# Report ZYNYZ® - Retifanlimab

| Product & Mechanism of action | Authorized indications Licensing status | Essential therapeutic features | NHS impact |
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| **Substance:** Retifanlimab<br><br>**Brand Name:** Zynyz<br><br>**Originator/licensee:** Incyte Biosciences Distribution B.V.<br><br>**Classification:** NCE<br><br>**ATC code:** L01FF10<br><br>**Orphan Status:**<br>**Eu:** Yes<br>**Us:** Yes<br><br>**Mechanism of action:**<br>The active substance retifanlimab is an antineoplastic agent that binds to PD-1receptor, blocks its interaction with its ligands PD-L1 and PD-L2, and potentiates T-cell response in the tumor microenvironment. [1] | **Authorized Indication:**<br>**EMA:** retifanlimab is indicated as monotherapy for the first-line treatment of adult pts with metastatic or recurrent locally advanced MCC not amenable to curative surgery or radiation therapy. [1]<br><br>**FDA**: for adult pts with metastatic or recurrent locally advanced MCC. [2]<br><br>**Route of administration:** EV<br><br>**Licensing status**<br>**EU CHMP P.O. date:** 22/02/2024<br>**FDA M.A. date:** 22/03/2023<br><br>**EU Speed Approval Pathway:** No<br>**FDA Speed Approval Pathway:** Yes<br><br>**-----**<br>**ABBREVIATIONS:**<br>**AE:** adverse event<br>**CHMP:** Committee for Medicinal Products for Human Use<br>**CR**: complete response<br>**ECOG:** Eastern Cooperative Oncology Group<br>**IRC:** independent central review committee<br>**M.A.:** Marketing Authorization<br>**MCC**: Merkel cell carcinoma<br>**ORR**: overall response rate<br>**P.O.:** Positive Opinion<br>**PD-1**: programmed cell death protein 1<br>**PR**: partial response<br>**Pts:** patients<br>**RECIST**: Response Evaluation Criteria in Solid Tumors<br>**TEAE:** treatment-emergent adverse event | **Summary of clinical EFFICACY:**<br>**POD1UM-201 (NCT03599713):**is an open-label, phase II, multiregional, single-arm study. Eligible pts have unresectable locally advanced/metastatic MCC, ECOG - PS 1, measurable disease per RECIST v1.1, are either chemotherapy (chemo)- naïve or have received three prior chemo regimens, and have had no prior treatment with anti-PD-1/anti-PD-L1 therapy.<br>The primary endpoint was ORR per RECIST v1.1 in chemo-naïve pts. 27 pts with MCC had received retifanlimab 500 mg IV Q4W (22 chemo-naïve; five refractory; all stage IV).<br>Of the 22 chemo-naïve pts enrolled, 18 have had one on-study tumor assessment or discontinued. There were 10 (56%) responders (investigator assessed) with two (11%) CP and eight (44%) PR. Of these, six are confirmed and four are unconfirmed ongoing responses. Three pts (17%) have stable disease [3].<br><br>**Summary of clinical SAFETY:**<br>Updated results from a phase II POD1UM-201 trial indicated that, serious AEs occurred in 22% of pts receiving retifanlimab. The most frequent serious AEs (i.e. 2% of pts) were fatigue, arrhythmia and pneumonitis.<br>Permanent discontinuation of retifanlimab due to an adverse reaction occurred in 11% of pts. The most common (=10%) AEs that occurred in pts receiving retifanlimab were fatigue, musculoskeletal pain, pruritus, diarrhea, rash, pyrexia and nausea.<br>As of January 8, 2020, among all treated pts (n=27), 16 (59%) had TEAE; six (22%) were ≥Grade 3; 11 (41%) had a treatment-related TEAE, three (11%) of which were ≥Grade 3.<br>The most common TRAEs were asthenia and pruritus (n=3 each). Seven (26%) had a TEAE of special interest (the only immune-related AE occurring in >1 pt was hypothyroidism [n=2]). Two pts (7%) discontinued treatment due to TEAEs (radiculopathy and polyarthritis). No fatal TEAEs have been reported. [4]<br><br>**Ongoing studies:**<br>● ***For the same indication:*** Yes<br>● ***For other indications:*** Yes<br><br>**Discontinued studies (for the same indication):**-<br><br>**References:**<br>[1] https://www.ema.europa.eu/en/medicines/human/EPAR/zynyz<br>[2] https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/761334Orig1s000correctedlbl.pdf<br>[3] https://www.annalsofoncology.org/article/S0923-7534(20)41209-8/fulltext<br>[4] https://doi.org/10.1016/j.annonc.2020.08.1213.<br>[5] https://www.drugs.com/price-guide/zynyz<br>[6] https://journals.lww.com/eurjcancerprev/abstract/2023/05000/epidemiology_of_merkel_cell_carcinoma_in_tuscany.13.aspx | **Cost of therapy:**In US the cost for Zynyz intravenous solution (500 mg/20 mL) is around $15,004 for a supply of 20 milliliters. [5]<br><br>**Epidemiology:**One study reported a dramatic increase in MCC diagnoses with a crude incidence rate of 1.15/100,000 in Italy. [6]<br><br>**POSSIBLE PLACE IN THERAPY**:The management of metastatic or recurrent locally advanced MCC typically involves a combination of surgical, radiation, and systemic therapies Platinum-based chemotherapy regimens, such as cisplatin or carboplatin combined with etoposide, have been the standard treatment for metastatic MCC.<br>Retifanlimabas monotherapy is the first-line treatment of adults with metastatic or recurrent locally advanced MCC not amenable to curative surgery or radiation therapy.<br><br>**OTHER INDICATIONS IN DEVELOPMENT:(NCT04472429**) Squamous Cell Anal Carcinoma, (**NCT04463771)** Endometrial Cancer.<br><br>**SAME INDICATION IN EARLIER LINE(S) OF TREATMENT**: -<br><br>**OTHER DRUGS IN DEVELOPMENT for the SAME INDICATION: -**<br><br>*Service reorganization: No<br>*Possible off label use: Yes |