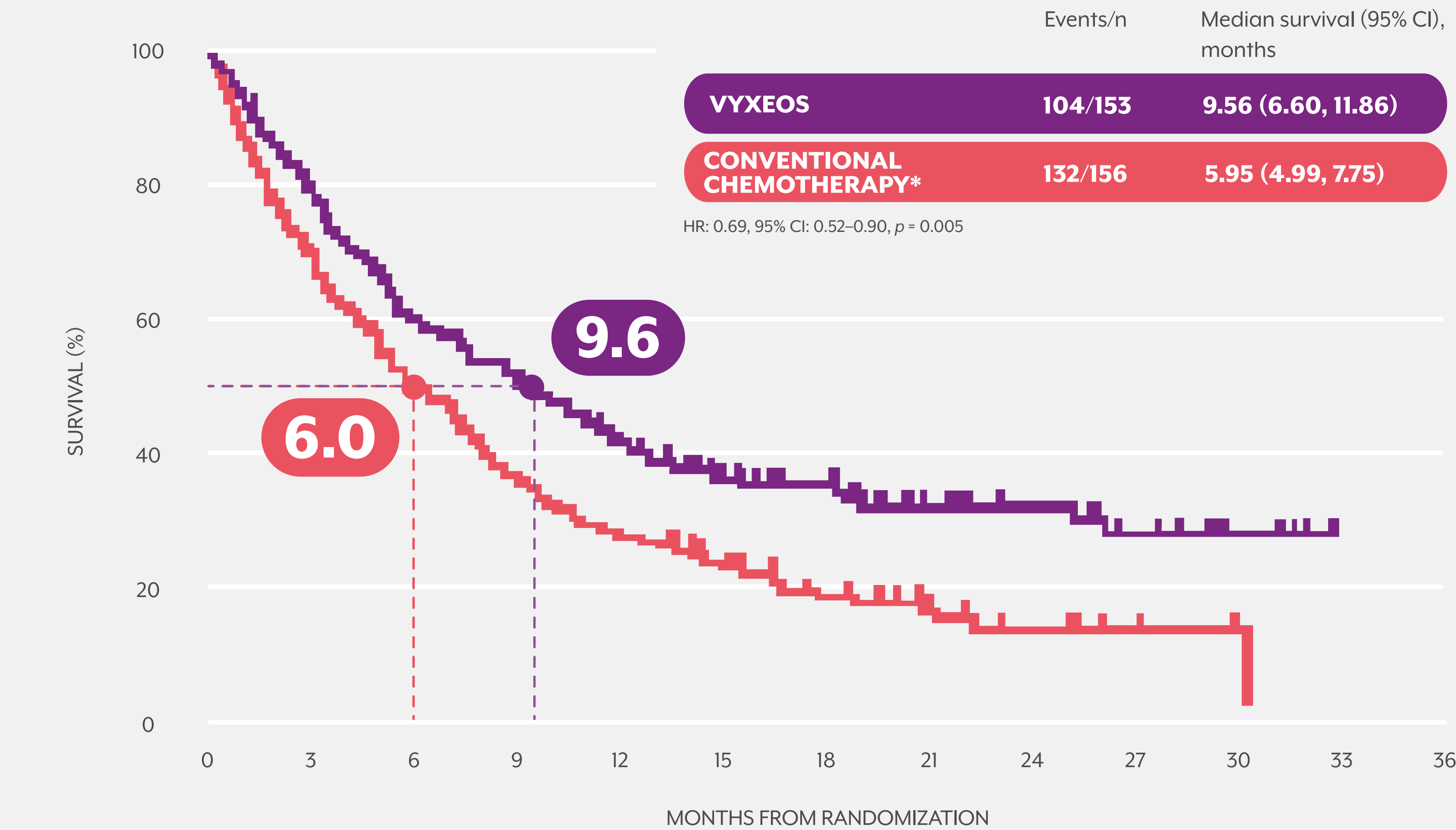
1. Current VYXEOS<sup>®</sup> Product Monograph, Jazz Pharmaceuticals Canada, Inc.
2. Lancet JE, Uy GL, Cortes JE, *et al.* CPX-351 (cytarabine and daunorubicin) liposome for injection versus conventional cytarabine plus daunorubicin in older patients with newly diagnosed secondary acute myeloid leukemia. *J Clin Oncol* 2018;36:2684–2692.
3. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines<sup>®</sup>) for Acute Myeloid Leukemia V.2.2021. © National Comprehensive Cancer Network, Inc. 2021. All rights reserved. Accessed January 2021. To view the most recent and complete version of the guideline, go online to NCCN.org.

EFFICACY RESULTS

VYXEOS DEMONSTRATED SUPERIORITY IN OVERALL SURVIVAL COMPARED TO CONVENTIONAL CHEMOTHERAPY IN PATIENTS AGED 60–75 WITH HIGH-RISK AML<sup>1\*</sup>

PRIMARY ENDPOINT

OVERALL SURVIVAL IN THE ITT POPULATION<sup>1</sup>



|                            |     |     |    |    |    |    |    |    |    |    |   |   |
|----------------------------|-----|-----|----|----|----|----|----|----|----|----|---|---|
| VYXEOS                     | 153 | 122 | 92 | 79 | 62 | 46 | 34 | 21 | 16 | 11 | 5 | 1 |
| Conventional chemotherapy* | 156 | 110 | 77 | 56 | 43 | 31 | 20 | 12 | 7  | 3  | 2 | 0 |

31%

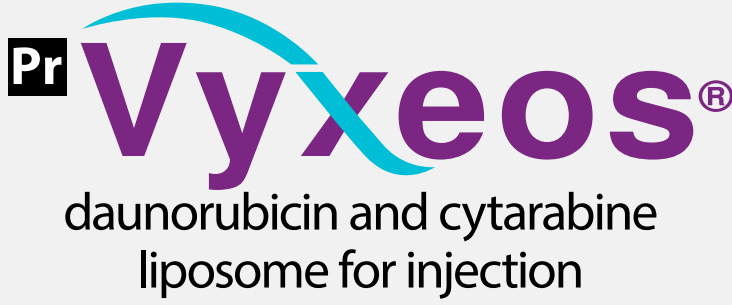
REDUCTION IN THE RELATIVE RISK OF DEATH FOR PATIENTS TREATED WITH VYXEOS VS CONVENTIONAL CHEMOTHERAPY<sup>1,2\*</sup>

Click to access the Lancet, *et al.* publication for full study results

Adapted from the VYXEOS Product Monograph.

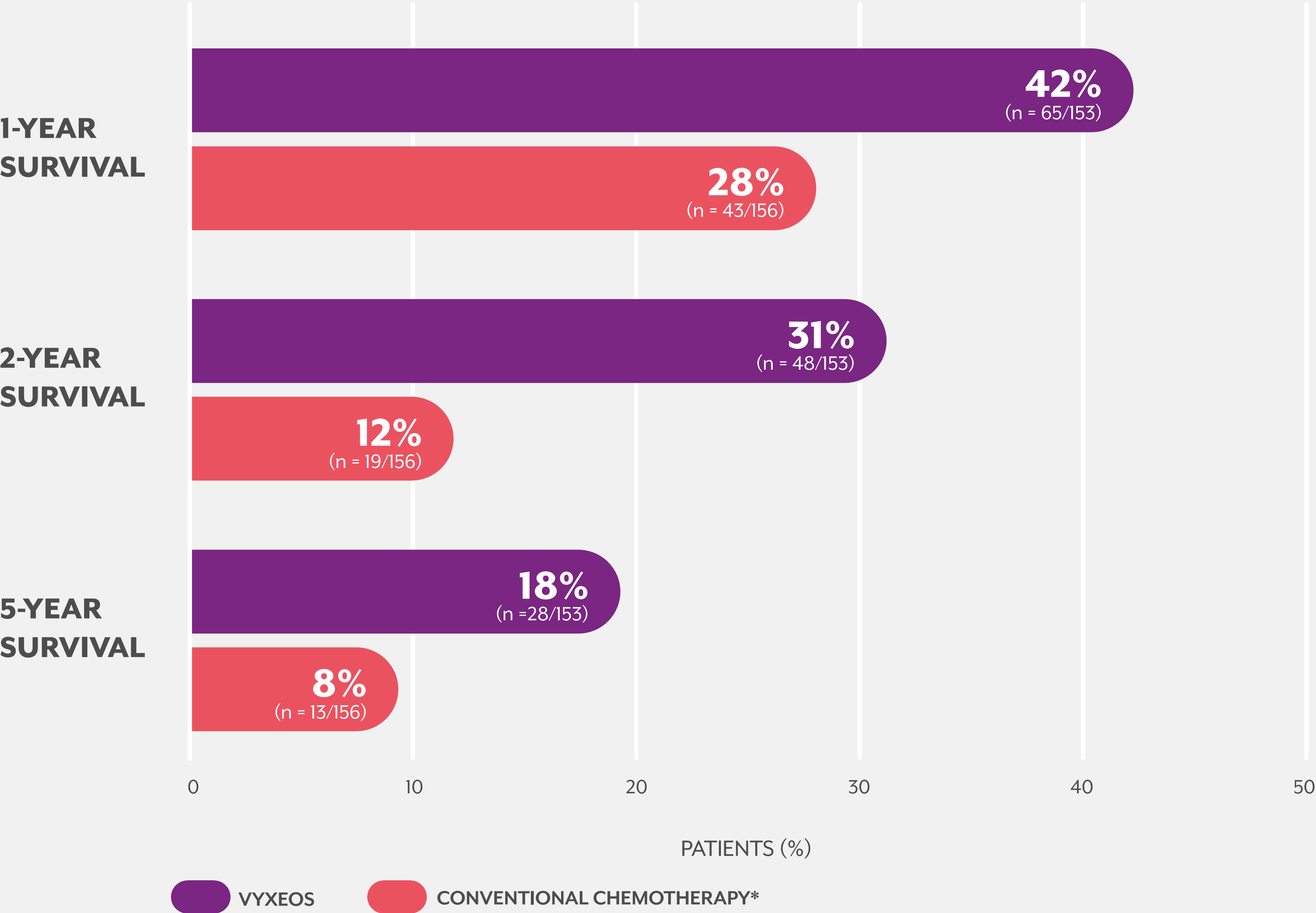
CI: Confidence interval  
HR: Hazard ratio  
ITT: Intent-to-treat  
\* Conventional chemotherapy includes the 7+3/5+2 regimen for induction and consolidation, using cytarabine and daunorubicin.<sup>2</sup>

1. Current VYXEOS® Product Monograph, Jazz Pharmaceuticals Canada, Inc.  
2. Lancet JE, Uy GL, Cortes JE, *et al.* CPX-351 (cytarabine and daunorubicin) liposome for injection versus conventional cytarabine plus daunorubicin in older patients with newly diagnosed secondary acute myeloid leukemia. *J Clin Oncol* 2018;36:2684–2692.



EFFICACY RESULTS

MORE PATIENTS TREATED WITH VYXEOS REACHED 1-, 2- AND 5-YEAR SURVIVAL LANDMARKS THAN WITH CONVENTIONAL CHEMOTHERAPY<sup>1,2\*</sup>



Adapted from Lancet, *et al* (2018) and the VYXEOS Product Monograph.

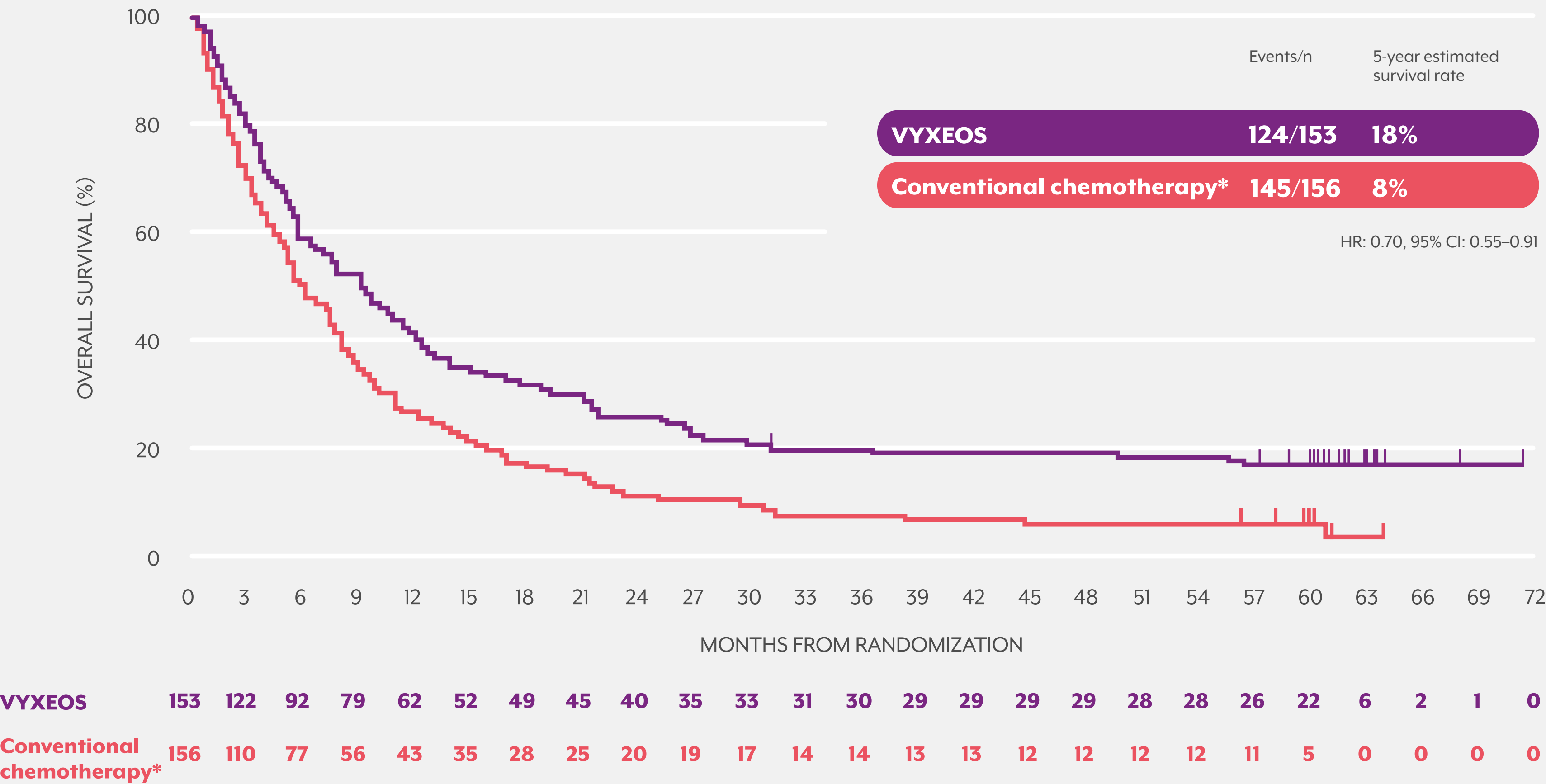


\* Conventional chemotherapy includes the 7+3/5+2 regimen for induction and consolidation, using cytarabine and daunorubicin.<sup>1</sup>  
1. Lancet JE, Uy GL, Cortes JE, *et al*. CPX-351 (cytarabine and daunorubicin) liposome for injection versus conventional cytarabine plus daunorubicin in older patients with newly diagnosed secondary acute myeloid leukemia. *J Clin Oncol* 2018;36:2684–2692.  
2. Current VYXEOS® Product Monograph, Jazz Pharmaceuticals Canada, Inc.

