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Chugai Obtains Approval for Polivy for the Treatment of Relapsed or Refractory Diffuse Large B-cell Lymphoma

- Polivy in combination with bendamustine (freeze-dried formulation) and rituximab becomes a new treatment option for diffuse large B-cell lymphoma
- Polivy is approved as a first-in-class anti-CD79b antibody-drug conjugate based on data including the Japanese phase II study and the overseas phase Ib/II study for relapsed or refractory diffuse large B-cell lymphoma

TOKYO, March 23, 2021 -- Chugai Pharmaceutical Co., Ltd. (TOKYO: 4519) announced today that it obtained approval from the Ministry of Health, Labour and Welfare (MHLW) for the anticancer agent/antimicrotubule binding anti-CD79b monoclonal antibody Polivy® intravenous infusion 30 mg and 140 mg [generic name: polatuzumab vedotin (genetical recombination)] in combination with bendamustine (freeze-dried formulation) and rituximab (BR therapy) for the treatment of relapsed or refractory (R/R) diffuse large B-cell lymphoma (DLBCL).

"I am very pleased that Polivy in combination with BR therapy now can be offered to patients as a new treatment option for R/R DLBCL, a disease with high unmet medical needs, in the hematologic cancer field following Rituxan® and Gazyva®," said Chugai's President and CEO Dr. Osamu Okuda. "We are preparing to bring this first-in-class anti-CD79b antibody-drug conjugate (ADC) to patients so that we may contribute to realize a better treatment."

The approval is based on data including the results from a multicenter overseas phase Ib/II clinical study (GO29365) that evaluated the efficacy and safety of Polivy in combination with BR therapy compared to BR therapy alone, and a multicenter, single-arm Japanese phase II study (JO40762/P-DRIVE study) that evaluated the efficacy and safety of the combination therapy in R/R DLBCL.

The efficacy and safety of Polivy and BR therapy (40 patients) compared with BR therapy alone (40 patients) was studied in the randomized phase II part of the GO29365 study in 80 patients with R/R DLBCL not eligible for autologous stem cell transplantation (ASCT). The primary endpoint of the complete response rate (CRR) at the time point of primary response assessment (PRA; 6 to 8 weeks after last dose of Polivy) as evaluated by an independent assessment committee using positron emission tomography-computed tomography (PET-CT) was 40% (16/40 patients; 95% CI: 24.9-56.7%) in the Polivy + BR therapy group, and 17.5% (7/40 patients; 95% CI: 7.3-32.8%) in the BR therapy group (data cut-off: April 30, 2018). Adverse reactions occurred in 36 (92.3%) patients out of 39 patients who received Polivy. The most common adverse reactions were neutropenia 53.8% (21/39 patients), thrombocytopenia 41.0% (16/39 patients), diarrhea and anemia 33.3% (13/39 patients) each, fatigue and nausea 23.1% (9/39 patients) each, and pyrexia and peripheral neuropathy 20.5% (8/39 patients) each.

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In the P-DRIVE study, the efficacy and safety of Polivy + BR therapy were studied in 35 patients with R/R DLBCL not eligible for ASCT. The primary endpoint of the CRR at the PRA as assessed by the principal investigator using PET-CT was 34.3% (12/35 patients), (95% CI: 19.1-52.2%) (data cut-off: December 24, 2019). Adverse reactions occurred in 33 (94.3%) patients out of 35 patients who received Polivy. The most common adverse reactions were anemia 37.1% (13/35 patients), nausea 31.4% (11/35 patients), thrombocytopenia and neutropenia 25.7% (9/35 patients) each, constipation, decreased platelet count and decreased neutrophil count 22.9% (8/35 patients) each, and malaise and decreased appetite 20.0% (7/35 patients) each.

A double-blind, placebo-controlled global phase III study (GO39942/POLARIX study) is ongoing for untreated DLBCL to compare the efficacy and safety of Polivy in combination with rituximab plus cyclophosphamide, doxorubicin, prednisolone (R-CHP) to rituximab plus cyclophosphamide, doxorubicin, vincristine, prednisolone (R-CHOP).

