Remibrutinib's Safety Across Immune-mediated Diseases Supports Development in MS

Short title: Remibrutinib Phase 2 Safety Profile

Presenting/Main author: Xavier Montalban

Xavier Montalban[1], Tanuja Chitnis[2], Mitzi Williams[3], Laura Airas[4], Sarbjit Saini[5], Michihiro Hide[6], Gordon Sussman[7], Jin Nakahara[8], Robert Bermel[9], Thomas Dörner[10], Brett Loop[11], Virginia DeLasHeras[12], Roman Willi[12], Bernd C. Kieseier[12,13], Sibylle Haemmerle[12], Artem Zharkov[12], Nathalie Barbier[12], Amin Azmon[12], Richard Siegel[14], Bruno Cenni[14], Heinz Wiendl[15], Marcus Maurer[16,17], Ana Giménez-Arnau[18]

[1]Department of Neurology-Neuroimmunology, Centre d'Esclerosi Múltiple de Catalunya (Cemcat), Hospital Universitari Vall d'Hebron, Barcelona, Spain; [2]Brigham and Women's Hospital, Department of Neurology, Boston, MA, USA; [3]Joi Life Wellness Group, Atlanta, GA, USA; [4]Turku University Hospital and University of Turku, Turku, Finland; [5]Johns Hopkins Asthma and Allergy Center, Baltimore, MD, USA; [6]Hiroshima City Hiroshima Citizens Hospital, Hiroshima, Japan; [7]University of Toronto, Toronto, Ontario, Canada; [8]Department of Neurology, Keio University School of Medicine, Tokyo, Japan; [9]Mellen Center for MS, Cleveland Clinic, Cleveland, OH, USA; [10]Department of Rheumatology and Clinical Immunology, Charite Universitätsmedizin Berlin; DRFZ, Berlin, Germany; [11]Novartis Pharmaceutical Corporation, Cambridge, MA, USA; [12]Novartis Pharma AG, Basel, Switzerland; [13]Department of Neurology, Heinrich-Heine University, Duesseldorf, Germany; [14]Novartis Institutes for Biomedical Research, Basel, Switzerland; [15]Department of Neurology with Institute of Translational Neurology, University of Münster, Münster, Germany; [16]Urticaria Center of Reference and Excellence (UCARE), Institute of Allergology, Charité – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin and Humboldt-Universität zu Berlin, Berlin, Germany; [17]Fraunhofer Institute for Translational Medicine and Pharmacology ITMP, Allergology and Immunology, Berlin, Germany; [18]Department of Dermatology, Hospital del Mar - IMIM, Universitat Pompeu Fabra, Barcelona, Spain.

INTRODUCTION

Remibrutinib, a potent, highly selective, covalent, oral Bruton's tyrosine kinase inhibitor, is currently being investigated in two Phase 3 trials for the treatment of relapsing multiple sclerosis (NCT05147220/NCT05156281). The highly selective profile of remibrutinib has the potential to result in a favorable safety profile by minimizing off-target effects.

OBJECTIVE

To report the integrated safety profile of remibrutinib using pooled data from completed Phase 2 clinical trials in chronic spontaneous urticaria (CSU), Sjögren syndrome (SjS) and asthma, including long-term treatment up to 52 weeks.

METHODS

Pooled data from completed Phase 2 studies of CSU (including 52-week open-label extension), SjS, and asthma were analyzed. Safety assessments included adverse events (AEs), serious AEs (SAEs), and AEs of special interest (AESI). Analyses were conducted for patients receiving

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any remibrutinib dose (N=391), and specifically for those receiving 100 mg dose (N=327), using exposure-adjusted incidence rates (EAIRs) per 100 patient-years.

RESULTS

Patients receiving any remibrutinib dose had an EAIR of 260.8 for AEs, the subgroup receiving 100 mg had an EAIR of 224.8. The EAIR for AEs leading to treatment discontinuation was 8.3 for both groups, and the EAIR for SAEs was 4.2 for the any dose group and 2.9 for the 100 mg subgroup. Infections and infestations were the most frequently reported AEs (EAIR - any dose: 68.0; 100 mg: 56.2), mild-to-moderate in severity, with mostly upper respiratory tract infections. Other reported grouped AEs with EAIR ≥20 were skin/subcutaneous tissue disorders, gastrointestinal disorders, nervous system disorders and musculoskeletal disorders. AESIs, other than infections, include bleeding (mostly minor cutaneous) and cytopenia (rare), which were mild-to-moderate in severity. Overall, EAIRs were generally similar for remibrutinib and placebo.

CONCLUSIONS

This integrated safety analysis confirmed the consistently favorable safety profile of remibrutinib across indications and doses, including 100 mg b.i.d. with up to 52 weeks long-term exposure.

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COI Disclosures

Xavier Montalban has received speaking honoraria and travel expenses for participation in scientific meetings, has been a steering committee member of clinical trials or participated in advisory boards of clinical trials in the past years with Abbvie, Actelion, Alexion, Bayer, Biogen, Bristol-Myers Squibb/Celgene, EMD Serono, Genzyme, Hoffmann-La Roche, Immunic, Janssen Pharmaceuticals, Medday, Merck, Mylan, Nervgen, Novartis, Sandoz, Sanofi-Genzyme, Teva Pharmaceutical, TG Therapeutics, Excemed, MSIF and NMSS.

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Ana Giménez-Arnau reports roles as a medical advisor for Uriach Pharma, Sanofi and Genentech, Novartis, FAES, GSK, AMGEN, Thermo Fisher and has research grants supported by Uriach Pharma, Novartis and Instituto Carlos III- FEDER; she also participates in educational activities for Uriach Pharma, Novartis, Genentech, Menarini, LEO- PHARMA, GSK, MSD, Almirall, AVENE and Sanofi.

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