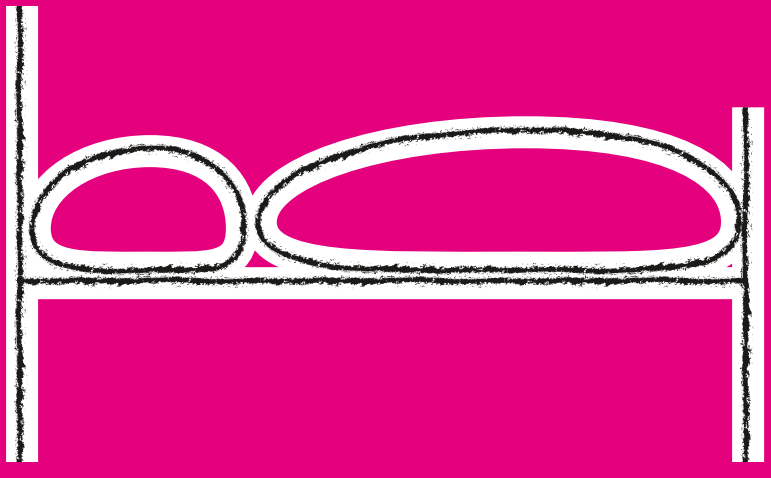
SCIENCE

ORAL LOLA IMPROVES HEALTH-RELATED QUALITY OF LIFE IN CIRRHOTIC PATIENTS WITH HEPATIC ENCEPHALOPATHY



Ong JP et al. Clin Drug Investig. 2011;31(4):213-20.

Hepa-Merz®
L-ornithine-L-aspartate

HEPA-MERZ® MARKEDLY IMPROVES HRQOL IN PATIENTS WITH HE

Introduction

- Health-related quality of life (HRQOL) is markedly impaired in patients with chronic liver disease, a condition associated with hepatic encephalopathy (HE)
- Both physical and mental aspects of HRQOL are affected in HE patients and neuropsychiatric disturbances are a hallmark of HE

Study

Objective

Evaluate the effect of Hepa-Merz® treatment on patient quality of life.

Design

8-week, open-label, prospective, multicentre observational study conducted in Germany on 191 cirrhosis patients with HE.

Patient population

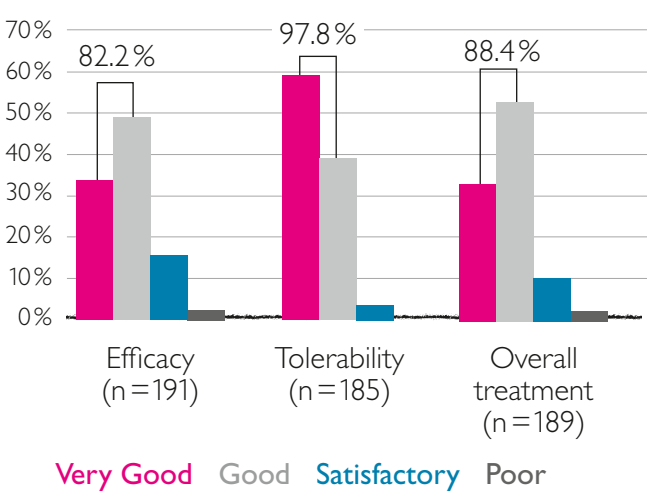
Causes of cirrhosis in the study population included alcoholic liver disease (87.2% of patients), drug-induced liver disease (5.9% of patients), metabolic disorder (5.9% of patients), viral hepatitis (5.3% of patients) and autoimmune liver disease (2.1% of patients).

Treatment

Patients were treated with Hepa-Merz® Granules (6 g sachets taken 3 times per day for 8 weeks) – Open-label study design mimics real-life product usage.

Results

Overall assessment of efficacy and tolerability by week 8 (data are % of patients)