[Reference information]
Polatuzumab Vedotin Achieved Primary Endpoint in the Japanese Phase II study for Relapsed or Refractory Diffuse Large B-cell Lymphoma (Press release issued by Chugai on February 13, 2020)
https://www.chugai-pharm.co.jp/english/news/detail/20200213150000_697.html

European Commission approves Roche's Polivy for people with previously treated aggressive lymphoma (Press release issued by Roche on January 21, 2020)
https://www.roche.com/media/releases/med-cor-2020-01-21.htm

Approval information

Product name:	Polivy® Intravenous Infusion 30 mg Polivy® Intravenous Infusion 140 mg
Generic name:	polatuzumab vedotin (genetical recombination)
Intended uses or indications:	Relapsed or refractory diffuse large B-cell lymphoma
Dosage and administration:	The usual adult dosage is 1.8 mg/kg (body weight) polatuzumab vedotin (genetical recombination) administered by intravenous infusion every 3 weeks for 6 doses, in combination with bendamustine hydrochloride and rituximab (genetical recombination). If the first infusion is well tolerated after 90 minutes, subsequent infusions may be administered over a shorter time of at least 30 minutes. Reduce the dose as necessary in accordance with the patient's condition.

About GO29365 study[1)]
GO29365 is a global, phase Ib/II study evaluating the safety and tolerability of Polivy in combination with bendamustine and rituximab (BR therapy) or obinutuzumab (BG therapy) in R/R follicular lymphoma or DLBCL. In the phase II randomized part of the study with 80 DLBCL patients, the efficacy and safety of Polivy in combination with BR therapy were studied compared to BR therapy alone. The primary endpoint

was complete response at the point of primary response assessment as evaluated by an independent assessment committee using PET-CT. Patients received six cycles of treatment, spaced three weeks apart.

About JO40762 (P-DRIVE) study

JO40762 (P-DRIVE) is an open label, single-arm study investigating Polivy in combination with BR therapy in 35 patients with R/R DLBCL. Primary endpoint is investigator's assessment of CRR by PET-CT at the timing of primary response assessment. Patients received six cycles of treatment, spaced three weeks apart.

About polatuzumab vedotin

Polatuzumab vedotin was developed by Roche using Seattle Genetics' ADC technology. It is a first-in-class anti-CD79b antibody-drug conjugate (ADC), comprising the anti-CD79b humanized monoclonal antibody and a tubulin polymerization inhibitor attached together using a linker. The CD79b protein is expressed specifically in the majority of B-cells, making it a promising target for the development of new therapies[2, 3]. Polatuzumab vedotin binds to CD79b and destroys these B-cells through the delivery of an anti-cancer agent, which is thought to suppress the effects on normal cells[4, 5]. Polatuzumab vedotin was granted accelerated approval in the US in June 2019 and conditional marketing authorization in the EU in January 2020, respectively.

About diffuse large B-cell lymphoma (DLBCL)

DLBCL is one of the histologic subtypes of non-Hodgkin's lymphoma (NHL), which is categorized as an aggressive disease that progresses on a monthly basis. DLBCL is the most common form of NHL, accounting for 30-40 percent of NHL[6-8]. DLBCL frequently occurs in middle-aged and older people, mainly in their 60's[9]. The median age at diagnosis has been reported to be 64[10].

The combination of rituximab and chemotherapy is the standard therapy for untreated DLBCL; however, recurrence has been observed in about 40% of patients due to insufficient therapeutic effect[11]. In addition, although autologous stem cell transplantation (ASCT) is recommended for eligible patients with recurrent or refractory DLBCL, ASCT cannot be performed in about half of these patients due to failure of salvage chemotherapy prior to ASCT[12]. Furthermore, no standard therapy has been established for patients ineligible for ASCT due to reasons including age or complications[13]. Therefore, more useful new treatment options for relapsed or refractory DLBCL are in great need.

Salvage chemotherapy: Salvage chemotherapy or salvage therapy is used to treat patients with hematologic malignancy who experienced no therapeutic effects (refractory), or recurrence/relapse of the disease. Applicable treatment may vary depending on the type of cancer. Combination therapies of multiple drugs including anticancer agents[14] are generally used.

Sources

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