Routine Laboratory Measures in the Controlled Treatment Period of Phase III Ocrelizumab Trials in Relapsing and Progressive Multiple Sclerosis

JS Wolinsky,1 L Kappos,2,3 X Montalban,4,5,6 C Chognot,7 H Koendgen,7 C Li7, A Pradhan,8 SL Hauser7

1McGovern Medical School, UTHealth, Houston, TX, USA; 2University Hospital Basel, University of Basel, Basel, Switzerland; 3Division of Neurology, University of Toronto, Toronto, ON, Canada; 4Vall d’Hebron University Hospital, Barcelona, Spain; 5Hoffmann-La Roche Ltd, Basel, Switzerland; 6Genentech, Inc., South San Francisco, CA, USA; 7University of California, San Francisco, San Francisco, CA, USA

BACKGROUND

The safety and efficacy of ocrelizumab (OCR) have been characterized in a Phase II study in patients with relapsing-remitting multiple sclerosis (RRMS; NCT01877715), and in the ORCHESTRA Phase III studies the enrolling patients with relapsing multiple sclerosis (RRMS; NCT01352724) and OCREVUS II (NCT01423273) or primary progressive multiple sclerosis (PPMS; ORATORIO) (NCT01941935).

• OCR reduced disease activity and disability progression in patients with RRMS (vs interferon (IFN)-b1a and IFNβ-1a) and PPMS (vs placebo).

• Patients with clinically relevant laboratory abnormalities were increases in liver enzymes (ALT and AP) and aspartate aminotransferase (AST), during the controlled treatment periods for OCR.

METHODS

In the OPERA I, OPERA II and ORATORIO studies, routine safety laboratory tests, including liver function and hematology, were conducted at baseline and every 12 weeks until the study end (Table 1). In addition, routine safety laboratory tests were conducted on Day 1 of the OPERA I and OPERA II studies. All laboratory samples collected during the OPERA I, OPERA II and ORATORIO studies were shipped to a central laboratory.

• Blood samples were collected to determine thyroid-stimulating hormone (TSH) levels.

• In the ORATORIO study, a clinically relevant increase in gamma-glutamyltransferase (GGT) was observed in a higher percentage of patients in the OCR group (35%) compared with the placebo group (6%).

OBJECTIVE

To present the routine laboratory measures in the controlled treatment period of the Phase III OCR trials in RRMS and PPMS.

RESULTS

Liver Function

• The proportions of patients with clinically relevant laboratory abnormalities were increases in liver enzymes in patients with RRMS and PPMS, including alanine aminotransferase (ALT) and aspartate aminotransferase (AST), during the controlled treatment period for OCR.

• In patients with RRMS in the pooled OPERA studies, there were increases in ALT (OCR 5.5% vs placebo 17.7% of patients with clinically relevant abnormalities) and AST (OCR 2.2% vs placebo 10.1%).

• In patients with PPMS in the ORATORIO study, there were increases in ALT (OCR 6.9% vs placebo 7.9%) and AST (OCR 2.9% vs placebo 3.3%).

• The proportions of patients with clinically relevant abnormalities for alkaline phosphatase (AP) in the pooled OPERA studies were OR 0.1% vs placebo 2.9%, and in the ORATORIO study were OCR 2.9% vs placebo 2.9%.

• For bilirubin, the total proportions of patients with clinically relevant laboratory abnormalities in the pooled OPERA studies was OCR 4.2% vs placebo 7.5%, and in the ORATORIO study was OCR 0.4% vs placebo 1.7%.

• In the ORATORIO study, a clinically relevant increase in gamma-glutamyltransferase (GGT) was observed in a higher percentage of patients in the OCR group (35%) compared with the placebo group (6%) during the controlled treatment period.

Electrolytes

• The proportions of patients with clinically relevant abnormalities in electrolyte levels (sodium and potassium) during the controlled treatment period for the pooled OPERA studies and the ORATORIO study were small and did not follow any particular pattern with OCR, FNβ-1a or placebo treatment (data not shown).

Renal Function

• The proportions of patients with clinically relevant laboratory abnormalities in renal function during the controlled treatment period for the pooled OPERA studies and the ORATORIO study were low, with no abnormalities reported for treatment in the OCR group (n=818) in the pooled OPERA studies (vs IFNβ-1a 2.9% vs placebo 2.9%).

• In the ORATORIO study, a clinically relevant increase in gamma-glutamyltransferase (GGT) was observed in a higher percentage of patients in the OCR group (35%) compared with the placebo group (6%) during the controlled treatment period.

Thyroid Function

• In the pooled OPERA studies, clinically relevant abnormal thyroid stimulating hormone (TSH) levels (increase) were observed in a lower percentage of patients in the OCR-treated group (0.4% vs 7%) compared with the IFNβ-1a group (1% vs 7%) during the controlled treatment period (data not shown).

• No clinically relevant abnormalities for TSH were reported for OCR and placebo in the ORATORIO study.

• TSH levels were determined in 39/486 (8.0%) OCR-treated patients and 14/239 (5.9%) placebo-treated patients.

CONCLUSIONS

• Overall, the proportions of patients with clinically relevant abnormal electrolyte, hematologic, renal and hepatic values were low with ocrelizumab.

• These data support an acceptable risk profile for ocrelizumab treatment.

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REFERENCES


DISCLOSURES

The studies were sponsored by Hoffmann-La Roche Ltd. Dr. Hauser is an employee of Hoffmann-La Roche Ltd and holds stock or stock options in the company. Dr. Wolinsky and Dr. Kappos are employees of Hoffmann-La Roche Ltd and hold stock or stock options in the company.