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Treating MS without continuous immunosuppression: an interview with Luciano Rossetti

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“Most current MS treatments rely on continuous administration with continuous immunosuppression, which is linked to a number of risks and a high-monitoring burden. However, MAVENCLAD[®] does not continuously suppress the immune system. Rather it selectively affects the adaptive immune system, while having a minimal effect on innate immune function.”

Luciano Rossetti, MD, Executive Vice President, Global Head of R&D at Merck KGaA, Darmstadt, Germany speaks to Laura Dormer, Commissioning Editor

Luciano Rossetti, MD, is Executive Vice President, Global Head of R&D at Merck KGaA, Darmstadt, Germany, and a member of the Healthcare Executive Committee. As Global Head of R&D, Rossetti leads the strategy for Merck KGaA, Darmstadt, Germany's discovery and development efforts in healthcare. He joined Merck KGaA in July 2014, and has since led the acceleration of several key programs through the pipeline and advanced the innovation of Merck KGaA's discovery teams into development. Under his leadership, R&D has been transformed, with significant potential to deliver the scientific, clinical, regulatory and medical excellence of its teams to patients in need. Before joining Merck KGaA, he served as Senior Vice President, responsible for Global Scientific Strategy and Late Stage Development at Merck Sharp & Dohme, or MSD. In the latter position, he was responsible for clinical development from Phase II to V across all therapeutic areas. Prior to joining MSD in 2006, he spent 18 years in academia during which he had considerable involvement with the pharmaceutical industry in both discovery and development. In his latest assignment, he was Professor of Medicine and led the Diabetes Research & Training Center at the Albert Einstein College of Medicine. He has authored more than 150 peer-reviewed scientific journal articles. He is a Post-Doctoral Fellow of Rome University Medical School and of Yale University Medical School. He holds a Doctorate in Medicine from the Trieste University Medical School, Italy.

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Please could you introduce yourself, & tell us about your role at Merck KGaA, Darmstadt, Germany?

My name is Luciano Rossetti and I am Global Head of R&D at Merck KGaA, Darmstadt, Germany. At Merck KGaA, we have been dedicated to pioneering new discoveries in neurology and immunology for more than two decades, grounded in our proud history of advancing multiple sclerosis (MS) care. Our priority is ensuring Merck KGaA continues to develop treatments which aim to address areas of high unmet patient needs – in particular, better and more durable efficacy; patient-friendly dosing regimens; and well-characterized safety profiles.

Could you describe how the recently approved MAVENCLAD[®] (cladribine tablets) is now being used in MS patients?

Since it's European Commission approval in August 2017 for the treatment of adults with highly active relapsing MS, MAVENCLAD is gradually being made available to patients in Europe. So far it has been launched in Germany, Canada, Australia, Argentina, United Arab Emirates, Israel, Luxembourg, Denmark, Norway, Scotland

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and the UK, where it is the first MS disease-modifying therapy that has gone straight to a positive recommendation in the NICE appraisal process. In addition, Merck KGaA has recently entered into a commercial agreement with National Health Service, England, the first of its kind in MS, which allows patients in England immediate access to MAVENCLAD, ahead of the NICE Final Guidance anticipated in early 2018.

At the ECTRIMS–ACTRIMS conference, Merck KGaA presented new data on the benefit–risk profile of MAVENCLAD. Could you tell us about these findings?

The safety and efficacy data presented recently at ECTRIMS–ACTRIMS in Paris confirm the previously established benefit–risk profile of MAVENCLAD. Analysis of data from the 2-year CLARITY study showed that MAVENCLAD significantly increased the proportion of patients with no evidence of disease activity compared with placebo (43.7 vs 9.0%) [1]. Safety data confirmed that the incidence of malignancy in patients treated with MAVENCLAD was not significantly different to the incidence in a matched population based on GLOBOCAN (0.97; 95% CI: 0.44–1.85) [2]. Additional safety data showed that although there was an increase in infections during grade 3 and 4 lymphopenia compared with grade 0–2 lymphopenia, the difference was mainly driven by mild-to-moderate upper respiratory tract and herpes infections.

Also, data presented at ECTRIMS–ACTRIMS provide further insights on how MAVENCLAD selectively targets the immune system in patients with MS. An analysis of T-cell subpopulations from the ORACLE-MS study provided a detailed assessment of the changes that occur in the adaptive immune system following MAVENCLAD treatment. Specifically, levels of CD4⁺ T cells were shown to be moderately and selectively reduced by up to 63% from baseline, and the greatest reductions in absolute cell numbers occurred at week 13 post-treatment for effector memory cells (54% reduction) and week 24 for central memory cells (63% reduction), with similar or slightly increased levels of these CD4⁺ cell subtypes at week 48 [3], supporting the theory that MAVENCLAD is a selective immune reconstitution therapy (SIRT).

How is this data significant for MS patients?

Most current MS treatments rely on continuous administration with continuous immunosuppression, which is linked to a number of risks and a high-monitoring burden. However, MAVENCLAD® does not continuously suppress the immune system. Rather it selectively affects the adaptive immune system, while having a minimal effect on innate immune function. In the studies we submitted for approval, MAVENCLAD showed sustained clinical efficacy for up to 4 years with a maximum of 20 days of oral treatment over 2 years.

Merck KGaA also presented a new report at ECTRIMS investigating the socioeconomic impact of MS on women in Europe; what were the report's key findings?

Merck KGaA commissioned this report because, although women are twice as likely to receive a diagnosis of MS than men, the gender-specific burden of the disease in women has received less attention and needs further research and understanding. The report found that there is a disproportionate impact of MS on women versus men, particularly in terms of diagnosis and comorbidities, life choices and relationships, caregiving and employment.

The report, which was based on 11 interviews with representatives from patient organizations around the world as well as a bespoke survey of women with MS, found that over 20% of those surveyed were misdiagnosed with a different illness prior to being diagnosed with MS. Since being diagnosed, over 40% of those surveyed had separated or divorced from their partner, with 88% reporting that MS had played a factor in their decision. 66% of women surveyed reported that MS had, at some point, affected their employment status. Of these women, 38% had left employment altogether.

To address these challenges, the report puts forward a number of policy recommendations, such as encouraging support from employers, particularly in providing more flexibility at work, and the provision of multidisciplinary support to ensure that the patients make informed life choices that manage the impact of MS on their futures.

Our support for patients and caregivers goes beyond the medications we provide. This report is one of a number of Merck KGaA's initiatives aimed at improving awareness, understanding and support for those impacted by MS.

Looking forward, can you elaborate on Merck KGaA's main areas of research focus in this area?

We are committed to deepening our understanding of MAVENCLAD as well as Rebif®, a therapy for the treatment of relapsing remitting MS. We are continuing to advance our understanding of these treatments and gather real-

world evidence, through ongoing and new Phase IV and investigator-initiated studies among patients with MS. Additionally, we are growing our pipeline with a range of new therapies to address patients' needs. Ultimately, our goal is to continue discovering and delivering treatments that significantly improve the lives of people living with MS and other chronic progressive diseases, especially those of the immune system.

Disclaimer

The opinions expressed in this interview are those of L Rossetti and do not necessarily reflect the views of Future Medicine Ltd.

Financial & competing interests disclosure

L Rossetti is a full-time employee of Merck KGaA, Darmstadt, Germany. The author has no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed.

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