Proudly Canadian

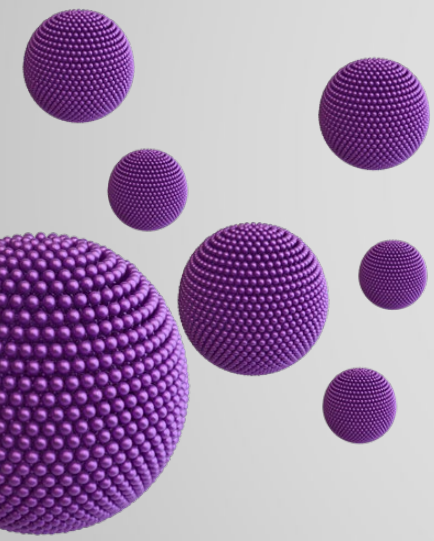
Pr Vyxeos®

daunorubicin and cytarabine liposome for injection

GREATER THAN THE SUM OF ITS PARTS

TOGETHER

The first dual-drug advanced liposomal formulation[1]



LONGER

Superior overall survival in patients with high-risk AML[2,3]*

Median overall survival: 9.6 months with VYXEOS vs 6 months with conventional chemotherapy†

(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)[2,3‡]

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).[3]

* 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.[2]

‡ 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 evaluating the efficacy and safety of VYXEOS in adults with newly diagnosed high-risk sAML.[2,3]

VYXEOS

THE FIRST DUAL-DRUG ADVANCED LIPOSOMAL FORMULATION[1]

Optimizing the delivery of daunorubicin and cytarabine[2]

SYNERGISTIC RATIO

Fixed 1:5 molar ratio of daunorubicin and cytarabine within an advanced liposomal formulation[3]

PROLONGED

Synergistic molar ratio maintained for a prolonged period of time – over 24 hours after administration[3]

HIGH CONCENTRATION

VYXEOS accumulates and persists in the bone marrow in high concentrations[3]*

PREFERENTIAL UPTAKE

VYXEOS is preferentially taken up by leukemia cells vs normal bone marrow cells[3]†

Adapted from the VYXEOS Product Monograph.

Scan to watch VYXEOS in action

Proudly Canadian

Formulated to optimize the synergistic activity of daunorubicin and cytarabine[2]

Designed using the CombiPlex® Platform by Celator Pharmaceuticals in Vancouver, BC (now a subsidiary of Jazz Pharmaceuticals)

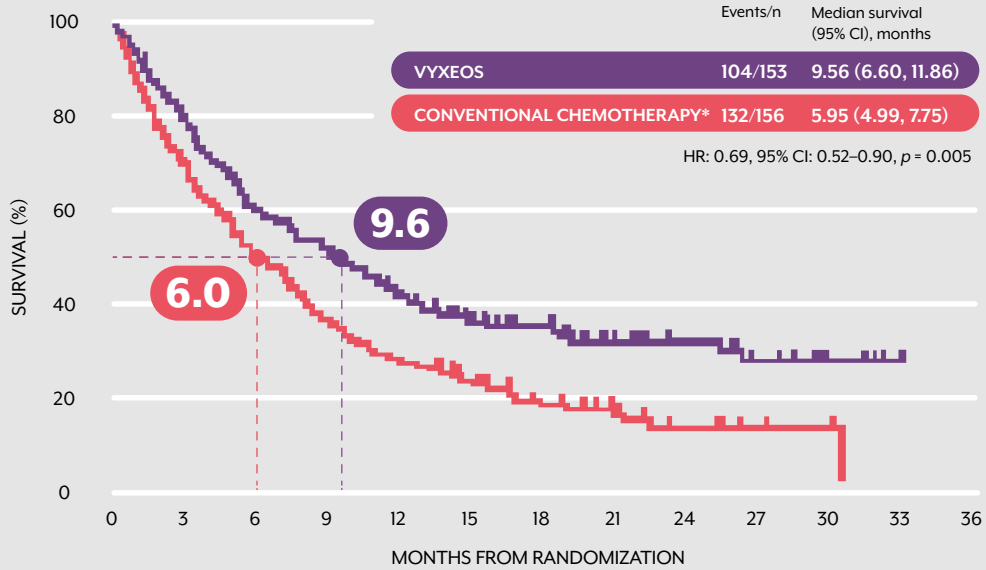
Tested in pre-clinical and clinical trials across multiple Canadian sites

BC: British Columbia
* As shown in animal models.
† As shown *in vitro*.

