Report POLIVY®polatuzumab vedotin

Product & Mechanism of action	Authorized indications Licensing status	Essential therapeutic features	NHS impact
Substance:polatuzumab vedotin **Brand Name:**Polivy **Originator/license:** Roche Registration GmbH **Classification:** NI **ATC code:** L01XC37 **Orphan Status:** **Eu:** Yes **Us:** Yes **Mechanism of action:**polatuzumab vedotin, is made up of a monoclonal antibody combined with MMAE. The monoclonal antibody attaches to a protein called CD79b on B cells, including cancerous B cells, and in doing so causes MMAE to be released inside them. MMAE then stops the B cells from dividing and causes them to die [1].	**Authorized Indication:** **EMA:** polatuzumab vedotin in combination with R-CHP is indicated for the treatment of adult pts with previously untreated DLBCL[2]. **Route of administration:** IV **Licensing status** **EU CHMP P.O. date:**24/03/2022 **FDA M.A. date:** 18/09/2020 **EU Speed Approval Pathway:**No **FDA Speed Approval Pathway:**No --- **ABBREVIATIONS:** **AEs:** Adverse events **CHMP**: Committee for Medicinal Product for Human Use **CI**: Confidence Interval **DLBCL**: diffuse large B-cell lymphoma **HR**: Hazard ratio **IV**: Intravenous **MA**: Marketing Authorization **MMAE**: monomethyl auristatin **NHL**: Non-Hodgkin Linfoma **PFS**: Progression-free survival **PO**: Positive Opinion **Pola-R-CHP**: polatuzumab, rituximab, cyclophosphamide, doxorubicin, and prednisone **Pts**: patients **R-CHOP**: rituximab, cyclophosphamide, doxorubicin, vincristine and prednisone **Vs**.: versus	**Summary of clinical EFFICACY:** **POLARIX (NCT03274492):** double-blind, placebo-controlled, international phase III trial to evaluate a modified regimen of R-CHOP (pola-R-CHP), in which vincristine was replaced with polatuzumab vedotin, as compared with standard R-CHOP, in adult pts (n=879) with previously untreated intermediate-risk or high-risk DLBCL. Pts were randomly assigned in a 1:1 ratio to receive six cycles of either pola-R-CHP (n=440) or R-CHOP (n=439), plus two cycles of rituximab alone. On day one of each cycle, pts received either IV polatuzumab vedotin at a dose of 1.8 mg per kg of body weight and a placebo matching IV vincristine (pola-R-CHP group) or a placebo matching polatuzumab vedotin and IV vincristine at a dose of 1.4 mg per m^2 of body surface area (R-CHOP group), plus IV doses of rituximab, cyclophosphamide, and doxorubicin. The primary efficacy end point was investigator-assessed PFS. The percentage of pts surviving without progressionwas significantly higher in the pola-R-CHP group than in the R-CHOP group (76.7% [95% CI, 72.7 to 80.8] vs. 70.2% [95% CI, 65.8 to 74.6] at two years; stratified HR for progression, relapse, or death, 0.73; 95% CI, 0.57 to 0.95; p=0.02) [3]. **Summary of clinical SAFETY:** The most common AEs of grade 3 or 4 were neutropenia (28.3% in the pola-R-CHP group vs. 30.8% in the R-CHOP group), febrile neutropenia (13.8% vs. 8.0% respectively), and anemia (12.0% and 8.4%, respectively). The percentages of pts who had infections of grade 3 or 4 were similar (15.2% vs. 12.6%). Peripheral neuropathy of any grade was reported in 52.9% of those who received pola-R-CHP and in 53.9% of those who received R-CHOP, and peripheral neuropathy of grade 2 or higher was reported in 13.8% and 16.7% of the pts, respectively. Serious AEs were reported in 34.0% of the pts who received pola-R-CHP and 30.6% of the pts who received R-CHOP. AEs that resulted in death were reported in 13 pts in the pola-CHP group and in 10 pts in the R-CHOP group; these events were primarily related to infections (pneumonia in four pts and three pts, respectively, and sepsis in one pt and three pts, respectively). [3]. **Ongoing studies:** ● ***For the same indication:***Yes ● ***For other indications:***Yes **Discontinued studies (for the same indication):**Yes **References:** 1. https://www.ema.europa.eu/en/documents/assessment-report/polivy-epar-public-assessment-report_en.pdf 2. https://www.ema.europa.eu/en/medicines/human/summaries-opinion/polivy-0 3. https://www.nejm.org/doi/full/10.1056/NEJMoa2115304 4. https://gallery.farmadati.it/Home.aspx 5. https://www.osservatoriomalattierare.it/i-tumori-rari/altri-tumori-rari/14242-linfoma-diffuso-a-grandi-cellule-b-benefici-duraturi-dalla-terapia-con-polat uzumab-vedotin 6. https://www.annalsofoncology.org/article/S0923-7534(19)47184-6/pdf 7. https://clinicaltrials.gov/ct2/home	**Cost of therapy:** The ex-factory cost for one 21-day cycle withpolatuzumab vedotin (for a 70 kg patient)is €18,319.09[4]. **Epidemiology:** DLBCL is the most common subtype of NHL: one in three cases of NHL is represented by DLBCL. Pts usually respond to first-line treatments, however in 40% of the cases the disease is recurrent [5]. The crude incidence for DLBCL in Europe is 3.8/100 000/year [6]. **POSSIBLE PLACE IN THERAPY** The standard first-line treatment of DLBCL is R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone). In a phase 1b-2 trial in which polatuzumab vedotin in combination with rituximab, cyclophosphamide, doxorubicin, and prednisone was investigated as first-line treatment for DLBCL, 89% of the pts had an overall survival and 77% had a complete response [3]. **OTHER INDICATIONS IN DEVELOPMENT:**Richter syndrome[7]. **SAME INDICATION IN EARLIER LINE(S) OF TREATMENT:**- [7]. **OTHER DRUGS IN DEVELOPMENT for the SAME INDICATION**:Zanubrutinib + R-CHOP[7]. *Service reorganization Y/N: Yes *Possible off label use Y/N: Yes

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