EFFICACY RESULTS

IMPROVED OVERALL SURVIVAL WAS MAINTAINED IN PATIENTS TREATED WITH VYXEOS VS CONVENTIONAL CHEMOTHERAPY\* AFTER A 5-YEAR FOLLOW-UP<sup>1</sup>

OVERALL SURVIVAL: 5-YEAR RESULTS<sup>1,2</sup>



Adapted from Lancet, *et al* (2020) and the VYXEOS Product Monograph.



MORE THAN TWICE AS MANY PATIENTS TREATED WITH VYXEOS WERE ALIVE AFTER 5 YEARS THAN THOSE TREATED WITH CONVENTIONAL CHEMOTHERAPY<sup>2\*</sup>

THE SURVIVAL BENEFIT WITH VYXEOS OVER CONVENTIONAL CHEMOTHERAPY\* WAS MAINTAINED INTO A LONGER TERM IN PATIENTS AGED 60-75 YEARS

See long-term survival data by age group

Click to access the Lancet *et al.* publication to more 5-year results

CI: Confidence interval  
HR: Hazard ratio  
\* Conventional chemotherapy includes the 7+3/5+2 regimen for induction and consolidation, using cytarabine and daunorubicin.<sup>3</sup>

1. Lancet JE, Uy GL, Newell LF, *et al.* Five-year final results of a phase III study of CPX-351 versus 7+3 in older adults with newly diagnosed high-risk/secondary AML. Presented at the Congress of the European Hematological Association (EHA) 2020.  
2. Current VYXEOS® Product Monograph, Jazz Pharmaceuticals Canada, Inc.  
3. Lancet JE, Uy GL, Cortes JE, *et al.* CPX-351 (cytarabine and daunorubicin) liposome for injection versus conventional cytarabine plus daunorubicin in older patients with newly diagnosed secondary acute myeloid leukemia. *J Clin Oncol* 2018;36:2684-2692.



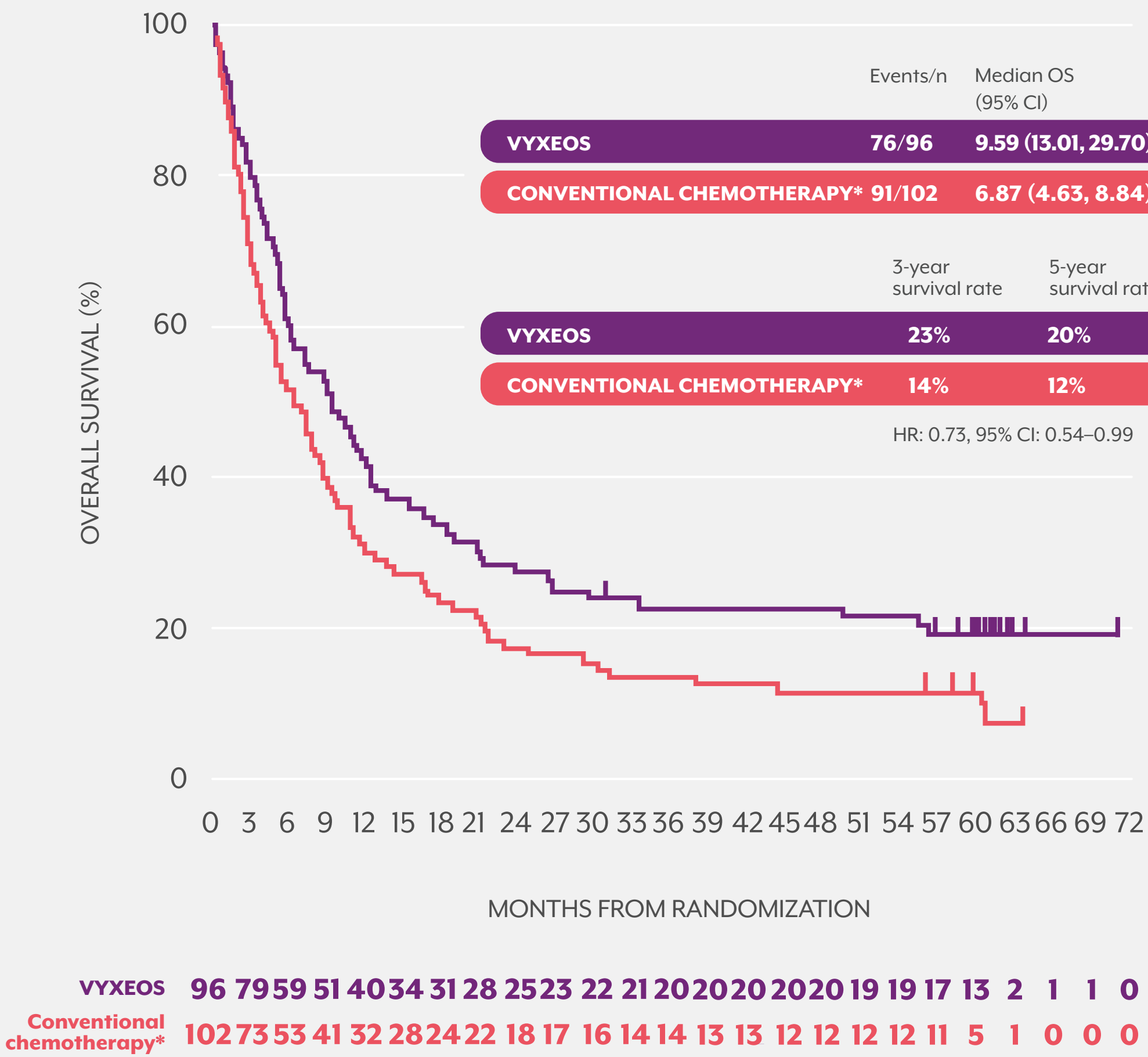
EFFICACY RESULTS

IMPROVED OVERALL SURVIVAL WAS MAINTAINED INTO A LONGER TERM IN PATIENTS OVER 60 TREATED WITH VYXEOS VS CONVENTIONAL CHEMOTHERAPY<sup>1\*</sup>

Age group: 60–69 years

Age group: 70–75 years

3-YEAR AND 5-YEAR SURVIVAL RATES IN PATIENTS AGED 60–69 YEARS<sup>1</sup>



Adapted from Data on File.

CI: Confidence interval  
HR: Hazard ratio

\* Conventional chemotherapy includes the 7+3/5+2 regimen for induction and consolidation, using cytarabine and daunorubicin.<sup>2</sup>

- 1. Jazz Pharmaceuticals. Data on File. Five-year results of a randomized, open-label, phase 3 trial of CPX-351 vs 7+3 chemotherapy in older adults with newly diagnosed high-risk/secondary AML.
- 2. Lancet JE, Uy GL, Cortes JE, *et al*. CPX-351 (cytarabine and daunorubicin) liposome for injection versus conventional cytarabine plus daunorubicin in older patients with newly diagnosed secondary acute myeloid leukemia. *J Clin Oncol* 2018;36:2684–2692.

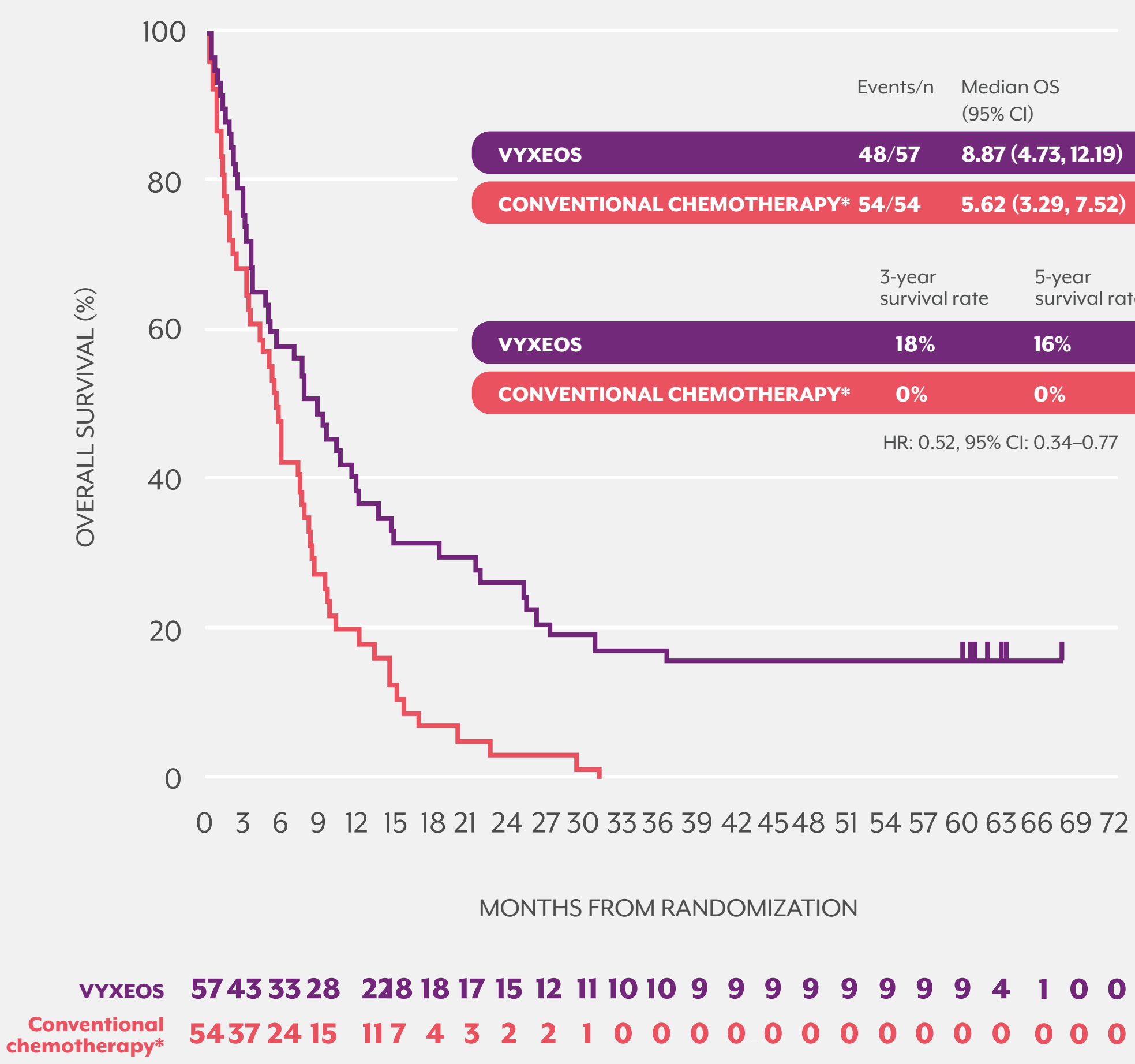
EFFICACY RESULTS

IMPROVED OVERALL SURVIVAL WAS MAINTAINED INTO A LONGER TERM IN PATIENTS OVER 60 TREATED WITH VYXEOS VS CONVENTIONAL CHEMOTHERAPY<sup>1\*</sup>

Age group: 60–69 years

Age group: 70–75 years

3-YEAR AND 5-YEAR SURVIVAL RATES IN PATIENTS AGED 70–75 YEARS<sup>1</sup>



CI: Confidence interval  
HR: Hazard ratio

\* Conventional chemotherapy includes the 7+3/5+2 regimen for induction and consolidation, using cytarabine and daunorubicin.<sup>2</sup>

1. Jazz Pharmaceuticals. Data on File. Five-year results of a randomized, open-label, phase 3 trial of CPX-351 vs 7+3 chemotherapy in older adults with newly diagnosed high-risk/secondary AML.

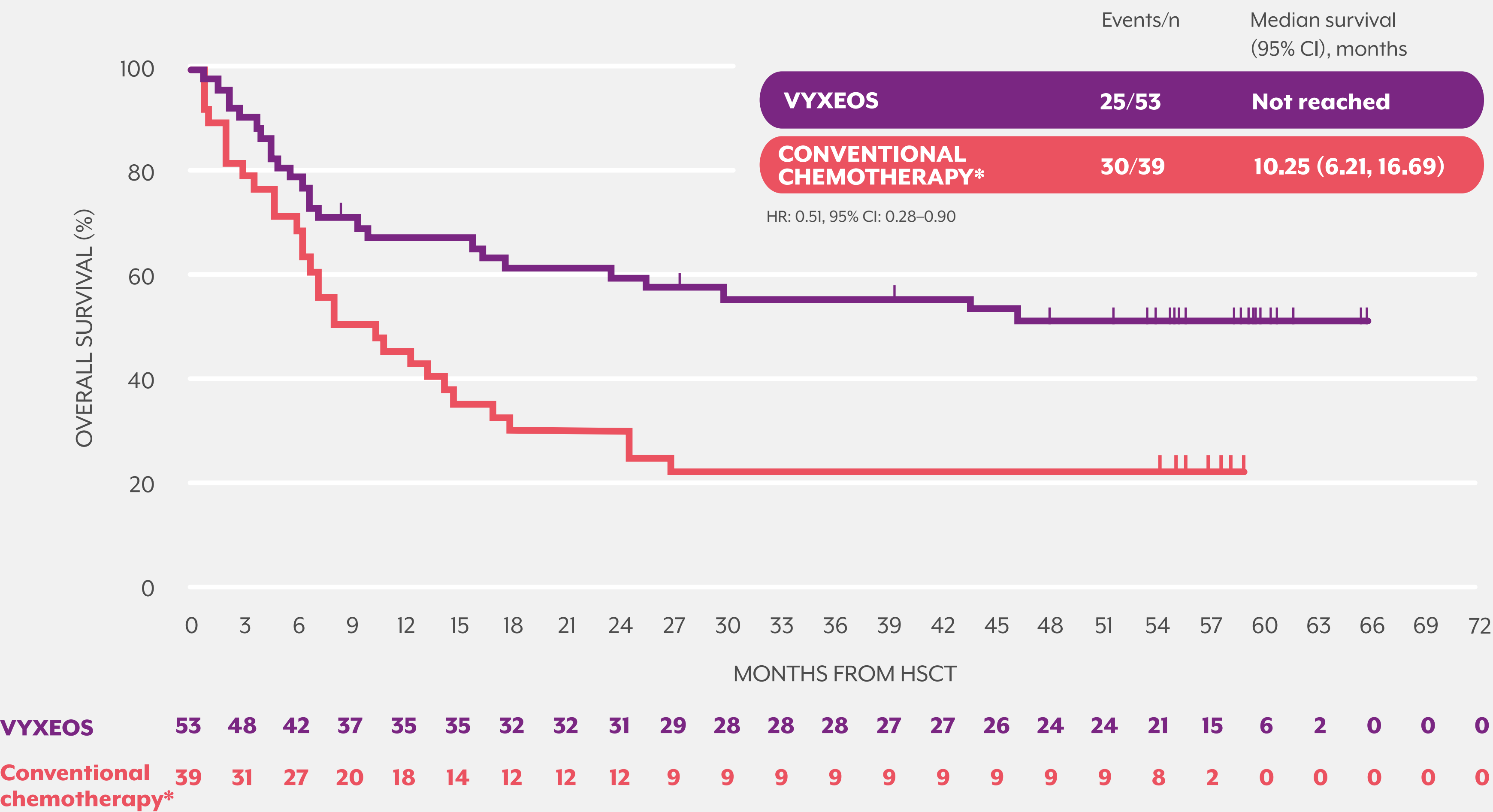
2. Lancet JE, Uy GL, Cortes JE, et al. CPX-351 (cytarabine and daunorubicin) liposome for injection versus conventional cytarabine plus daunorubicin in older patients with newly diagnosed secondary acute myeloid leukemia. *J Clin Oncol* 2018;36:2684–2692.