VYXEOS DEMONSTRATED SUPERIORITY IN OVERALL SURVIVAL COMPARED TO CONVENTIONAL CHEMOTHERAPY IN PATIENTS AGED 60–75 WITH HIGH-RISK AML[3*†]

PRIMARY ENDPOINT

OVERALL SURVIVAL IN THE ITT POPULATION[3]



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

Adapted from the VYXEOS Product Monograph.

31% Reduction in the relative risk of death for patients treated with VYXEOS vs conventional chemotherapy[2,3*]

ITT: Intent-to-treat
CI: Confidence interval
HR: Hazard ratio
* Conventional chemotherapy includes the 7+3/5+2 regimen for induction and consolidation, using cytarabine and daunorubicin.[2]
† High-risk AML defined as t-AML or AML-MRC.

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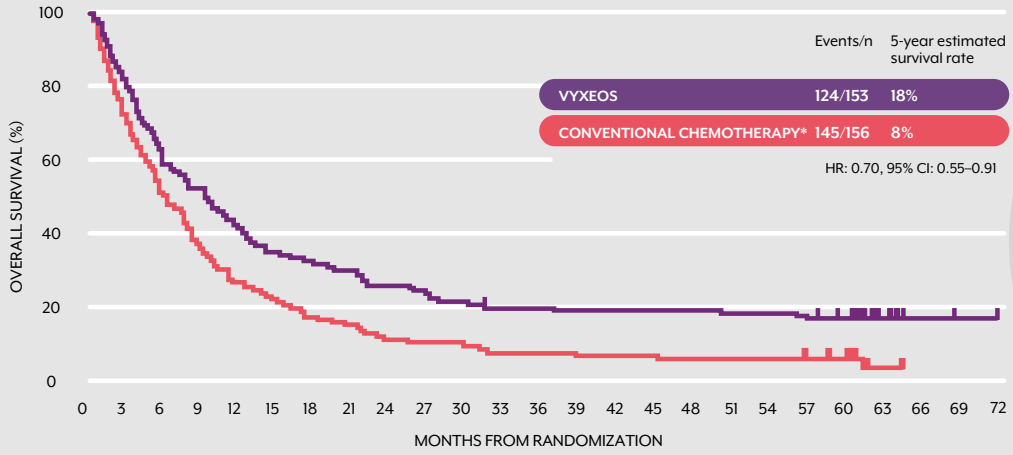
44 mg / 100 mg

IMPROVED OVERALL SURVIVAL WAS MAINTAINED IN PATIENTS TREATED WITH VYXEOS VS CONVENTIONAL CHEMOTHERAPY* AFTER A 5-YEAR FOLLOW-UP[3,4]

OVERALL SURVIVAL: 5-YEAR RESULTS[3,4]



More than twice as many patients treated with VYXEOS were alive after 5 years than those treated with conventional chemotherapy[3]*

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

SECONDARY ENDPOINT

Patients receiving VYXEOS achieved significantly greater response rates and overall remission vs conventional chemotherapy[3]*

COMPLETE RESPONSE (CR)

37% (n = 57/153) **26%** (n = 40/156)

HR: 1.69, 95% CI: 1.03–2.78
p = 0.040

OVERALL REMISSION (CR+CRi)

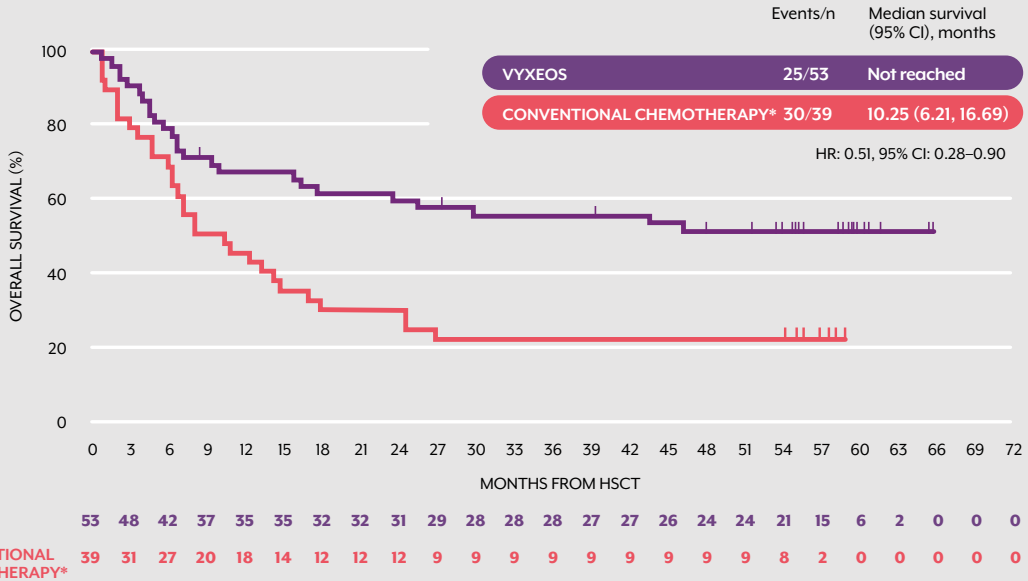
48% (n = 73/153) **33%** (n = 52/156)

