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News release

New Data Analysis Shows Link between Blood Involvement and Response to Treatment in Cutaneous T-cell Lymphoma (CTCL) Patients

Patients treated with POTELIGEO®▼ (mogamulizumab) with higher levels of abnormal T-cells in the blood reported higher quality of life, compared to vorinostat, new data analysis released today at the European Hematology Association meeting[1]

GALASHIELS, UK 10 June 2021 – Kyowa Kirin International PLC (Kyowa Kirin), a wholly owned subsidiary of Kyowa Kirin Co., Ltd., today announced a new analysis of data showing statistically significant improvements in quality of life in cutaneous T-cell lymphoma (CTCL) patients treated with mogamulizumab with blood involvement, compared to vorinostat.[1] The new findings from the MAVORIC trial compared the impact of treatment with POTELIGEO® (mogamulizumab) and vorinostat by patient blood tumour burden in adult patients with mycosis fungoides (MF) and Sézary syndrome (SS), two types of CTCL.

Professor Doctor Pier Luigi Zinzani of the Institute of Hematology "L. e A. Seràgnoli" at the University of Bologna said: “This new analysis helps us to understand more about the importance of blood involvement in CTCL, which is relatively common in the more advanced stages of the disease and may be present in some less advanced cases. We know that increasing levels of malignant T-cells in the blood correlate with increased risk of CTCL disease progression and an overall reduction in patient survival. Treatment with mogamulizumab has also been shown to be more effective in CTCL patients who have blood involvement as part of their disease and treatment with mogamulizumab also generates quality of life benefits for CTCL patients with blood involvement. This new information underlines the importance of blood monitoring in the clinical management of CTCL patients.”

In the study, patients classified as B0 were considered to have no blood involvement and patients classified as B1 and B2 were considered to have blood involvement.[1] B1 is a measurable low level of blood involvement of between 250 to 1000 abnormal T-cells per µL. B2 is higher level of blood involvement, greater than 1000 abnormal T-cells per µL, detected using flow cytometry.

Statistically significant differences in quality of life were seen for patients with blood involvement, with patients treated with mogamulizumab seeing improvements in the Skindex-29 and ItchyQoL questionnaires, compared to vorinostat. Quality of life improvements were also seen in patients treated with mogamulizumab with blood involvement assessed by the Pruritus Likert Scale and the FACT-G Total Score questionnaire**s**, compared to vorinostat. For patients with no blood involvement there was no statistically significant differences in quality of

life between mogamulizumab and vorinostat.[1]

MF and SS are subtypes of CTCL, a rare type of non-Hodgkin's lymphoma that can affect the skin, blood, lymph nodes and internal organs.[2] As a chronic and generally incurable disease associated with disfiguring skin lesions, intractable itching, sleep disturbance, and psychosocial problems, CTCL has a serious negative effect on quality of life.[1] MAVORIC is the largest multinational, randomised, Phase 3 trial of systemic CTCL therapy. MAVORIC evaluated the safety and efficacy of mogamulizumab versus vorinostat in patients who had received at least one previous systemic therapy.[3] This new post hoc analysis of the MAVORIC trial looked at data from patients' quality of life using a range of recognised and validated assessment tools.[1]

The MAVORIC trial met its primary endpoint of overall investigator-assessed progression-free survival (PFS), which was shown to be significantly greater for patients treated with mogamulizumab compared to vorinostat, at 7.7 months and 3.1 months, respectively (P<0.0001).[3]

About Mycosis Fungoides (MF) and Sézary syndrome (SS)

Cutaneous T-cell lymphomas (CTCL) are rare, serious and potentially life-threatening, forms of non-Hodgkin's lymphoma,[2] affecting around 240 persons per 1,000,000 population across Europe.[4] Mycosis fungoides (MF) and Sézary syndrome (SS) are the two best studied types of CTCL,[5] together accounting for around two thirds of all CTCLs.[6,7]