Adapted from Data on File.

EFFICACY RESULTS: POST-HOC ANALYSIS

POST-HOC ANALYSIS SUGGESTS THAT OVERALL SURVIVAL WAS MAINTAINED ABOVE 50% AT 5 YEARS IN PATIENTS WHO RECEIVED VYXEOS AND UNDERWENT HSCT<sup>1,2</sup>

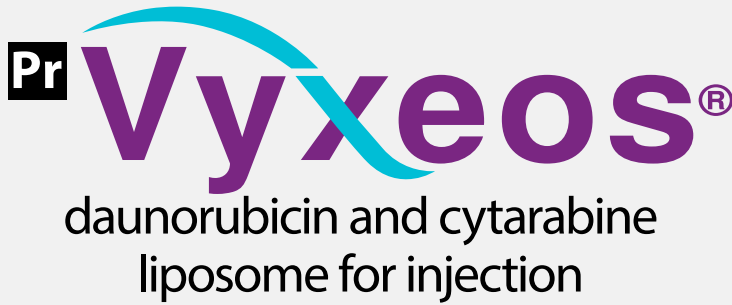
OVERALL SURVIVAL LANDMARKED FROM DATE OF HSCT<sup>1,2</sup>



Adapted from Lancet, *et al* (2020) and the VYXEOS Product Monograph.

CI: Confidence interval  
HR: Hazard ratio  
HSCT: Hematopoietic stem cell transplantation  
\* Conventional chemotherapy includes the 7+3/5+2 regimen for induction and consolidation, using cytarabine and daunorubicin.<sup>1</sup>

1. Lancet JEt, Uy GL, Newell LF, *et al*. Five-year final results of a phase III study of CPX-351 versus 7+3 in older adults with newly diagnosed high-risk/secondary AML. Presented at the Congress of the European Hematological Association (EHA) 2020.  
2. Current VYXEOS® Product Monograph, Jazz Pharmaceuticals Canada, Inc.



EFFICACY RESULTS: POST-HOC ANALYSIS

THE PROPORTION OF PATIENTS TREATED WITH VYXEOS OR CONVENTIONAL CHEMOTHERAPY WHO REACHED HSCT<sup>1,2</sup>

HSCT WAS REACHED BY  
35% OF PATIENTS

Treated with VYXEOS (n = 53/153)

vs

25% OF PATIENTS

Receiving conventional chemotherapy\*  
(n = 39/151)<sup>1</sup>

p = 0.098

See the data

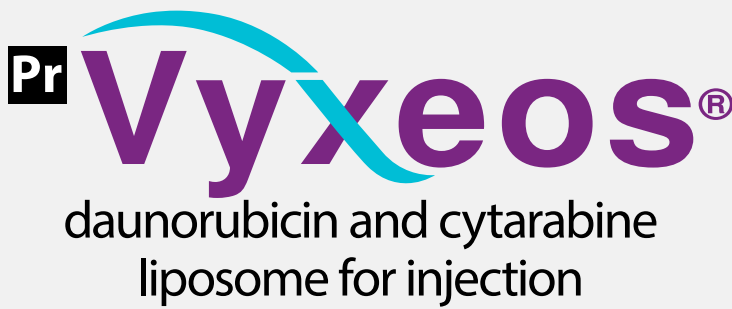


↓ 49%

REDUCED RELATIVE RISK OF DEATH FOR PATIENTS RECEIVING TRANSPLANT WHEN TREATED WITH VYXEOS VS CONVENTIONAL CHEMOTHERAPY<sup>1,2\*</sup>

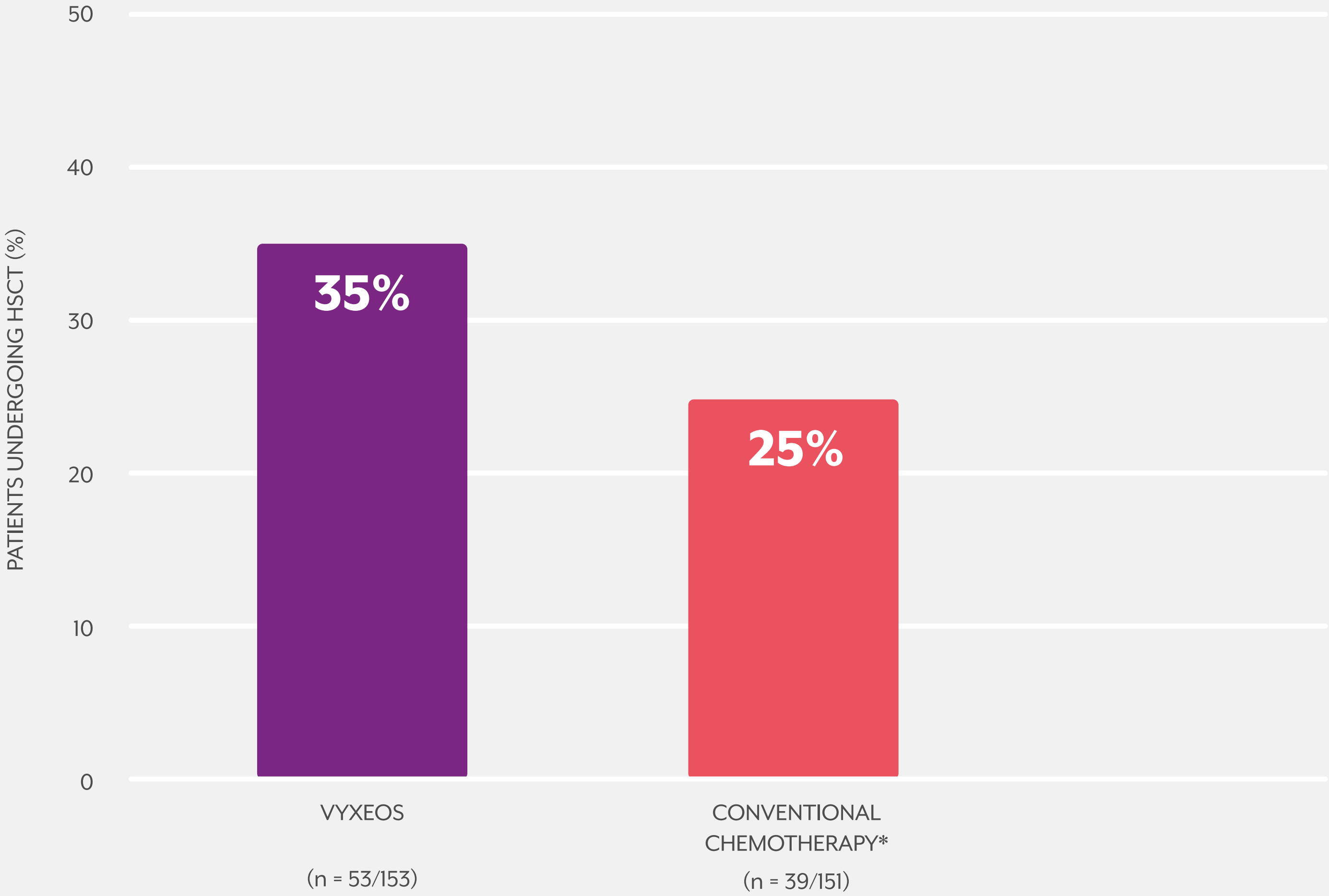
HSCT: Hematopoietic stem cell transplantation  
\* Conventional chemotherapy includes the 7+3/5+2 regimen for induction and consolidation, using cytarabine and daunorubicin.<sup>2</sup>

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# THE PROPORTION OF PATIENTS TREATED WITH VYXEOS OR CONVENTIONAL CHEMOTHERAPY WHO REACHED HSCT<sup>1\*</sup>



Adapted from the VYXEOS Product Monograph.

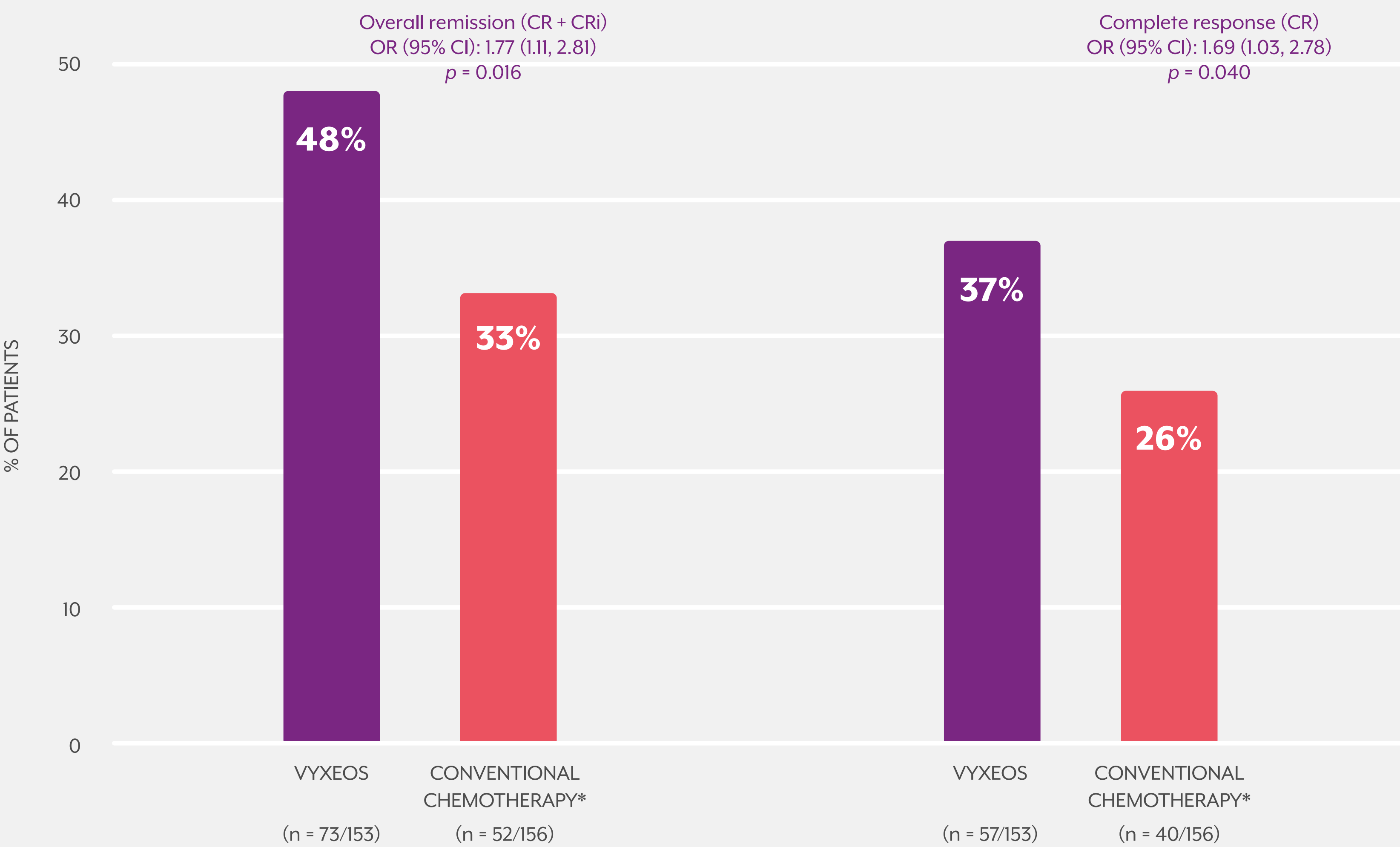
HSCT: Hematopoietic stem cell transplantation  
\* Conventional chemotherapy includes the 7+3/5+2 regimen for induction and consolidation, using cytarabine and daunorubicin.<sup>2</sup>

1. Current VYXEOS® Product Monograph, Jazz Pharmaceuticals Canada, Inc.  
2. Lancet JE, Uy GL, Newell LF, *et al.* Five-year final results of a phase III study of CPX-351 versus 7+3 in older adults with newly diagnosed high-risk/secondary AML. Presented at the Congress of the European Hematological Association (EHA) 2020.

EFFICACY RESULTS

PATIENTS TREATED WITH VYXEOS ACHIEVED SIGNIFICANTLY GREATER RESPONSE RATES VS CONVENTIONAL CHEMOTHERAPY<sup>1\*</sup>

SECONDARY ENDPOINT  
RESPONSE RATES IN PATIENTS TREATED WITH VYXEOS VS CONVENTIONAL CHEMOTHERAPY<sup>1\*</sup>

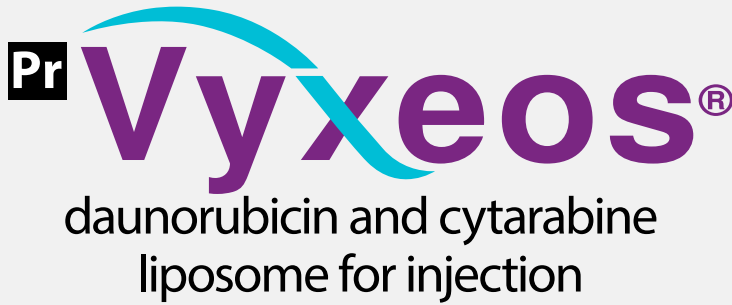


CONSIDER WHAT COMPLETE REMISSION  
COULD MEAN FOR YOUR AML PATIENTS

Adapted from the VYXEOS Product Monograph.

CI: Confidence interval  
CRi: Complete response with incomplete platelet or neutrophil recovery  
OR: Odds ratio  
\* Conventional chemotherapy includes the 7+3/5+2 regimen for induction and consolidation, using cytarabine and daunorubicin.<sup>2</sup>

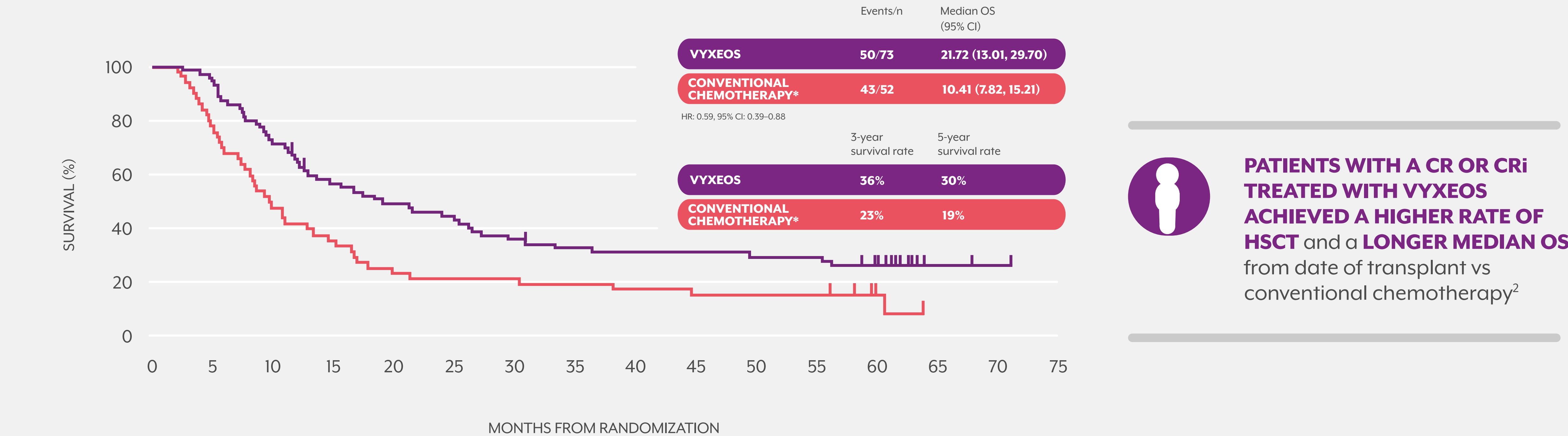
1. Current VYXEOS® Product Monograph, Jazz Pharmaceuticals Canada, Inc.  
2. Lancet JE, Uy GL, Cortes JE, *et al.* CPX-351 (cytarabine and daunorubicin) liposome for injection versus conventional cytarabine plus daunorubicin in older patients with newly diagnosed secondary acute myeloid leukemia. *J Clin Oncol* 2018;36:2684–2692.



