Ocrevus and Elevated Liver Enzymes

This article responds to your request for information on Ocrevus® (ocrelizumab) and elevated liver enzymes.

In brief

- There is no evidence to date to suggest a causal relationship between Ocrevus administration and elevated liver enzymes.

Abbreviations

ALT=alanine aminotransferase

AP=alkaline phosphatase

AST=aspartate aminotransferase

GGT=gamma-glutamyltransferase

IFN=interferon

Ocrevus prescribing recommendations

Ocrevus is a monoclonal antibody and is cleared via catabolism rather than hepatic metabolism. Elevated liver enzymes is not listed as an adverse event of Ocrevus in the prescribing information.[1] There are no recommendations regarding withholding Ocrevus in a patient with elevated liver enzymes.[1]

Elevated liver enzymes in Ocrevus clinical trials

Management of elevated liver enzymes

Patients were excluded from the pivotal clinical trials (OPERA I and II, and ORATORIO) if AST or ALT levels were greater than or equal to twice the upper level of normal at baseline.

If clinically significant deviations of laboratory values occurred, Ocrevus was withheld until the events resolved and laboratory values were within normal ranges.[2,3] Table 1 details the reference and marked abnormality ranges as defined in the studies.

Table 1. Overview of hepatic laboratory parameters in the studies[4]

Laboratory parameter	Reference range	Marked abnormality range	Direction of change	Clinically relevant change from baseline
ALT	M: 0–55 U/L* F: 0–30 U/L†	0–110 U/L	Increase	≥50%
AST	M: 0–40 U/L* F: 0–25 U/L†	0–80 U/L	Increase	≥50%
AP	M: 0–115 U/L* F: 0–100 U/L†	0–220 U/L	Increase	≥50%
Bilirubin (Total)	0–17 µmol/L*	0–34 µmol/L	Increase	≥75%
GGT	M: 0–94 U/L* F: 0–70 U/L†	0–190 U/L	Increase	≥50%

Occurrence of elevated liver enzymes

In the studies, the proportions of patients with marked abnormal hepatic laboratory values were generally low with Ocrevus and remained fairly constant during the controlled treatment periods.The most common clinically relevant laboratory abnormalities were increases in liver enzymes, including ALT and AST.[4]

These increases were not accompanied by increases in bilirubin levels. There were no reports of Hy's Law cases during the controlled treatment period. Most of the marked laboratory abnormalities were single occurrences and were not sustained or replicated.[4]

Details related to liver function measures during the controlled treatment period of OPERA I and II and ORATORIO are presented in Tables 2.

Table 2. Patients with clinically relevant abnormalities in liver function in OPERA I and II and ORATORIO studies[4]

	OPERA I and II		ORATORIO	
Laboratory parameter	**IFN beta-1a 44 mcg (n=826)**	**Ocrevus 600 mg (n=825)**	**Placebo (n=239)**	**Ocrevus 600 mg (n=825)**
ALT	17.7%	5.1%	7.5%	6.9%
AST	10.1%	2.2%	3.3%	2.9%
AP	0.4%	0.1%	0.8%	0.6%
Bilirubin (Total)	0.1%	0.5%	1.7%	0.4%
GGT	9.1%	4.3%	4.6%	6.9%

References

1. Roche Internal Regulatory Report (Accessed on 8 August 2023).

2. Hauser S, Bar-Or A, Comi G, et al. Ocrelizumab versus Interferon Beta-1a in Relapsing Multiple Sclerosis. N Engl J Med 2017;376:221-234. https://www.ncbi.nlm.nih.gov/pubmed/28002679

3. Montalban X, Hauser S, Kappos L, et al. Ocrelizumab versus Placebo in Primary Progressive Multiple Sclerosis. N Engl J Med 2017;376:209-220. https://www.ncbi.nlm.nih.gov/pubmed/28002688

4. Wolinsky J, Kappos L, Montalban X, et al. Routine laboratory measures in the controlled treatment period of Phase III ocrelizumab trials in relapsing and progressive multiple sclerosis. Presented at the American Academy of Neurology Annual Meeting in Los Angeles, CA; April 21-27, 2018. AAN Poster #425.