MF and SS can affect the skin, blood, lymph nodes (part of the body's immune system which is spread throughout the body) and internal organs.[2] MF and SS can be very distressing for patients and have a significant negative impact upon many aspects of patients' lives.[3,8] Disease stage in MF and SS is the most important prognostic factor,[9] and draws upon the type and extent of skin involvement, as well as the presence or absence of extracutaneous disease in lymph nodes, viscera, and blood.[10] Hence, assessment of all four anatomical 'compartments' is recommended, first at diagnosis and then to assess patient response to treatment.[10,11]

Neoplastic T lymphocytes in MF and SS, consistently express CC chemokine receptor 4 (CCR4),[3] making this a relevant target for treatment at all stages of disease. All disease stages can include blood involvement[10,12] and blood tumour burden may be relevant for prognosis[13] and treatment[6,10,14,15] in MF and SS.

Due to its likeness to more common skin conditions such as eczema and psoriasis,[16] CTCL can take, on average, between 2 and 7 years for individuals to receive a confirmed diagnosis.[17] It is critical for doctors to accurately diagnose CTCL as early as possible as the patient's prognosis can be affected if the disease progresses to later stages.[13] Whilst most individuals that present with early stage do not progress to a more

advanced stage,[18] patients with advanced disease have significantly poorer outcomes with only around half of patients (52%) surviving for just 5 years.[19]

About POTELIGEO (mogamulizumab) and the MAVORIC Trial

POTELIGEO (mogamulizumab), a humanised monoclonal antibody that selectively binds to CCR4,[20] elicits anti-tumour activity by antibody-dependent cellular cytotoxicity (ADCC).[3]

Following a positive opinion from Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA), the European Commission (EC) granted marketing authorisation for mogamulizumab in November 2018 for the treatment of adult patients with MF or SS who have received at least one prior systemic therapy.[20] The CHMP's opinion was based on results of the MAVORIC trial, the largest randomised study of systemic therapy in MF and SS,[3] and the first trial to compare systemic therapies using progression-free survival as a primary endpoint.[3]

MAVORIC evaluated the safety and efficacy of mogamulizumab versus vorinostat in patients who had received at least one previous systemic therapy:[3]

- Mogamulizumab more than doubled median progression-free survival (PFS) in patients with relapsed or refractory MF/SS, compared with vorinostat (7.7 months vs 3.1 months), which is a relative reduction in the risk of disease progression of 47% (HR=0.53, 95% CI: 0.41–0.69; P<0.0001).[3]
- Overall, significantly more patients responded to mogamulizumab than vorinostat (overall response rate [ORR] 28.0% versus 4.8% (P<0.0001).[3]
- Median time-to-next-treatment (TTNT), an additional measure of clinical benefit and disease control, was significantly superior in patients treated with mogamulizumab compared to those that received vorinostat (11.0 months vs 3.5 months; P<0.0001).[3]
- In post hoc analyses, patients with B1 and B2 levels of blood tumour burden that received mogamulizumab have been shown to draw significantly more benefit in terms of PFS,[21] TTNT,[21] and improvement in mSWAT[22] compared to patients that received vorinostat.
- Mogamulizumab shows good tolerability with a manageable safety profile.[3,,23,24,25]

Important Prescribing information and Safety Information

Refer to the full Summary of Product Characteristics (SmPC) for prescribing information and the full safety information: https://www.ema.europa.eu/en/medicines/human/EPAR/poteligeo#product-information-section

About Kyowa Kirin

Kyowa Kirin strives to create and deliver novel medicines with life-changing value. As a Japan-based Global

Specialty Pharmaceutical Company with a heritage of 70+ -years, we apply cutting-edge science including an expertise in antibody research and engineering, to address the needs of patients and society across multiple therapeutic areas including Nephrology, Oncology, Immunology/Allergy and Neurology. Across our four regions – Japan, Asia Pacific, North America and EMEA/International – we focus on our purpose, to make people smile, and are united by our shared values of commitment to life, teamwork/Wa, innovation, and integrity. You can learn more about the business of Kyowa Kirin at: https://www.kyowakirin.com/

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