EFFICACY RESULTS: POST-HOC ANALYSIS

POST-HOC ANALYSIS OF PATIENTS WHO ACHIEVED CR OR CRi<sup>1</sup>

OVERALL SURVIVAL WAS GREATER AT 5 YEARS IN PATIENTS WITH A CR OR CRi AND TREATED WITH VYXEOS VS CONVENTIONAL CHEMOTHERAPY<sup>1\*</sup>

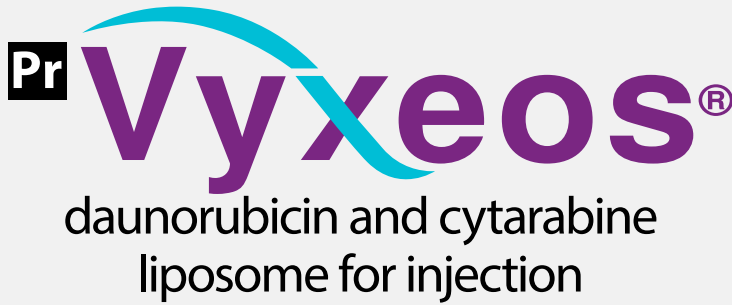


|                            |    |    |    |    |    |    |    |    |    |    |    |    |    |   |   |   |
|----------------------------|----|----|----|----|----|----|----|----|----|----|----|----|----|---|---|---|
| VYXEOS                     | 73 | 69 | 54 | 41 | 36 | 33 | 27 | 24 | 23 | 23 | 22 | 22 | 18 | 2 | 1 | 0 |
| Conventional chemotherapy* | 52 | 41 | 26 | 20 | 15 | 13 | 13 | 12 | 11 | 10 | 10 | 10 | 3  | 0 | 0 | 0 |

Adapted from Lancet, *et al* (2020).

CI: Confidence interval  
CRi: Complete response with incomplete platelet or neutrophil recovery  
HR: Hazard ratio  
HSCT: Hematopoietic stem cell transplantation  
OS: Overall survival  
\* Conventional chemotherapy includes the 7+3/5+2 regimen for induction and consolidation, using cytarabine and daunorubicin.<sup>3</sup>

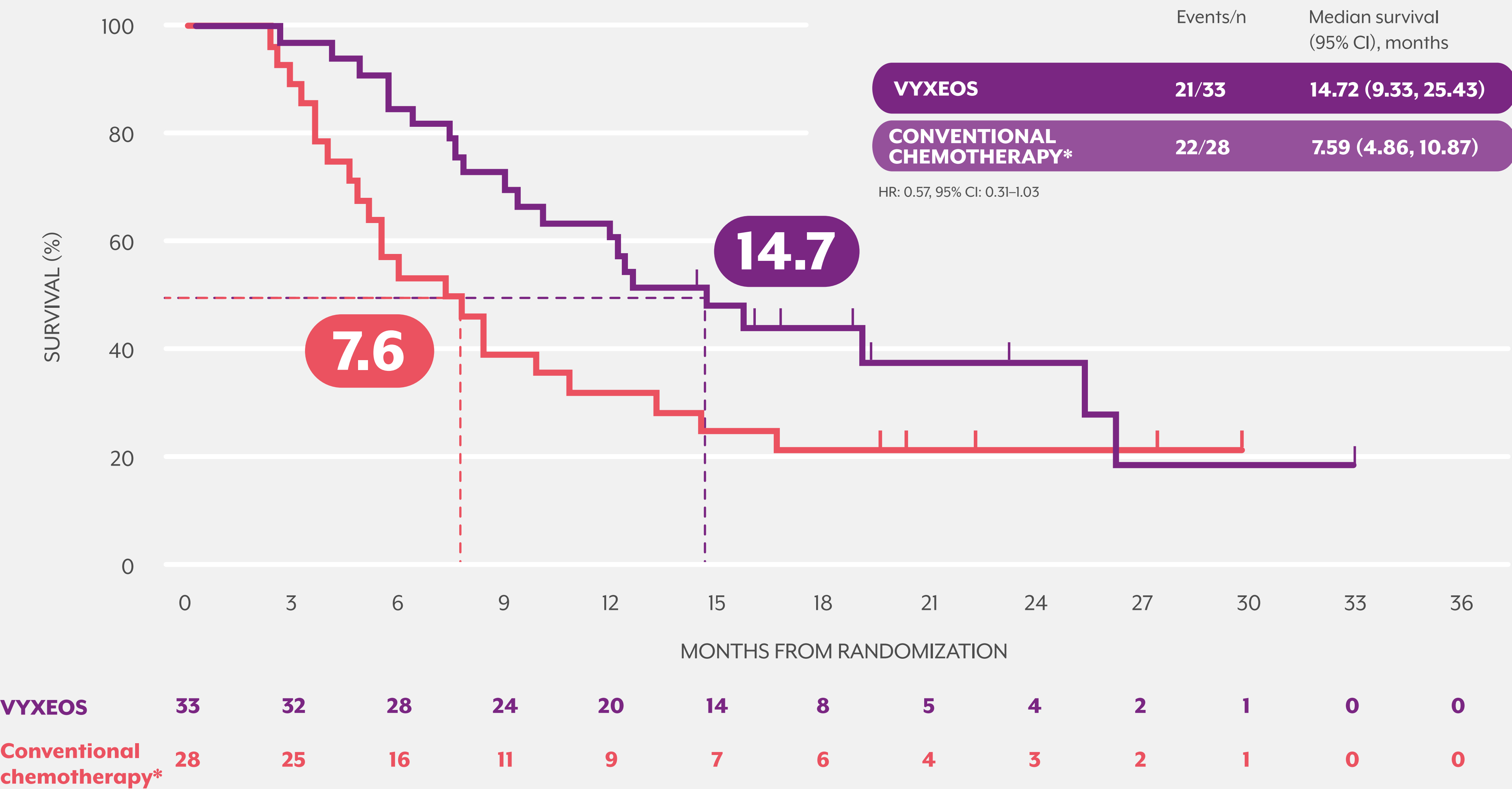
1. Lancet JE, Uy GL, Newell LF, *et al*. Five-year final results of a phase III study of CPX-351 versus 7+3 in older adults with newly diagnosed high-risk/secondary AML. Presented at the Congress of the European Hematological Association (EHA) 2020.  
2. Faderl S, Uy GL, Schiller GJ, *et al*. Outcomes in older patients with newly diagnosed, high-risk/secondary AML (sAML) who achieve remission with CPX-351 versus 7+3 Induction. Presented at the ISAL XVII 2019.  
3. Lancet JE, Uy GL, Cortes JE, *et al*. CPX-351 (cytarabine and daunorubicin) liposome for injection versus conventional cytarabine plus daunorubicin in older patients with newly diagnosed secondary acute myeloid leukemia. *J Clin Oncol* 2018;36:2684-2692.



EFFICACY RESULTS: POST-HOC ANALYSIS

POST-HOC ANALYSIS SUGGESTS THAT MEDIAN OS WAS OVER ONE YEAR FOR PATIENTS TREATED WITH VYXEOS WHO ACHIEVED CR OR CRi BUT DID NOT UNDERGO HSCT<sup>1</sup>

OVERALL SURVIVAL IN PATIENTS WHO ACHIEVED REMISSION BUT DID NOT UNDERGO TRANSPLANT<sup>1</sup>

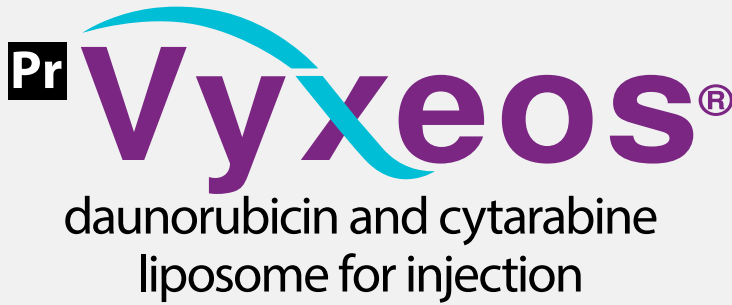


Click to access the Lin *et al.* publication for full results

Adapted from Lin, *et al* (2021).

CI: Confidence interval  
CRi: Complete response with incomplete platelet or neutrophil recovery  
HR: Hazard ratio  
HSCT: Hematopoietic stem cell transplantation  
OS: Overall survival  
\* Conventional chemotherapy includes the 7+3/5+2 regimen for induction and consolidation, using cytarabine and daunorubicin.<sup>2</sup>

1. Lin TL, Rizzieri DA, Ryan DH, *et al.* Older adults with newly diagnosed high-risk/secondary AML who achieved remission with CPX-351: phase 3 post hoc analyses. *Blood Adv* 2021;5(6):1719-1728.  
2. Lancet JE, Uy GL, Cortes JE, *et al.* CPX-351 (cytarabine and daunorubicin) liposome for injection versus conventional cytarabine plus daunorubicin in older patients with newly diagnosed secondary acute myeloid leukemia. *J Clin Oncol* 2018;36:2684-2692.



EFFICACY RESULTS: POST-HOC ANALYSIS

POST-HOC ANALYSIS SUGGESTS VYXEOS PROVIDED THE GREATEST BENEFIT WHEN USED FOR INDUCTION AND CONSOLIDATION<sup>1</sup>

Patients who received VYXEOS for induction and consolidation therapy achieved over 2 years median overall survival<sup>1</sup>

VYXEOS (n = 49)

25.4 months

CONVENTIONAL CHEMOTHERAPY\* (n = 32)

8.5 months

HR: 0.44, 95% CI: 0.25–0.77

Adapted from Kolitz, *et al* (2020).



Patients were able to receive up to 2 cycles of VYXEOS for induction and consolidation<sup>1</sup>

INDUCTION CYCLES

CONSOLIDATION CYCLES



INDUCTION

CONSOLIDATION

See overall survival (OS) data

Click to access the Kolitz *et al.* publication for full results

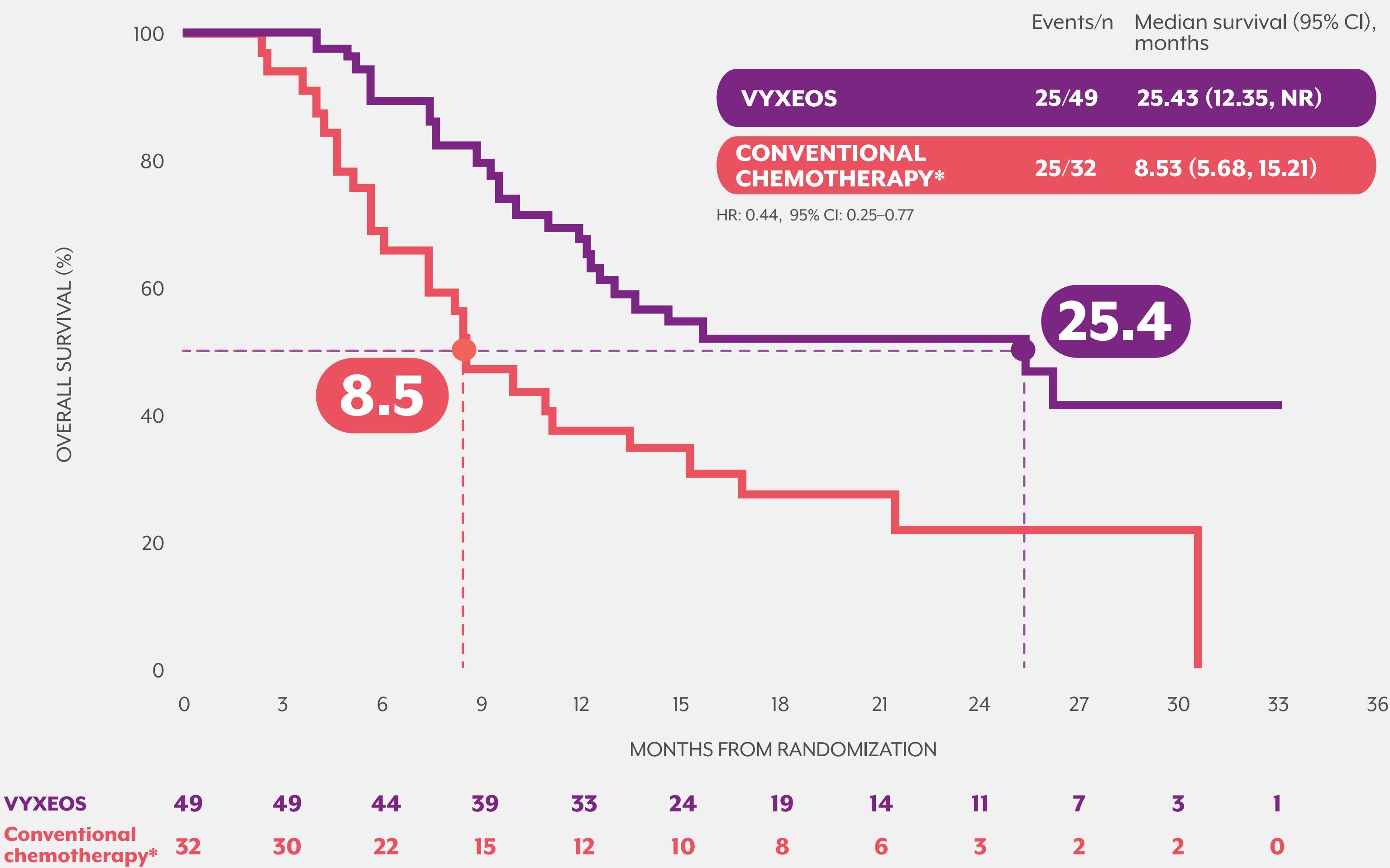
Adapted from Kolitz, *et al* (2020).

CI: Confidence interval  
HR: Hazard ratio

\* Conventional chemotherapy includes the 7+3/5+2 regimen for induction and consolidation, using cytarabine and daunorubicin.<sup>2</sup>

1. Kolitz JE, Strickland SA, Cortes JE, *et al.* Outcomes in older patients with newly diagnosed, high-risk/secondary acute myeloid leukemia (sAML) who received consolidation in a phase 3 study of CPX-351 versus conventional 7+3/5+2 cytarabine and daunorubicin. *Leuk Lymphoma* 2020;61(3):631–640.
2. Lancet JE, Uy GL, Cortes JE, *et al.* CPX-351 (cytarabine and daunorubicin) liposome for injection versus conventional cytarabine plus daunorubicin in older patients with newly diagnosed secondary acute myeloid leukemia. *J Clin Oncol* 2018;36:2684–2692.

# OVERALL SURVIVAL IN PATIENTS WHO RECEIVED INDUCTION AND CONSOLIDATION<sup>1</sup>



Adapted from Kolitz, *et al* (2020).