HR: 1.77, 95% CI: 1.11–2.81
p = 0.016

HR: Hazard ratio
CI: Confidence interval
CRi: Complete response with incomplete platelet or neutrophil recovery
* Conventional chemotherapy includes the 7+3/5+2 regimen for induction and consolidation, using cytarabine and daunorubicin.[2]

POST-HOC ANALYSIS SUGGESTS THAT OVERALL SURVIVAL WAS MAINTAINED ABOVE 50% AT 5 YEARS IN PATIENTS WHO RECEIVED VYXEOS AND UNDERWENT HSCT[3,4]

OVERALL SURVIVAL LANDMARKED FROM DATE OF HSCT[3,4]



HSCT WAS REACHED BY 35% OF PATIENTS
treated with VYXEOS
(n = 53/153)
vs
25% OF PATIENTS
receiving conventional chemotherapy*
(n = 39/151)[3]

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

The median overall survival was over one year for patients treated with VYXEOS who achieved CR or CRi but did not undergo HSCT[5]

LONGER OVERALL SURVIVAL WITHOUT HSCT

Median OS

14.7 months | **7.6 months**

HR: 0.57, 95% CI: 0.31–1.03

49%

REDUCED RELATIVE RISK OF DEATH FOR PATIENTS RECEIVING TRANSPLANT WHEN TREATED WITH VYXEOS VS CONVENTIONAL CHEMOTHERAPY[2,3]*

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.[2]

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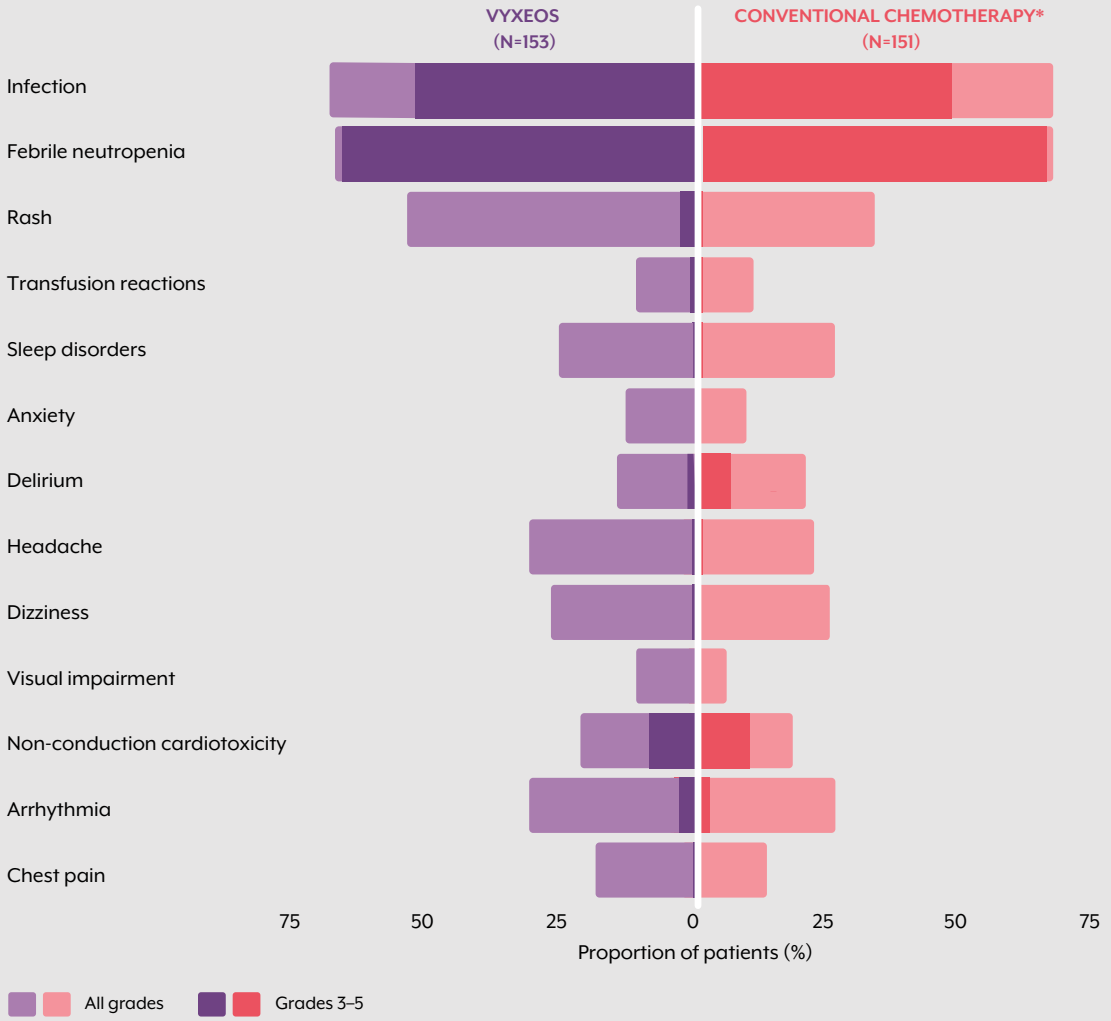
OVERALL FREQUENCY AND SEVERITY OF ADVERSE EVENTS WAS COMPARABLE FOR VYXEOS AND CONVENTIONAL CHEMOTHERAPY IN HIGH-RISK AML PATIENTS[3]*†

