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Interim Analysis of the START Study – Extensive Electrocardiographic Monitoring Confirms the Good Cardiac Safety Profile of Fingolimod

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Background: Fingolimod was the first oral therapy approved for the treatment of RRMS. As a sphingosine 1-phosphate receptor (S1PR) modulator, it activates S1PR at the surface of cardiac myocytes after treatment initiation. This activation results in transient pulse rate reduction and in rare cases in atrioventricular conduction blocks.

Objective: This interim analysis of the START study evaluates in a large cohort the cardiac safety of fingolimod after the first dose and analyzes individual arrhythmic episodes in detail.

Methods: The START study (NCT01585298) is a prospective, 1-week, multicenter, open-label study enrolling up to 7,000 RRMS patients in more than 250 centers in Germany, according to the EU label criteria of fingolimod. The study consists of a screening period, a baseline visit at which the first fingolimod dose is taken, and a final visit after one week. During screening and at the final visit, a 12-lead ECG is carried out. The procedure at baseline is as follows: prior to the first intake of fingolimod, a 12-lead ECG is recorded. After the first dose, a continuous 6h Holter ECG is recorded, while pulse and blood pressure are measured simultaneously, every hour. A final 12-lead ECG is performed afterwards. All ECG recordings are centrally evaluated by cardiologists.

Results: The previous START interim analysis was based on 2455 patients. In this cohort 0.9% of the patients developed bradycardia (< 45 bpm) at any time during the 6h observation period. 39 out of 2455 patients (1.6%) developed a 2nd degree AV-block Mobitz type I or 2:1 block. No AV-block Mobitz type II or AV Block III were observed. Only one patient complained about mild symptoms (chest discomfort, fatigue) and no treatment was necessary. All cardiac events were transient. The results of the most recent analysis including approx. 3500-4000 patients will be presented focusing on an in-depth Holter-ECG-analysis of those patients having developed bradycardia or AV-block 2nd degree and higher.

Conclusions: This study confirms the good cardiac safety profile of fingolimod. Bradycardia and AV conduction abnormalities detected in continuous ECG-monitoring are rare and benign.