CI: Confidence interval  
HR: Hazard ratio  
NR: Not reached

\* Conventional chemotherapy includes the 7+3/5+2 regimen for induction and consolidation, using cytarabine and daunorubicin.<sup>2</sup>

1. Kolitz JE, Strickland SA, Cortes JE, *et al*. Outcomes in older patients with newly diagnosed, high-risk/secondary acute myeloid leukemia (sAML) who received consolidation in a phase 3 study of CPX-351 versus conventional 7+3/5+2 cytarabine and daunorubicin. *Leuk Lymphoma* 2020;61(3):631–640.  
2. Lancet JE, Uy GL, Cortes JE, *et al*. CPX-351 (cytarabine and daunorubicin) liposome for injection versus conventional cytarabine plus daunorubicin in older patients with newly diagnosed secondary acute myeloid leukemia. *J Clin Oncol* 2018;36:2684–2692.

EFFICACY RESULTS

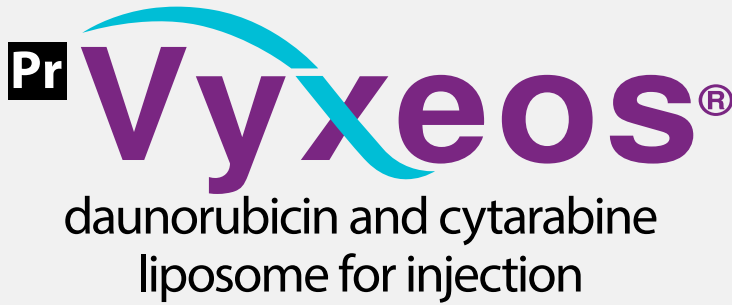
IMPROVED OS IN PATIENTS TREATED WITH VYXEOS VS CONVENTIONAL CHEMOTHERAPY AT 5 YEARS\*

OVERALL SURVIVAL BY SUBGROUP AND BASELINE CHARACTERISTICS

|                           | VYXEOS |                    | Conventional chemotherapy |                   |                       |  |
|---------------------------|--------|--------------------|---------------------------|-------------------|-----------------------|--|
| Subgroup                  | No.    | Median OS, months  | No.                       | Median OS, months | HR (95% CI) for death |  |
| ECOG PS                   |        |                    |                           |                   |                       |  |
| 0                         | 37     | 14.72 (7.00–33.58) | 45                        | 8.41 (5.13–11.07) | 0.55 (0.33–0.90)      |  |
| 1                         | 101    | 9.33 (6.37–11.60)  | 89                        | 5.55 (3.58–7.36)  | 0.67 (0.49–0.91)      |  |
| 2                         | 15     | 3.98 (1.61–6.24)   | 22                        | 5.13 (2.53–9.40)  | 1.09 (0.55–2.13)      |  |
| Karyotype                 |        |                    |                           |                   |                       |  |
| Favourable/intermediate   | 71     | 14.72 (9.07–20.96) | 63                        | 8.41 (5.13–11.07) | 0.65 (0.45–0.96)      |  |
| Poor                      | 72     | 6.42 (4.96–9.66)   | 83                        | 5.16 (3.19–7.33)  | 0.66 (0.47–0.92)      |  |
| WBC category              |        |                    |                           |                   |                       |  |
| < 20 × 10 <sup>9</sup> /L | 131    | 10.61 (7.69–13.01) | 131                       | 6.64 (5.13–8.18)  | 0.64 (0.49–0.83)      |  |
| ≥ 20 × 10 <sup>9</sup> /L | 22     | 3.60 (1.48–7.49)   | 24                        | 3.42 (1.41–7.26)  | 0.83 (0.46–1.52)      |  |
|                           |        |                    |                           |                   |                       |  |

CI: Confidence interval  
ECOG: Eastern Cooperative Oncology Group  
HR: Hazard ratio  
OS: Overall survival  
PS: Performance status  
\* Conventional chemotherapy includes the 7+3/5+2 regimen for induction and consolidation, using cytarabine and daunorubicin.

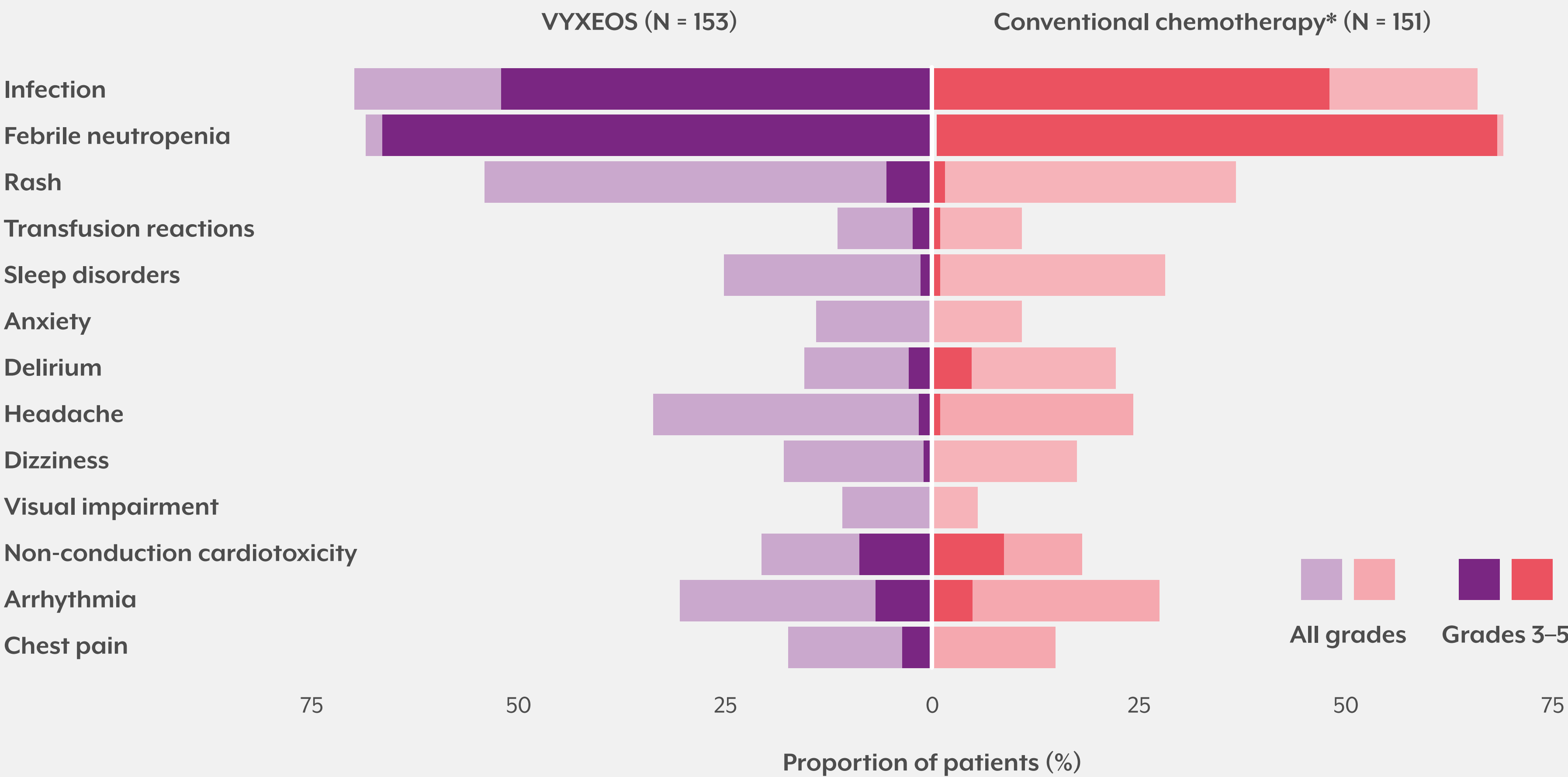
Lancet JE, Uy GL, Newell LF, *et al.* Five-year final results of a phase III study of CPX-351 versus 7+3 in older adults with newly diagnosed high-risk/secondary AML. Presented at the Congress of the European Hematological Association (EHA) 2020.



SAFETY PROFILE

OVERALL FREQUENCY AND SEVERITY OF ADVERSE EVENTS WAS COMPARABLE FOR VYXEOS AND CONVENTIONAL CHEMOTHERAPY IN HIGH-RISK AML PATIENTS<sup>1,2\*†</sup>

COMMON ADVERSE REACTIONS (≥ 10% INCIDENCE IN THE VYXEOS ARM) DURING THE INDUCTION PHASE‡



Adapted from the VYXEOS Product Monograph.

18% (28/153) of patients treated with VYXEOS discontinued treatment due to adverse events vs 13% (20/151) of patients treated with conventional chemotherapy\*

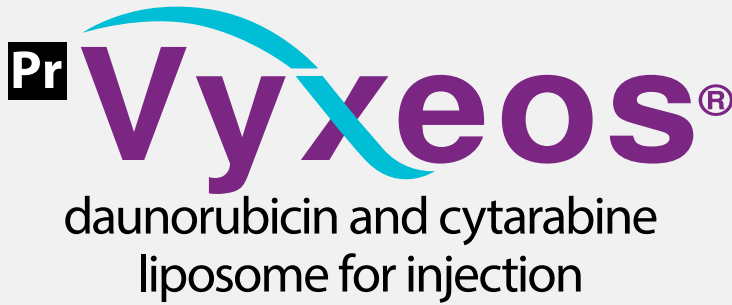
\* Conventional chemotherapy includes the 7+3/5+2 regimen for induction and consolidation, using cytarabine and daunorubicin.<sup>2</sup>

† High-risk AML defined as t-AML and AML-MRC.

‡ Adverse reactions were graded using NCI CTCAE version 3.0.<sup>1</sup>

1. Current VYXEOS® Product Monograph, Jazz Pharmaceuticals Canada, Inc.

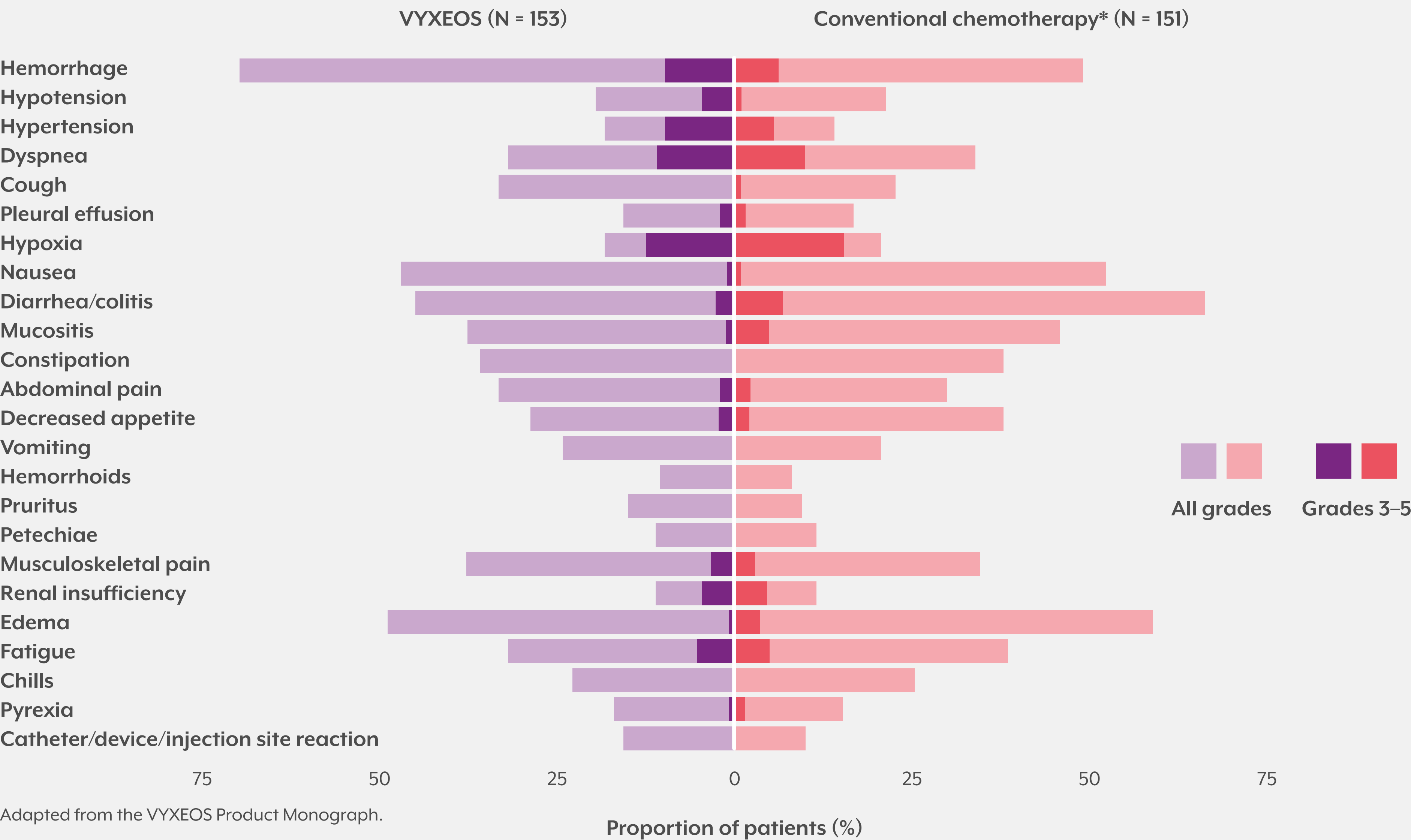
2. Lancet JE, Uy GL, Cortes JE, *et al.* CPX-351 (cytarabine and daunorubicin) liposome for injection versus conventional cytarabine plus daunorubicin in older patients with newly diagnosed secondary acute myeloid leukemia. *J Clin Oncol* 2018;36:2684–2692.