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



Adapted from the VYXEOS Product Monograph.

* Conventional chemotherapy includes the 7+3/5+2 regimen for induction and consolidation, using cytarabine and daunorubicin.[2]
† High-risk AML defined as t-AML or AML-MRC.
‡ Adverse reactions were graded using NCI CTCAE version 3.0.[3]

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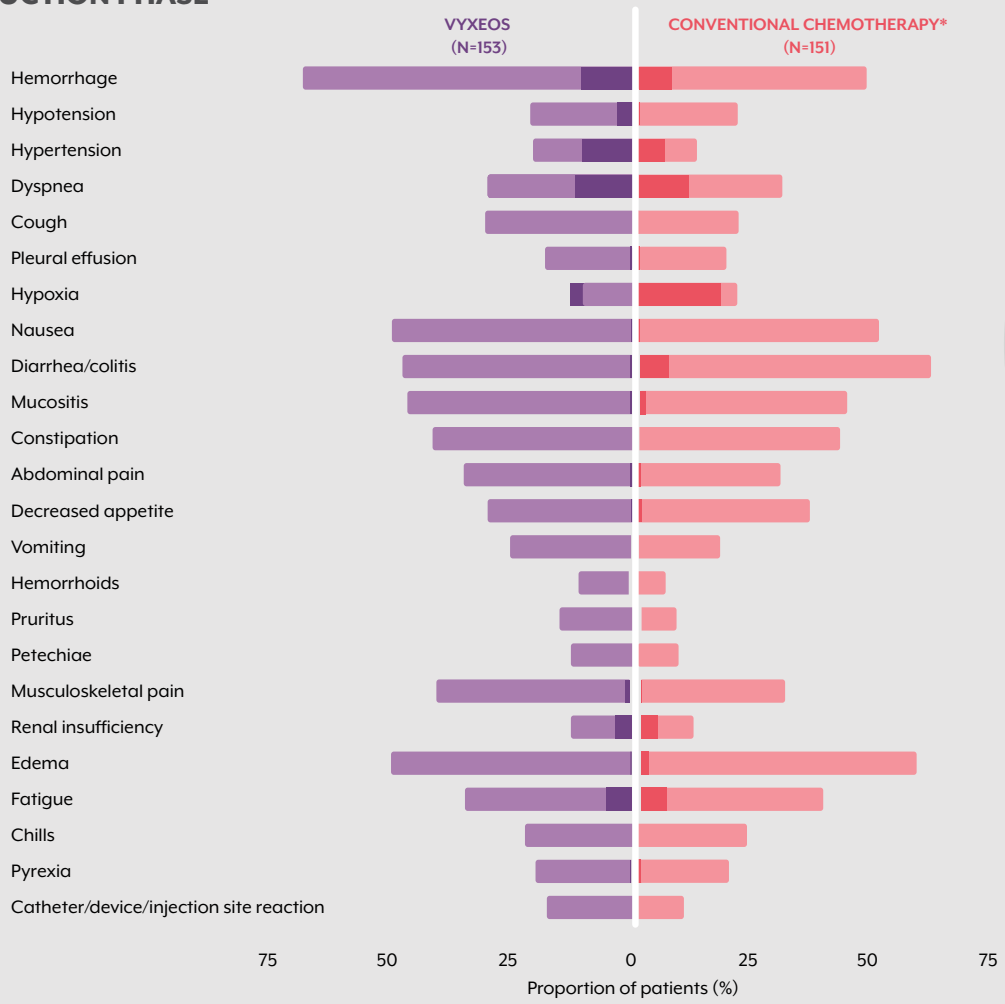

Adapted from the VYXEOS Product Monograph.

