NEWS RELEASE

NIPPON SHINYAKU CO., LTD.

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Vyxeos® Combination for I.V. Injection Receives Approval for the Treatment of High-risk AML in Japan

Kyoto, Japan, March 26, 2024 - Nippon Shinyaku Co., Ltd. (Nippon Shinyaku; Headquarters, Kyoto; President, Toru Nakai) announced today that the Ministry of Health, Labour and Welfare (MHLW) has approved Vyxeos® Combination for I.V. Injection (Daunorubicin hydrochloride/cytarabine liposomal drug for injection) for the treatment of high-risk acute myeloid leukemia (AML) in Japan.

AML is a disease of clonal proliferation of immature myeloid cells, and results from genetic abnormalities in myeloblasts which are immature blood cells. The uncontrollable growth of leukemia cells in the bone marrow prevents the production of normal blood which results in various symptoms such as infections and bleeding.[1] Although multiple AML drugs have been launched in recent years and the outcomes for some patient groups have improved, many patients still do not have long-term survival. Novel therapeutic agents with greater efficacy are needed.[2]

Vyxeos® is a liposomal formulation of a fixed combination of cytarabine and daunorubicin, the standard drugs for AML treatment, at 5:1 molar ratio. The 5:1 molar ratio has been shown to maximize synergistic antitumor activity in AML. After the drug is taken up by leukemia cells in the bone marrow, cytarabine and daunorubicin are released to exert its anti-tumor effect.

Nippon Shinyaku acquired a license for Vyxeos® from Jazz Pharmaceuticals plc (Headquarters: Dublin, Ireland, Chairman and CEO: Bruce C. Cozadd) on March 30, 2017, and has been developing it in Japan. The approval is based on data from a Phase I/II study conducted by Nippon Shinyaku in Japan and a Phase III study conducted by Jazz in overseas for patients with high-risk AML*, which is considered to have poorer prognosis compared to other forms of AML. The Phase III study met its primary endpoint, as Vyxeos demonstrated a superior improvement in overall survival compared to the standard of care 7+3 treatment regimen for the first time. The median overall survival for the Vyxeos treatment group was 9.56 months compared with 5.95 months for the 7+3 treatment group (1-sided p-value = 0.003; HR [95% confidence interval] = 0.69 [0.52, 0.90]).[3]

Vyxeos® is approved for the treatment of therapy-related AML and AML with myelodysplastic changes in more than 30 countries or regions around the world, including Europe and the United States. Vyxeos® was designated as an orphan drug by MHLW for the indication of AML in May 2022.

Nippon Shinyaku believes that it will contribute to the treatment of high-risk AML by delivering Vyxeos® appropriately to healthcare professionals and their patients who need it.

* The definition of high-risk AML is if any of the following conditions below apply.
・therapy-related AML
・AML with a history of myelodysplastic syndromes (MDS)
・de novo AML with MDS-related cytogenetic abnormalities
・AML with a history of chronic myelomonocytic leukemia (CMML)

References

1. Japanese Society of Hematology. Practical Guidelines for Hematological Malignancies, 2023, Kanehara & Co., Ltd. (Japanese only).
2. Gurnari C et al. Deciphering the Therapeutic Resistance in Acute Myeloid Leukemia. Int J Mol Sci. 2020; 21(22):8505.
3. Lancet 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(26):2684-2692.

Summary of Vyxeos®

Brand name	Vyxeos® Combination for I.V. Injection
Generic name	Daunorubicin hydrochloride/cytarabine liposomal drug for injection
Dosage Forms and Strengths	Freeze-dried preparation for injection containing 47mg of daunorubicin hydrochloride (44mg as daunorubicin) and 100mg of cytarabine
Indication	High-risk acute myeloid leukemia
Dosage and Administration	(1) Remission induction therapy Usually, as remission induction therapy, 100 units (44mg as daunorubicin and 100mg as cytarabine)/m^2 (body surface area) of Vyxeos® Combination for I.V. Injection shall be administered over 90 minutes once daily for up to two cycles. This drug shall be intravenously administered by drip infusion on Days 1, 3, and 5 of Cycle 1. This drug shall be intravenously administered by drip infusion on Days 1 and 3 of Cycle 2 to patients who do not achieve remission during Cycle 1, if there are no unacceptable toxicities, two to five weeks after the start of Cycle 1. (2) Consolidation therapy Usually, as consolidation therapy, 65 units (29mg as daunorubicin and 65mg as cytarabine)/m^2 (body surface area) of Vyxeos® Combination for I.V. Injection shall be administered over 90 minutes once daily for up to two cycles. This drug shall be intravenously administered by drip infusion on Days 1 and 3 of Cycle 1, five to eight weeks after the start of the last remission induction therapy. This drug shall be intravenously administered by drip infusion on Days 1 and 3 of Cycle 2 to patients without disease progression after the start of administration of Cycle 1, if there are no unacceptable toxicities, five to eight weeks after the start of Cycle 1 of the consolidation therapy. One dose unit of this drug contains 0.44mg of daunorubicin and 1mg of cytarabine.

About Nippon Shinyaku

Based on Nippon Shinyaku's business philosophy, "Helping people lead healthier, happier lives," we aim to be an organization trusted by the community through creating unique medicines that will bring hope to patients and families suffering from illness. Please visit our website (https://www.nippon-shinyaku.co.jp/english/) for products or detailed information.

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