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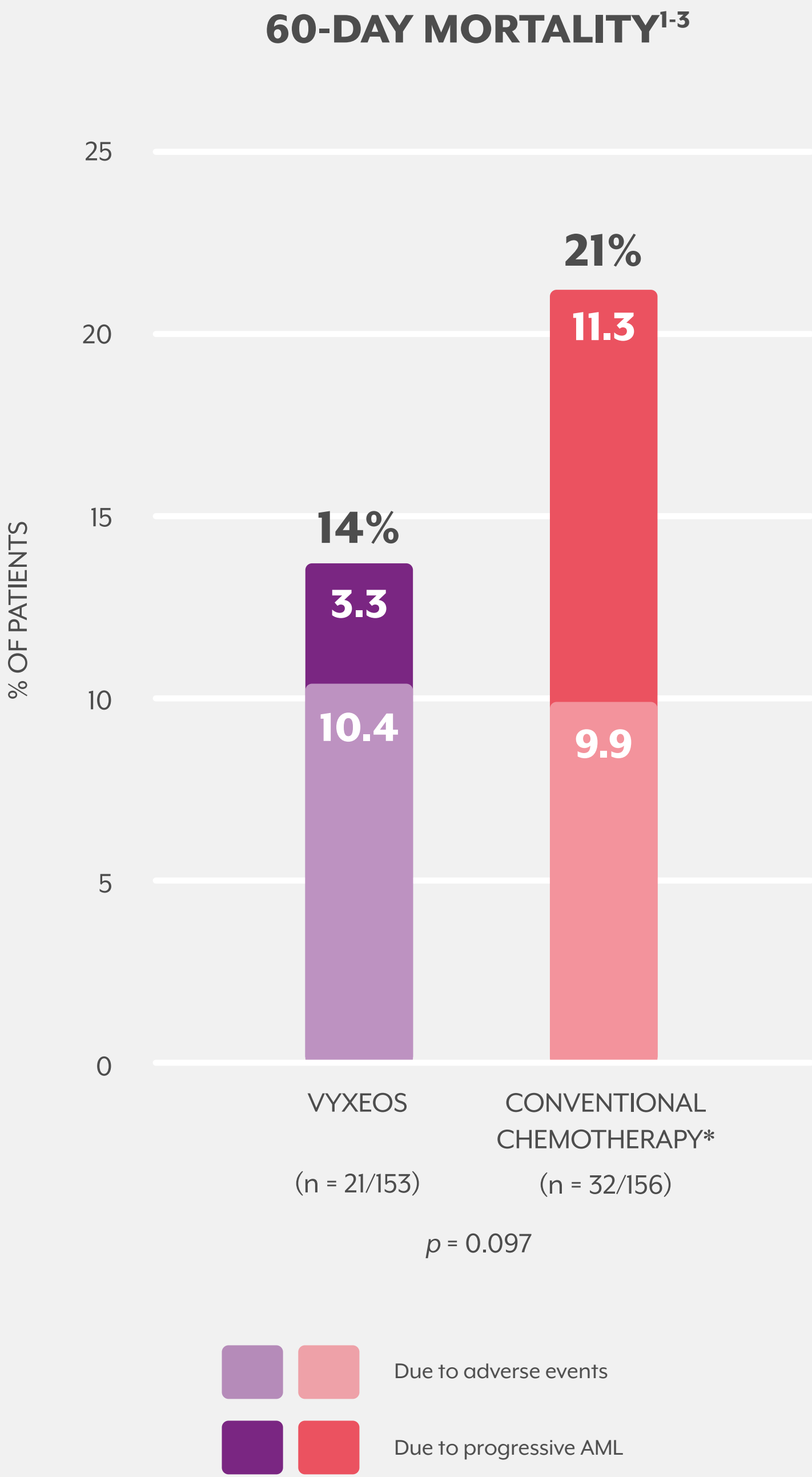
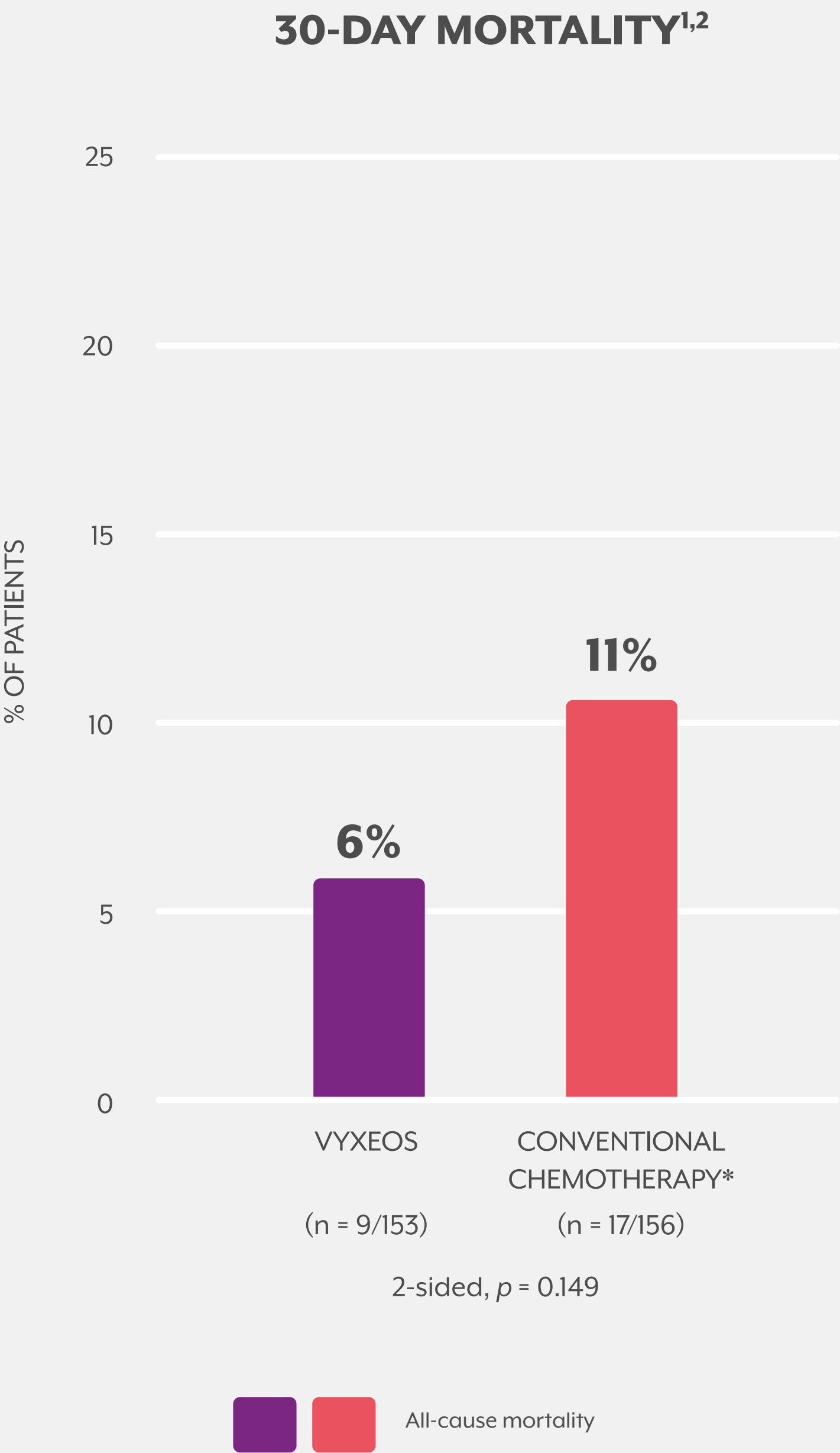
1. Current VYXEOS® Product Monograph, Jazz Pharmaceuticals Canada, Inc.

2. Lancet JE, Uy GL, Cortes JE, et al. CPX-351 (cytarabine and daunorubicin) liposome for injection versus conventional cytarabine plus daunorubicin in older patients with newly diagnosed secondary acute myeloid leukemia. *J Clin Oncol* 2018;36:2684–2692.

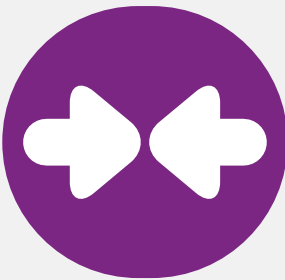


EFFICACY RESULTS

EARLY MORTALITY RATES WERE LOWER WITH VYXEOS THAN WITH CONVENTIONAL CHEMOTHERAPY<sup>1-3\*</sup>



60-day mortality due to disease progression was lower for VYXEOS than conventional chemotherapy<sup>2\*</sup>



60-day mortality due to adverse events was comparable between both arms<sup>2</sup>

Adapted from the VYXEOS Product Monograph, Lancet, *et al* (2018) and Data on File.

\* Conventional chemotherapy includes the 7+3/5+2 regimen for induction and consolidation, using cytarabine and daunorubicin.<sup>2</sup>

1. Current VYXEOS® Product Monograph, Jazz Pharmaceuticals Canada, Inc.

2. Lancet JE, Uy GL, Cortes JE, *et al*. CPX-351 (cytarabine and daunorubicin) liposome for injection versus conventional cytarabine plus daunorubicin in older patients with newly diagnosed secondary acute myeloid leukemia. *J Clin Oncol* 2018;36:2684–2692.

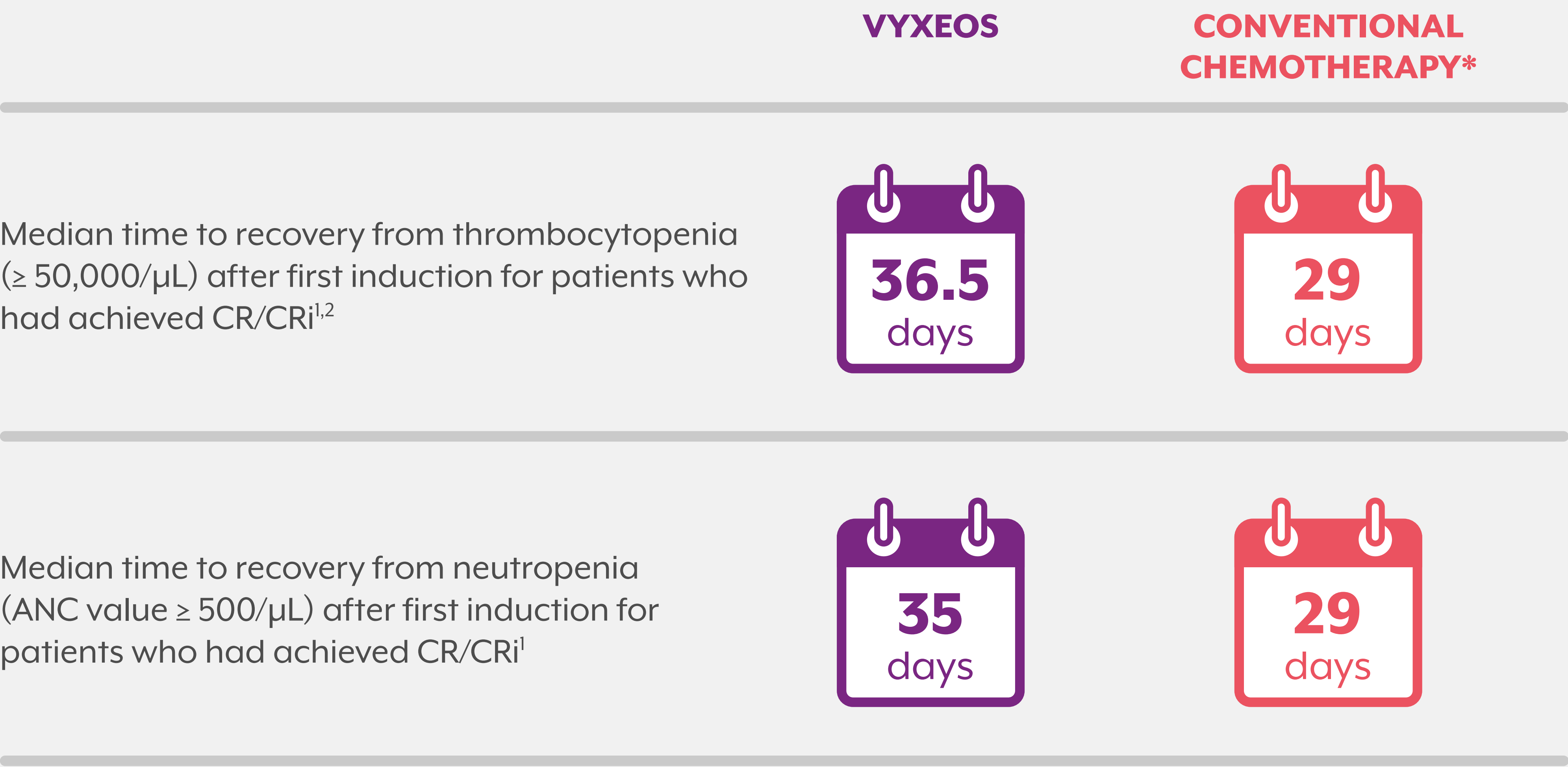
3. Jazz Pharmaceuticals. Data on File. Early mortality.



SAFETY PROFILE

THROMBOCYTOPENIA AND NEUTROPENIA WITH VYXEOS

Patients may require additional monitoring as VYXEOS is associated with prolonged thrombocytopenia and neutropenia vs conventional chemotherapy<sup>1,2\*</sup>



See data from phase 3 trial

Adapted from the VYXEOS Product Monograph and Lancet, *et al* (2018).

\* Conventional chemotherapy includes the 7+3/5+2 regimen for induction and consolidation, using cytarabine and daunorubicin.<sup>2</sup>

1. Current VYXEOS® Product Monograph, Jazz Pharmaceuticals Canada, Inc.

2. Lancet JE, Uy GL, Cortes JE, *et al*. CPX-351 (cytarabine and daunorubicin) liposome for injection versus conventional cytarabine plus daunorubicin in older patients with newly diagnosed secondary acute myeloid leukemia. *J Clin Oncol* 2018;36:2684–2692.



# PROLONGED CYTOPENIAS FOR PATIENTS IN THE PHASE 3 TRIAL<sup>1</sup>



|                                         | INDUCTION 1     |                                        | CONSOLIDATION 1* |                                        |
|-----------------------------------------|-----------------|----------------------------------------|------------------|----------------------------------------|
|                                         | VYXEOS          | CONVENTIONAL CHEMOTHERAPY <sup>†</sup> | VYXEOS           | CONVENTIONAL CHEMOTHERAPY <sup>†</sup> |
|                                         | n = 58<br>n (%) | n = 34<br>n (%)                        | n = 48<br>n (%)  | n = 32<br>n (%)                        |
| PROLONGED THROMBOCYTOPENIA <sup>‡</sup> | 16 (28)         | 4 (12)                                 | 12 (25)          | 5 (16)                                 |
| PROLONGED NEUTROPENIA <sup>‡</sup>      | 10 (17)         | 1 (3)                                  | 5 (10)           | 1 (3)                                  |

Adapted from the VYXEOS Product Monograph.

\* Patients receiving at least one consolidation.  
† Conventional chemotherapy includes the 7+3/5+2 regimen for induction and consolidation, using cytarabine and daunorubicin.<sup>2</sup>  
‡ Platelets < 50 Gi/LW or neutrophils < 0.5 Gi/L lasting past cycle day 42 in the absence of active leukemia.<sup>1</sup>

1. Current VYXEOS® Product Monograph, Jazz Pharmaceuticals Canada, Inc.  
2. Lancet JE, Uy GL, Cortes JE, *et al.* CPX-351 (cytarabine and daunorubicin) liposome for injection versus conventional cytarabine plus daunorubicin in older patients with newly diagnosed secondary acute myeloid leukemia. *J Clin Oncol* 2018;36:2684–2692.

DOSING AND ADMINISTRATION

VYXEOS CAN BE ADMINISTERED IN 90-MINUTE INFUSIONS FOR BOTH INDUCTION AND CONSOLIDATION IN ADULTS WITH HIGH-RISK AML\*

RECOMMENDED DOSING SCHEDULE

FIRST INDUCTION

Days 1 3 5

Daunorubicin 44 mg/m<sup>2</sup> and cytarabine 100 mg/m<sup>2</sup>



SECOND INDUCTION + CONSOLIDATION†

Days 1 3

Second induction: Daunorubicin 44 mg/m<sup>2</sup> and cytarabine 100 mg/m<sup>2</sup>

Consolidation: Daunorubicin 29 mg/m<sup>2</sup> and cytarabine 65 mg/m<sup>2</sup>

Adapted from the VYXEOS Product Monograph.



Treatment should be continued as long as patients continue to benefit or until disease progression, up to a maximum of 2 induction and 2 consolidation courses

Click to watch  
how to prepare  
VYXEOS

Dosing should be delayed or permanently discontinued, if necessary. For more information about dosing and administration, please [click here](#) to see the Product Monograph.

\* High-risk AML defined as t-AML or AML-MRC.  
† Administered as subsequent course of therapy if needed.  
Current VYXEOS® Product Monograph, Jazz Pharmaceuticals Canada, Inc.