Patients treated with VYXEOS displayed lower 60-day mortality rates related to disease progression vs conventional chemotherapy[6*]

* Conventional chemotherapy includes the 7+3/5+2 regimen for induction and consolidation, using cytarabine and daunorubicin.[2]
† High-risk AML defined as t-AML or AML-MRC.
‡ Adverse reactions were graded using NCI CTCAE version 3.0.[3]

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VYXEOS CAN BE ADMINISTERED FOR BOTH INDUCTION AND CONSOLIDATION IN ADULT PATIENTS WITH HIGH-RISK AML[3]*

INDUCTION + **CONSOLIDATION**

INDUCTION CYCLES → **CONSOLIDATION CYCLES**

or or

FIRST INDUCTION

Days 1 3 5

Daunorubicin 44 mg/m² and cytarabine 100 mg/m²

Treatment should be continued as long as patients continue to benefit or until disease progression, up to a maximum of 2 courses for induction and consolidation each.[3]

SECOND INDUCTION + CONSOLIDATION

Days 1 3

Second induction: Daunorubicin 44 mg/m² and cytarabine 100 mg/m²

Consolidation: Daunorubicin 29 mg/m² and cytarabine 65 mg/m²

Reduce infusion time with a 90-minute infusion for your high-risk AML patients.[3]*

Adapted from the VYXEOS Product Monograph.

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

PREPARATION AND ADMINISTRATION[3]

Calculate VYXEOS dose based on patient's BSA and determine the number of vials required.

Remove the vials of VYXEOS from the refrigerator and **equilibrate** at room temperature for 30 minutes.

DO NOT HEAT

Reconstitute each vial with 19 mL of sterile water for injections using a 20 mL sterile syringe and start a 5-minute timer immediately. **Carefully swirl the contents** of the vial for 5 minutes while gently inverting the vial every 30 seconds.

Rest for 15 minutes after reconstitution. If the reconstituted product is not immediately diluted into an infusion bag, **store** in a refrigerator (2°C to 8°C) for up to 4 hours.

DO NOT VORTEX OR SHAKE VIGOROUSLY

Gently invert each vial 5 times prior to withdrawing the concentrate for dilution.

Aseptically withdraw the calculated volume of reconstituted VYXEOS from the vial(s) with a sterile syringe and transfer it to an infusion bag containing 500 mL of sodium chloride 9 mg/mL (0.9%) solution for injection, or 5% glucose. **Discard any unused portions.**

Gently invert the bag to mix the solution. If the diluted infusion solution is not used immediately, store in a refrigerator (2°C to 8°C) for up to 4 hours.

Scan to watch how to prepare VYXEOS

BSA: Body surface area

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Indications and 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
- 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
- Increased susceptibility to infections
- 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 for important information relating to adverse reactions, drug interactions, and dosing information, which has not been discussed in this piece.

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

Further information for healthcare professionals can be found at

www.vyxeos.ca

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SUMMARY

DISCOVER VYXEOS FOR YOUR HIGH-RISK AML PATIENTS*

GREATER THAN THE SUM OF ITS PARTS[1,2]

VYXEOS IS THE FIRST DUAL-DRUG ADVANCED LIPOSOMAL FORMULATION[1]

INCREASED OVERALL SURVIVAL VS CONVENTIONAL CHEMOTHERAPY* WITH A DEMONSTRATED SAFETY PROFILE IN ADULT PATIENTS WITH HIGH-RISK AML[2†]

IMPROVED OVERALL SURVIVAL VS CONVENTIONAL THERAPY* WAS MAINTAINED AFTER A 5-YEAR FOLLOW-UP

INCREASED POST-TRANSPLANT SURVIVAL OVER A LONGER TERM VS CONVENTIONAL CHEMOTHERAPY[3,4]*

90 minutes

REDUCED INFUSION TIME VS CONVENTIONAL CHEMOTHERAPY* USING A 90-MINUTE INFUSION SCHEDULE FOR BOTH INDUCTION AND CONSOLIDATION[2]

* Conventional chemotherapy includes the 7+3/5+2 regimen for induction and consolidation, using cytarabine and daunorubicin.[2]
† High-risk AML defined as newly diagnosed t-AML or AML-MRC.

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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.
5. 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.
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CA-VYX-2300020

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