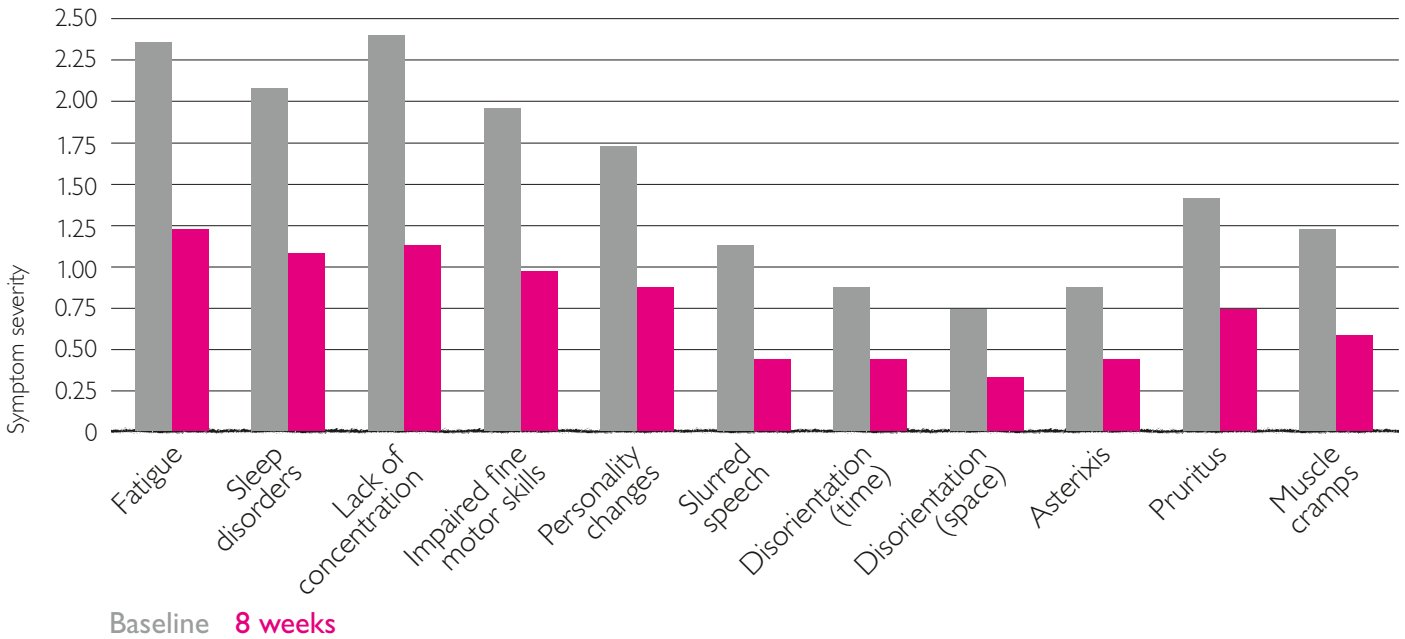


Patients noticeably improved during 8 weeks of therapy with Hepa-Merz®

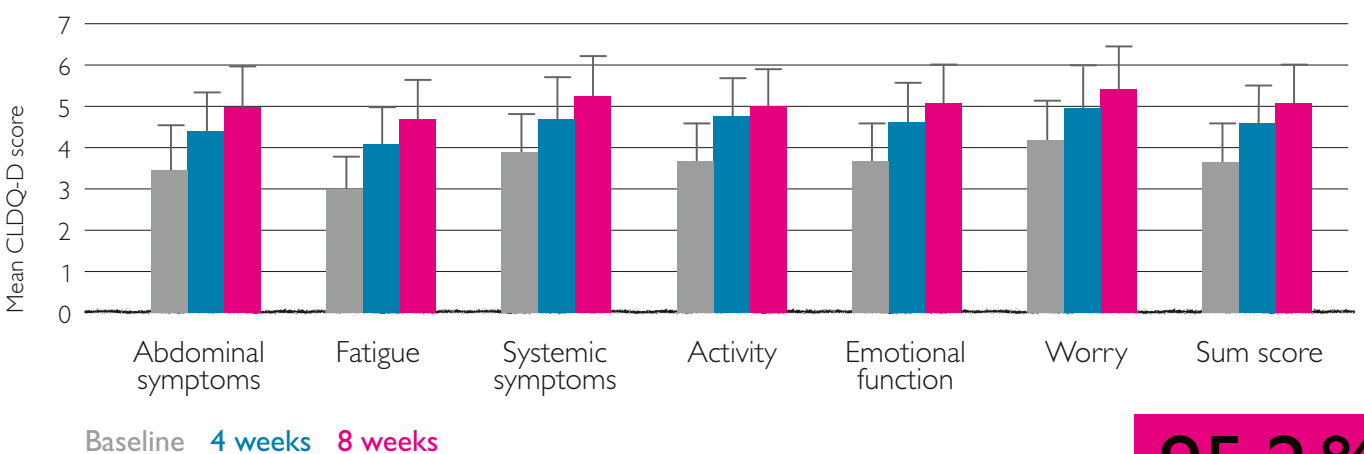
- Physicians reported that 70% of patients were "much" or "very much" improved after 8 weeks of therapy as measured by the modified Clinical Global Impression-Improvement scale (CGI-I) – 22.4% of patients were "moderately improved," 6.0% saw no change, and 1.6% were considered to be worse by the end of treatment
- The proportion of markedly or severely ill patients was reduced by 63% by the end of the study (59.5% at study entry to 22% at 8 weeks)

HEPA-MERZ® IMPROVES ALL MEASURES OF HRQOL

Hepa-Merz® Effectively reduced the full range of HE-related symptoms*



Hepa-Merz® treatment resulted in significant improvement across all HRQOL measures[7,**]



95.2%
of patients
reported improved HRQOL[7]

The domain "fatigue" showed the most substantial improvement (67.5%), followed by "abdominal symptoms" (50.8%) and "emotional functioning" (42.0%)

Hepa-Merz® was well tolerated by 98% of study patients
No drug-related adverse events were reported during the observation period

Hepa-Merz®
L-ornithine-L-aspartate

HEPA-MERZ® IS A WELL TOLERATED OPTION TO IMPROVE HRQOL IN PATIENTS WITH HE

Conclusion

Treatment with Hepa-Merz® granules results in improved quality of life and is well tolerated.