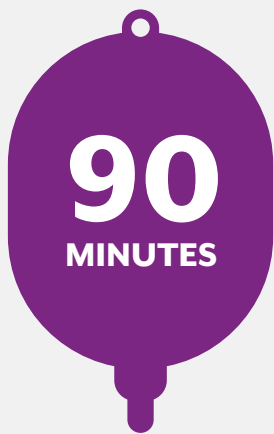


DOSING AND ADMINISTRATION

VYXEOS REDUCES THE LENGTH OF INFUSION TIME FOR YOUR PATIENTS

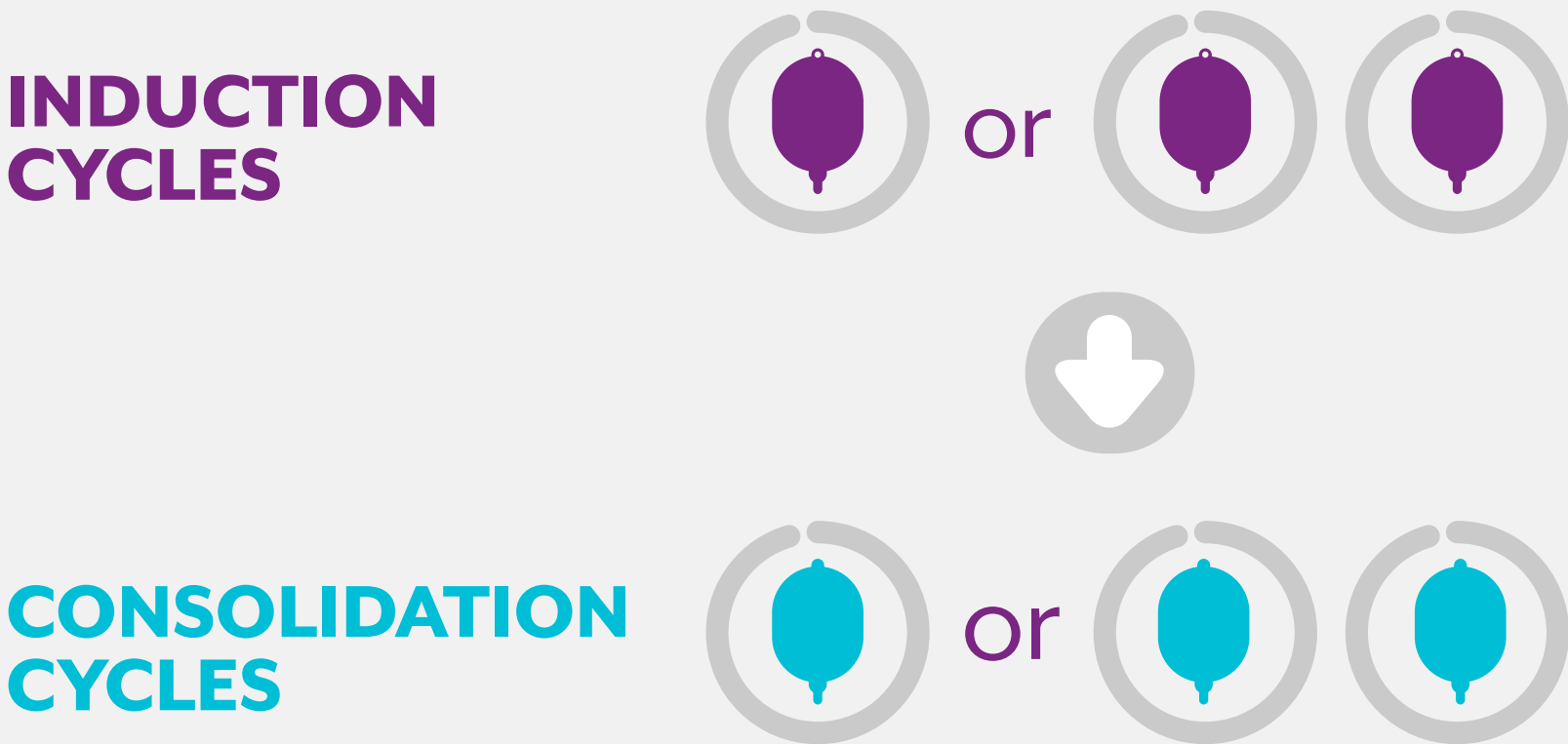
ESTIMATED TOTAL HOURS SPENT RECEIVING INFUSIONS PER CYCLE<sup>1-7,\*</sup>

|                  | VYXEOS                   | CONVENTIONAL CHEMOTHERAPY |                           |                         |
|------------------|--------------------------|---------------------------|---------------------------|-------------------------|
|                  |                          | 7+3/5+2                   | FLAG-IDA                  | HDAC                    |
| INDUCTION        | 4.5 hours<br>over 5 days | 168 hours<br>over 7 days  | 27 hours<br>over 5 days   | 18 hours<br>over 5 days |
| SECOND INDUCTION | 3 hours<br>over 3 days   | 120 hours<br>over 5 days  | 27 hours<br>over 5 days   | 18 hours<br>over 5 days |
| CONSOLIDATION    | 3 hours<br>over 3 days   | 120 hours<br>over 5 days  | 24.5 hours<br>over 4 days | 18 hours<br>over 5 days |



VYXEOS PROVIDED THE GREATEST BENEFIT WHEN USED FOR BOTH INDUCTION AND CONSOLIDATION THERAPY<sup>2</sup>

A full course of VYXEOS consists of up to 2 cycles of induction and up to 2 cycles of consolidation<sup>1</sup>



Adapted from the VYXEOS Product Monograph, Lancet, *et al* (2018) and Kolitz, *et al* (2020).

FLAG-IDA: Fludarabine, cytarabine and idarubicin  
HDAC: High-dose cytarabine  
\* Based on 3/2 x 90-minute infusion schedules for VYXEOS and 7/5-day continuous infusion schedule for conventional chemotherapy.

1. Current VYXEOS® Product Monograph, Jazz Pharmaceuticals Canada, Inc.

2. Lancet JE, Uy GL, Cortes JE, *et al*. CPX-351 (cytarabine and daunorubicin) liposome for injection versus conventional cytarabine plus daunorubicin in older patients with newly diagnosed secondary acute myeloid leukemia. *J Clin Oncol* 2018;36:2684–2692.

3. Kolitz JE, Strickland SA, Cortes JE, *et al*. Outcomes in older patients with newly diagnosed, high-risk/secondary acute myeloid leukemia (sAML) who received consolidation in a phase 3 study of CPX-351 versus conventional 7+3/5+2 cytarabine and daunorubicin. *Leuk Lymphoma* 2020;61:631–640.

4. University Health Network. Princess Margaret Cancer Centre clinical practice guidelines: Acute myeloid leukemia. Accessed June 2023 at: [https://www.uhn.ca/PrincessMargaret/Health\\_Professionals/Programs\\_Departments/Leukemia/Documents/CPG\\_Leukemia\\_AcuteMyeloidLeukemia.pdf](https://www.uhn.ca/PrincessMargaret/Health_Professionals/Programs_Departments/Leukemia/Documents/CPG_Leukemia_AcuteMyeloidLeukemia.pdf).

5. Virchis A, Koh M, Rankin P, *et al*. Fludarabine, cytosine arabinoside, granulocyte-colony stimulating factor with or without idarubicin in the treatment of high risk acute leukaemia or myelodysplastic syndromes. *Br J Haematol* 2004;124:26–32.

6. Alberta Health Services. High dose cytarabine: AML, adult cancer inpatient order set. Accessed June 2023 at: <https://extranet.ahsnet.ca/teams/policydocuments/1/klink/et-klink-ckv-high-dose-cytarabine-aml-adult-cancer-order-set-inpatient.pdf>.

7. Alberta Health Services. Clinical practice guideline: Acute myeloid leukemia. Accessed June 2023 at: <https://www.albertahealthservices.ca/assets/info/hp/cancer/if-hp-cancer-guide-lyhe006-aml.pdf>.

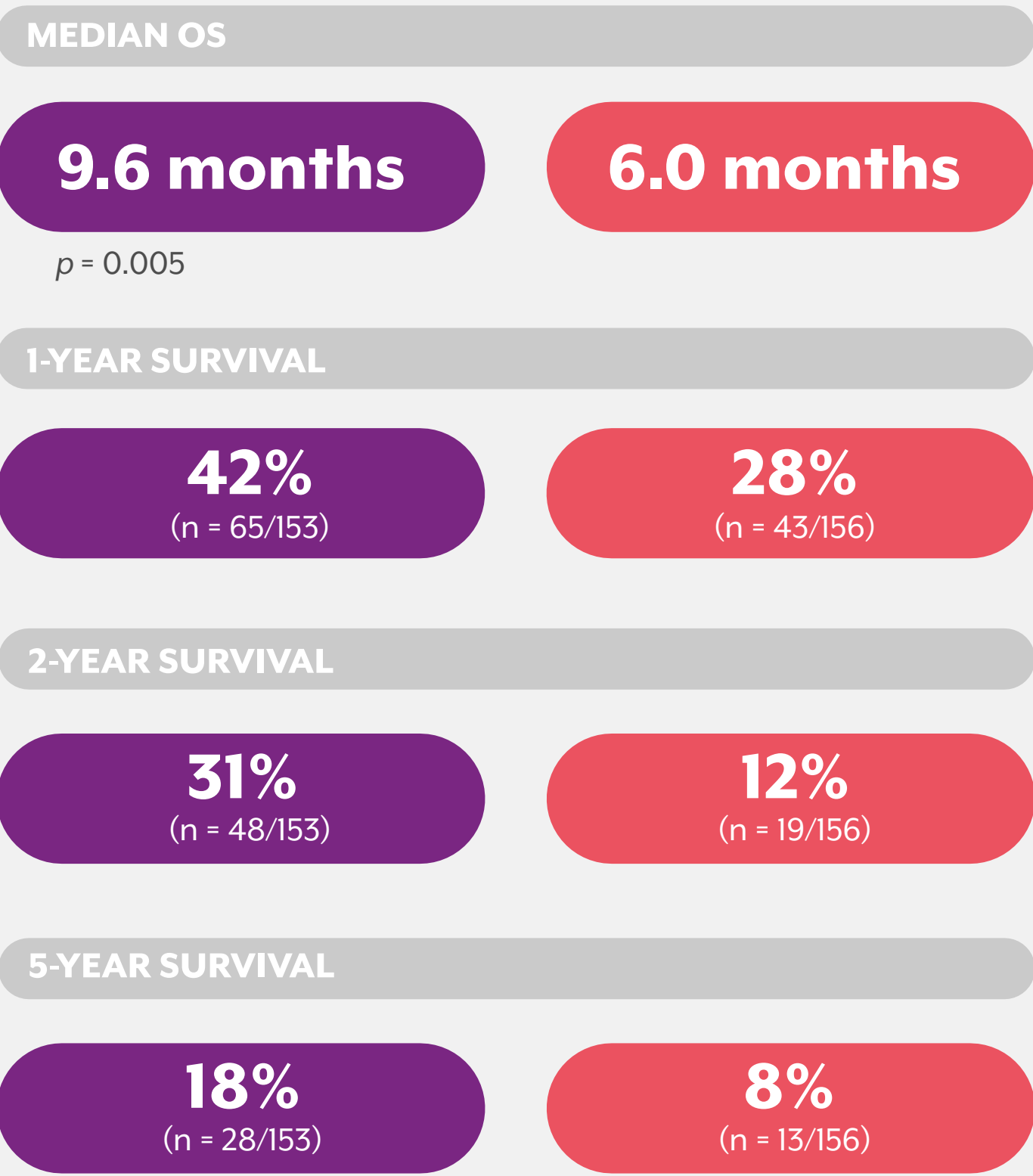


SUMMARY

DISCOVER VYXEOS FOR YOUR HIGH-RISK AML PATIENTS\*

Designed to optimize the delivery of daunorubicin and cytarabine through synergistic activity<sup>1</sup>

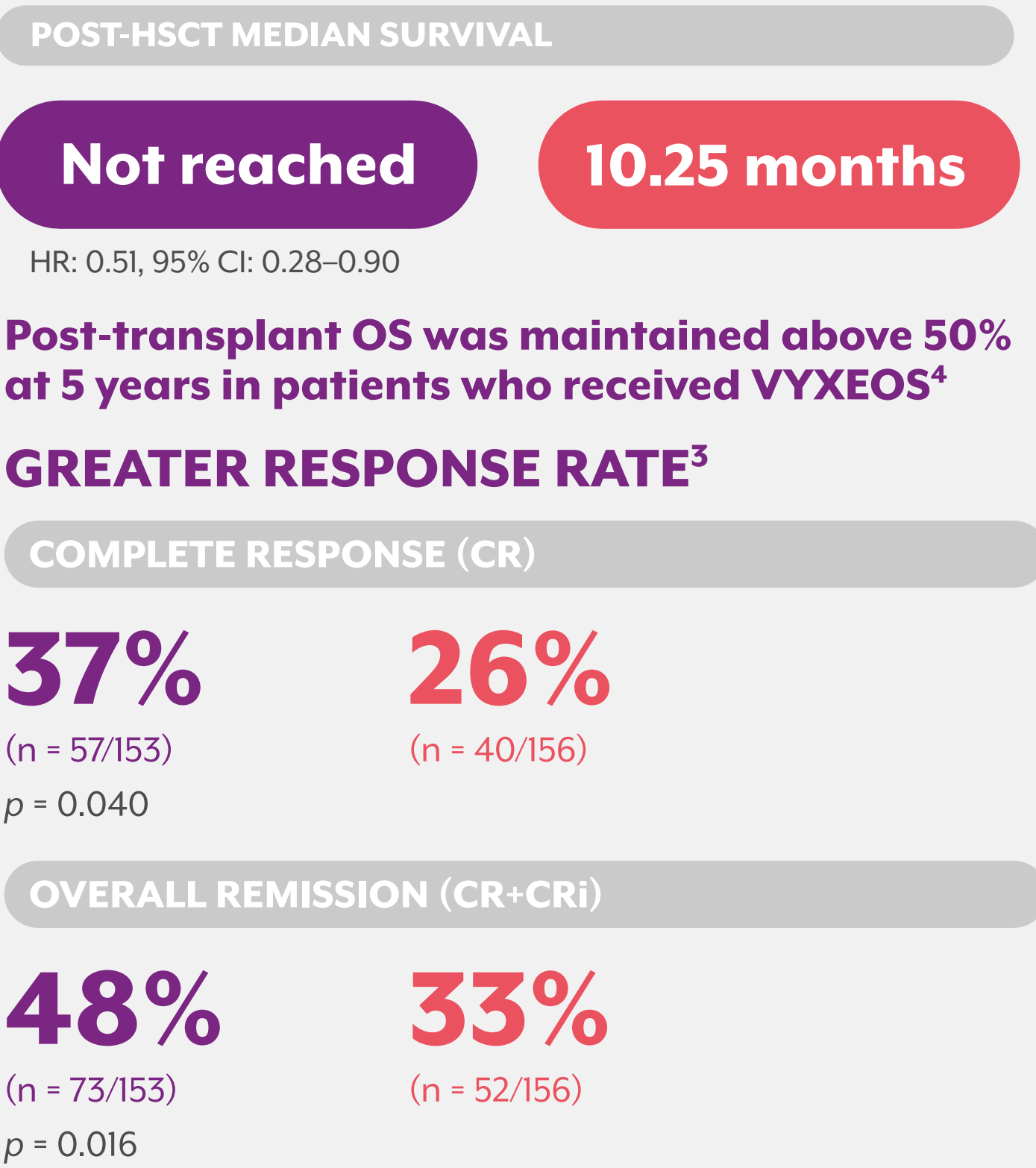
GREATER SURVIVAL<sup>2,3</sup>



VYXEOS

Conventional chemotherapy<sup>†</sup>

LONGER POST-TRANSPLANT SURVIVAL<sup>3</sup>



CRi: Complete response with incomplete platelet or neutrophil recovery  
HSCT: Hematopoietic stem cell transplantation  
\* High-risk AML defined as t-AML or AML-MRC.  
<sup>†</sup> Conventional chemotherapy includes the 7+3/5+2 regimen for induction and consolidation, using cytarabine and daunorubicin.<sup>2</sup>

1. Tolcher AW, Mayer LD. Improving combination cancer therapy: the CombiPlex® development platform. *Future Oncol* 2018;14:1317–1332.

