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MEETING ABSTRACT

A5.3 Statin-associated immune-mediated necrotising myopathy: a retrospective study of WHO pharmacovigilance safety reports
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Background: Statins represent an effective treatment for hyperlipidemia. Recently, immune-mediated necrotising myopathy (IMNM), a new form of a non-self-limited statin myopathy, became evident. The incidence of IMNM is approximately 2 to 3 patients per 100,000 patients treated with statins, mostly older than 50 years. Clinically, IMNM mostly manifests as symmetrical proximal muscle weakness of the arms and legs. Laboratory values can show significantly raised creatinine kinase (CK) levels up to 13,000 U/l. The onset of the disease may be acute (days to weeks) or subacute (weeks)—with even ongoing symptoms after discontinuation of statin therapy. Treatment options of autoimmune-related myopathy consists of immunosuppressive regimens. All reported cases of IMNM in the WHO pharmacovigilance database were analysed to characterise this rare phenomenon.

Methods: International individual case safety reports (ICSR) concerning IMNM until October 1st, 2016, were extracted from VigiBase™, the WHO database of pharmacovigilance. The responsible authorities were contacted to maximise ICSR information and improve quality of the reports by implementing information of the corresponding case narratives. Duplicates of similar pairs of ICSR were identified. Demographic data, drug administration information, e.g. dose and duration, seriousness of the adverse drug reactions (ADR), latency time and patients’ outcomes were analysed.

Results: Overall, 159 ICSR related to IMNM were identified. 101 ICSR with IMNM under statin administration from 17 countries (52 from North America, 45 Europe, 3 Australia, 1 Japan) were used for analysis after identification of duplicates. The majority of the European cases (n = 51%) were reported by physicians, in contrast to only 9.6% from North American reports. Males and females were equally affected (59 males vs. 41 females). The average age was 67 years (range 16–87). 100 reports were classified as serious, 6 of them were subgrouped as life-threatening and 7 as disabling/incapacitating. The mean latency time between diagnosis of IMNM and start of treatment was over 4 years (range 1–300 months). The median CK values were 6460 U/l (range 24–35000). For 33 patients HMGCoA antibody testing was documented: 24 (73%) of those patients were tested HMGCoA-positive. In total, 8 patients recovered from IMNM, 6 only recovered with sequelae and 28 were recovering during the reported ICSR. A 63-year-old American female patient died due to IMNM. In 76 patients one statin was reported, in 22 ICSR 2 statins, and in 3 patients 3 statins were documented. Atorvastatin was the most frequently coded statin in 80% of the reports (simvastatin 27%, rosuvastin 18%, pravastatin 3%). The median daily statin dose was 40 mg (range 5–80 mg) for a median time of 36 weeks (range 1–232 weeks).

Discussion: IMNM associated with statin treatment was reported in different countries worldwide with the main focus in Europe and Northern America. IMNM was described with serious consequences even with fatal outcomes. Atorvastatin was the most frequently reported statin.

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