Hepa-Merz® Prescribing Information

Hepa-Merz® Granules. Active substance: L-ornithine-L-aspartate. **Composition:** One sachet with 5 g of Granules contains: **Active substance:** 3 g L-ornithine-L-aspartate. **Excipients:** citric acid, saccharin sodium, sodium cyclamate, povidone 25, fructose, flavorings, orange yellow S (E110). Note for diabetics: One sachet of Hepa-Merz® Granules contains 1.13 g of fructose (corresponds to approx. 0.11 BU). **Therapeutic indications:** Treatment of concomitant disease and sequelae due to impaired detoxification activity (e.g. in cirrhosis of the liver) with the symptoms of latent and manifest hepatic encephalopathy. **Contraindications:** Absolute: Hypersensitivity to L-ornithine-L-aspartate, orange yellow S or any of the other excipients. Severely impaired renal function (renal insufficiency). A serum creatinine value over 3 mg/100 ml can be used as a guideline value. Relative: Pregnancy and lactation: No clinical data are available relating to intake of Hepa-Merz® Granules during pregnancy. No exhaustive animal studies have been performed for L-ornithine-L-aspartate, to investigate its toxicity in relation to reproduction. Administration of Hepa-Merz® Granules during pregnancy should therefore be avoided. If, however, treatment with Hepa-Merz® Granules is considered necessary, careful consideration should be given to the benefit versus risk ratio. It is not known whether L-ornithine-L-aspartate is excreted into the breast milk. Administration of Hepa-Merz® Granules should therefore be avoided during lactation. If, however, treatment with Hepa-Merz® Granules is considered necessary, careful consideration should be given to the benefit versus risk ratio. **Undesirable effects:** Uncommon (≥ 1/1000 to < 1/100): Nausea, vomiting, stomach ache, flatulence, diarrhea. Very rare (< 1/10000): Pain in the limbs. These undesirable effects are usually transient and do not require withdrawal of the medicine. Orange yellow S (E110) can trigger allergic reactions. **Warnings:** Hepa-Merz® Granules contain fructose. Patients with rare hereditary problems of fructose intolerance should not take this medicine. **Further precautions:** As a result of the disease, the ability to drive and operate machinery may be impaired during treatment with L-ornithine-L-aspartate.

Hepa-Merz® Infusion concentrate. Active substance: L-ornithine-L-aspartate. **Composition:** One ampoule of 10 ml contains: **Active substance:** 5 g L-ornithine-L-aspartate. **Excipients:** Water for injections. **Therapeutic indications:** Latent and manifest hepatic encephalopathy. **Contraindications:** Absolute: Hypersensitivity to L-ornithine-L-aspartate. Severe renal impairment (renal failure). A serum creatinine level in excess of 3 mg/100 ml can be taken as a guide. Relative: Pregnancy and lactation: There are no clinical data available on the use of Hepa-Merz® Infusion concentrate in pregnancy. L-ornithine-L-aspartate has been investigated for reproduction toxicity only to a limited extent in experimental animal studies. The administration of Hepa-Merz® Infusion concentrate in pregnancy should therefore be avoided. If treatment with Hepa-Merz® is nevertheless thought to be necessary, the benefits and risks should be carefully assessed. It is not known whether L-ornithine-L-aspartate passes into breast milk. Administration of Hepa-Merz® should therefore be avoided during lactation. If treatment with Hepa-Merz® is nevertheless thought to be necessary, the benefits and risks should be carefully assessed. **Undesirable effects:** Uncommon (≥ 1/1000 to < 1/100): Nausea. Rare (≥ 1/10000 to < 1/1000): vomiting. Frequency not known (frequency cannot be estimated from the available data): hypersensitivity, anaphylactic reaction. Generally however, the gastrointestinal symptoms are transient, and do not necessitate discontinuation of treatment. They disappear on reduction of the dose or the infusion rate. **Further precautions:** Hepa-Merz® concentrate for solution for infusion can be mixed with the usual infusion solutions. So far no peculiarities have been observed with regard to miscibility. However, the ampoules should be admixed to the infusion solution only immediately before application. At high doses of Hepa-Merz® Infusion concentrate, serum and urine urea levels should be monitored. If liver function is substantially impaired, the infusion rate must be adjusted to the individual patient in order to prevent nausea and vomiting. Depending on the underlying disease, the ability to drive and operate machines may also be impaired on treatment with L-ornithine-L-aspartate. Hepa-Merz® Infusion concentrate must not be injected into an artery. Status: January 2013. Merz Pharmaceuticals GmbH, 60048 Frankfurt.

Reference: Ong JP, Oehler G, Krüger-Jansen C, Lambert-Baumann J, Younossi ZM. Oral L-ornithine-L-aspartate improves health-related quality of life in cirrhotic patients with hepatic encephalopathy: an open-label, prospective, multicentre observational study. Clin Drug Investig. 2011;31(4): 213-220.

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**Self-assessment by patient using German-validated version of Chronic Liver Disease Questionnaire (CLDQ-D). This figure has been reproduced with permission from Adis, a Wolters Kluwer usiness[7]

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