2. Lancet JE, Uy GL, Cortes JE, *et al*. CPX-351 (cytarabine and daunorubicin) liposome for injection versus conventional cytarabine plus daunorubicin in older patients with newly diagnosed secondary acute myeloid leukemia. *J Clin Oncol* 2018;36:2684–2692.

3. Current VYXEOS® Product Monograph, Jazz Pharmaceuticals Canada, Inc.

4. Lancet JE, Uy GL, Newell LF, *et al*. Five-year final results of a phase III study of CPX-351 versus 7+3 in older adults with newly diagnosed high-risk/secondary AML. Presented at the Congress of the European Hematological Association (EHA) 2020.

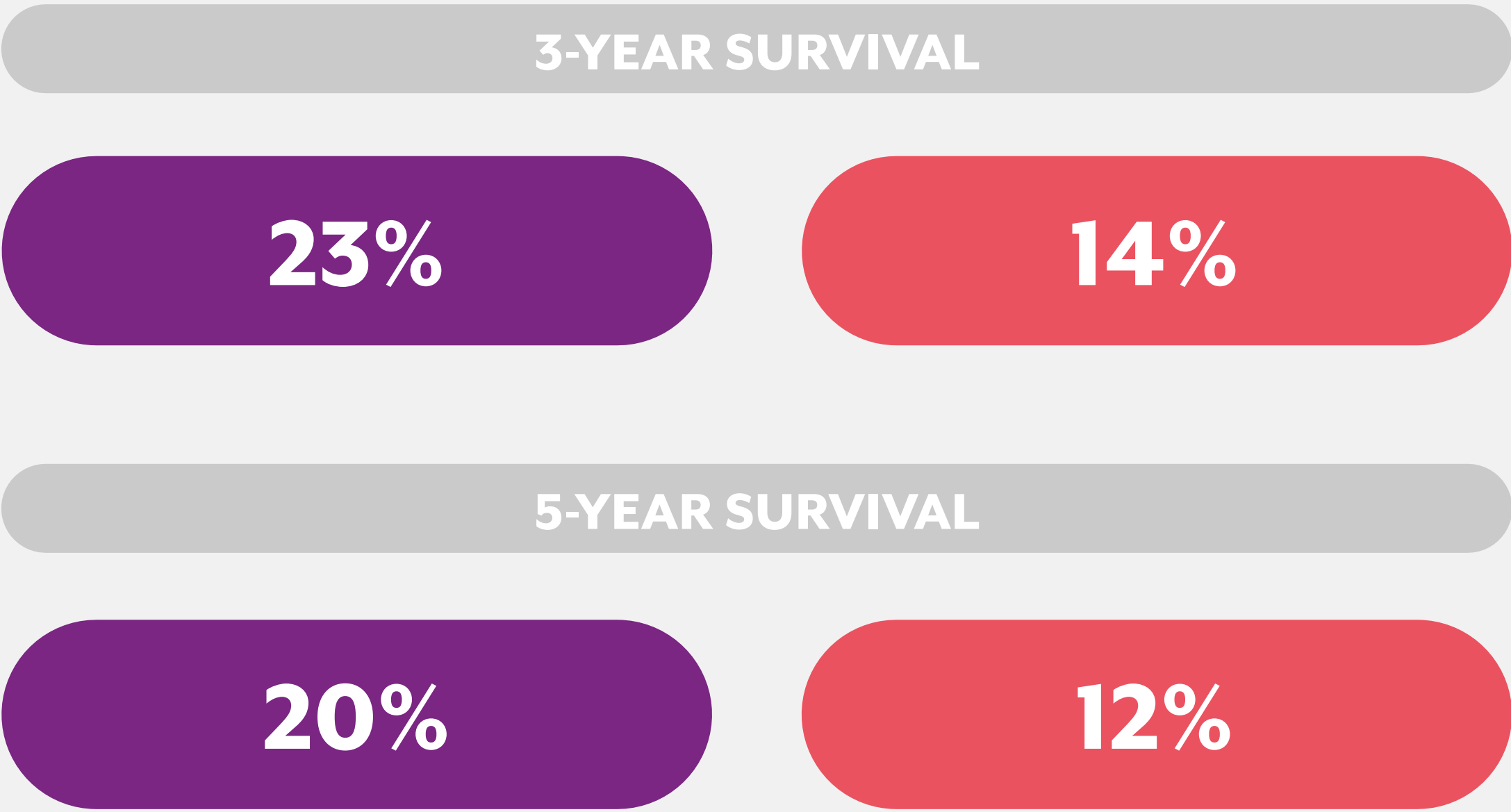
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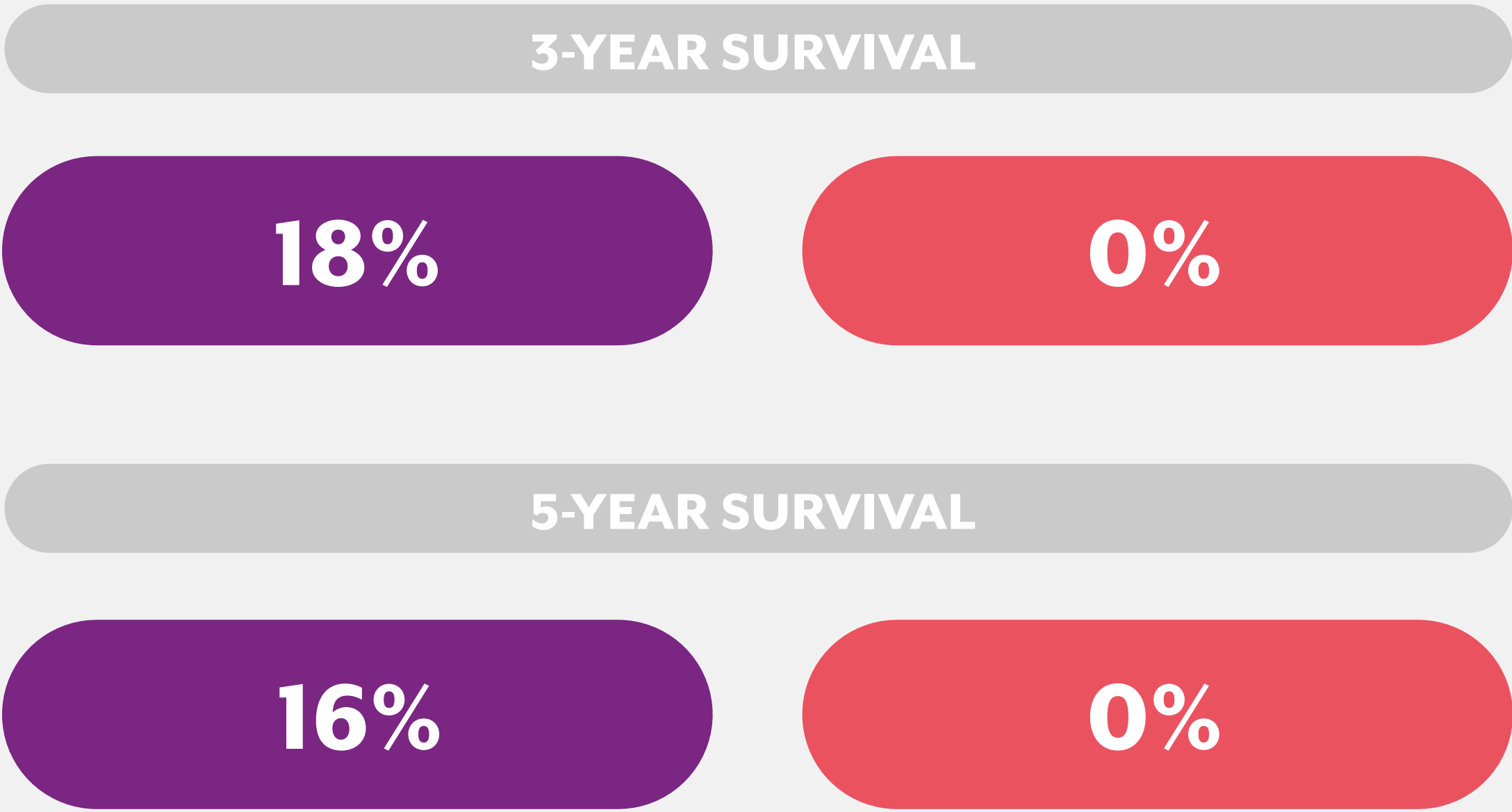
IMPROVED SURVIVAL MAINTAINED  
OVER A LONGER TERM IN PATIENTS OVER 60

IN PATIENTS OF 60–69 YEARS<sup>2</sup>



HR: 0.73, 95% CI: 0.54–0.99

IN PATIENTS OF 70–75 YEARS

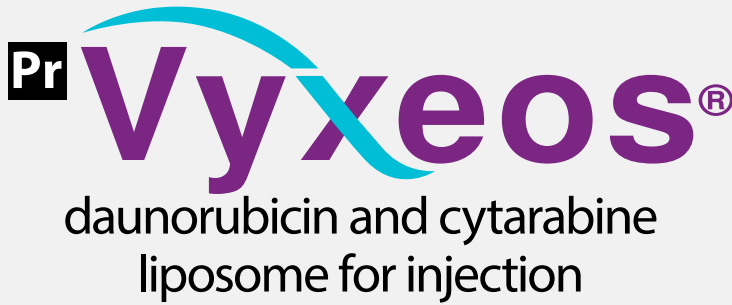


HR: 0.52, 95% CI: 0.34–0.7

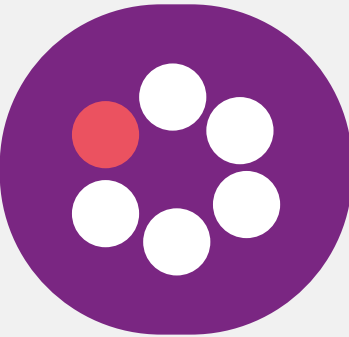
VYXEOS    Conventional chemotherapy<sup>†</sup>

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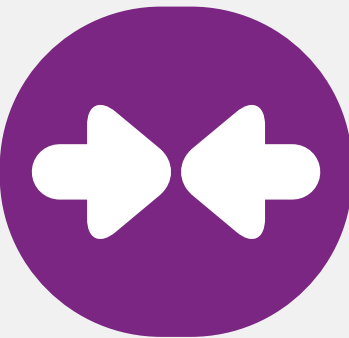
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2. Jazz Pharmaceuticals. Data on File. Five-year results of a randomized, open-label, phase 3 trial of CPX-351 vs 7+3 chemotherapy in older adults with newly diagnosed high-risk/secondary AML.  
3. Lancet JE, Uy GL, Newell LF, *et al*. Five-year final results of a phase III study of CPX-351 versus 7+3 in older adults with newly diagnosed high-risk/secondary AML. Presented at the Congress of the European Hematological Association (EHA) 2020.



# GREATER THAN THE SUM OF ITS PARTS<sup>1</sup>



VYXEOS IS THE FIRST DUAL-DRUG ADVANCED LIPOSOMAL FORMULATION<sup>1</sup>



VYXEOS HAS A DEMONSTRATED SAFETY PROFILE IN ADULT PATIENTS WITH HIGH-RISK AML<sup>2†</sup>

90 minute

INDUCTION



CONSOLIDATION

REDUCED INFUSION TIME VS CONVENTIONAL CHEMOTHERAPY\*  
USING A 90-MINUTE INFUSION SCHEDULE FOR BOTH  
INDUCTION AND CONSOLIDATION<sup>2</sup>



\* Conventional chemotherapy includes the 7+3/5+2 regimen for induction and consolidation, using cytarabine and daunorubicin.<sup>2</sup>  
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1. Tolcher AW, Mayer LD. Improving combination cancer therapy: the CombiPlex® development platform. *Future Oncol* 2018;14:1317–1332.  
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Clinical use:

**Pediatrics (< 18 years):** The safety and effectiveness of VYXEOS in the treatment of newly diagnosed t-AML and AML-MRC has not been established in children and adolescent patients under 18 years of age.

**Geriatrics (≥ 65 years of age):** No significant differences in safety were observed in patients aged 65 or older.

**Serious warnings and precautions:** VYXEOS has different dosage recommendations than daunorubicin hydrochloride injection, cytarabine injection, daunorubicin citrate liposome injection, and cytarabine liposome injection. Verify drug name and dose prior to preparation and administration to avoid dosing errors.

Relevant warnings and precautions:

- VYXEOS must not be substituted or interchanged with other daunorubicin and/or cytarabine-containing products
- Tissue necrosis
- Cardiotoxicity is a known risk of anthracycline treatment
- Driving and operating machinery
- VYXEOS should be used in patients with a history of Wilson’s disease or other copper-related disorder only if the benefits outweigh the risks. Discontinue VYXEOS in patients with signs or symptoms of acute copper toxicity
- Gastrointestinal mucositis and diarrhea
- Hematologic: Severe myelosuppression resulting in fatal infections and hemorrhage has been reported in patients after administration with VYXEOS. Patient blood counts should be regularly monitored during VYXEOS treatment and appropriate supportive measures should be used for clinical complications due to myelosuppression

- Hepatic impairment may increase the risk of toxicity associated with daunorubicin and cytarabine. Evaluation of hepatic function using conventional clinical laboratory tests is recommended prior to administration of VYXEOS and periodically during treatment. VYXEOS should only be used in patients with severe hepatic impairment if the benefits outweigh the risks
- Serious hypersensitivity reactions including anaphylactic reactions have been reported with daunorubicin and cytarabine
- Increased susceptibility to infections
- Renal impairment may increase the risk of toxicity associated with daunorubicin and cytarabine. Evaluation of renal function using conventional clinical laboratory tests is recommended prior to administration of VYXEOS and periodically during treatment. VYXEOS should only be used in patients with end-stage renal disease if the benefits outweigh the risks
- Cardiac function and blood uric acid levels should be closely monitored. Appropriate therapy should be initiated if hyperuricemia develops
- Pregnancy: There are no data on the use of VYXEOS in pregnant women. Patients should be advised to avoid becoming pregnant during VYXEOS treatment. Male patients and women of childbearing potential must use effective methods of contraception during treatment and for 6 months following last dose of VYXEOS
- Male fertility may be compromised by treatment with VYXEOS according to animal studies
- Nursing women should be advised not to breastfeed during treatment with VYXEOS

For more information:

Consult the VYXEOS Product Monograph at: [www.jazzpharma.com](http://www.jazzpharma.com) for important information relating to adverse reactions, drug interactions, and dosing information that have not been discussed in this piece.

The Product Monograph is also available by calling our medical department at: 1-800-520-5568.

VYXEOS® is a registered trademark of Celator Pharmaceuticals, Inc. (a Jazz Pharmaceuticals subsidiary).

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