

ILC 2017: Long-term antibiotic prophylaxis can decrease short-term mortality in patients with life-threatening advanced liver disease

Norfloxacin reduces the risk of infections and death at 6 months in patients with Child-Pugh class C cirrhosis

April 20, 2017, Amsterdam, The Netherlands: A multicentre, randomised, controlled study presented today found that long-term oral antibiotic therapy with norfloxacin improved the prognosis of people with life-threatening advanced liver disease. The study, presented at The International Liver Congress™ 2017 in Amsterdam, The Netherlands, showed that norfloxacin administration for 6 months was associated with a reduced risk of death and infection at 6 months in patients with Child-Pugh class C cirrhosis (scarring of the liver), a very severe and advanced stage of liver disease.

The French study demonstrated that at 12 months, following 6 months after termination of treatment, the cumulative incidence of death was similar between those treated with norfloxacin and those treated with placebo. However, the infection rates remained lower in the norfloxacin group at 12 months.

Patients with advanced liver disease who have cirrhosis have differing prognoses. The Child-Pugh classification system, which is used to estimate prognosis in cirrhosis, rates levels of cirrhosis from A to C, with C being the most advanced cases. Child-Pugh class C indicates that the person has decompensation of the liver,¹ which is a life threatening condition in which extensive scarring of the organ results in its inability to function properly.² Decompensated cirrhosis is a leading reason for liver transplantation. Over 8,500 people in Europe³ and over 16,000 people in the United States are waiting for a liver transplant, with this number expected to increase.⁴

"This study shows that long-term oral antibiotic therapy may improve the prognosis of patients with life-threatening liver disease. However, overuse of broad spectrum antibiotics is a subject that has been thoroughly debated over the years," said Dr Richard Moreau, Beaujon, Hospital, Clichy, France, and lead author of the study. "The results from this study provide evidence that 6 months of norfloxacin therapy reduces the risk of infections and death in the short-term, but not in the longer-term."

This randomised, placebo-controlled, phase 3 trial assigned 291 patients with Child-Pugh class C cirrhosis to receive either a 400mg norfloxacin tablet or placebo once a day for 6 months. Patients were followed up for an additional 6 months for infections, death and other liver-related complications.

After 6 months of treatment, fewer patients had died in the norfloxacin group than the placebo group (22 [15.3%] versus 36 [24.5%]). Seventeen (11.8%) patients had received a

liver transplant in the norfloxacin group compared with 15 (10.2%) in the placebo group. At 6 months follow-up, the cumulative incidence of death was lower in the norfloxacin than placebo group (15.5% versus 24.8%), although at 12 months the cumulative incidence of death was similar in the two groups. At 6 months follow-up, fewer patients receiving norfloxacin had developed an infection compared with the placebo group (30 [20.8%] versus 46 [31.3%]). The cumulative incidence of infection at 6 months was lower in the norfloxacin group, and at 12 months remained lower compared with the placebo group. The cumulative incidence of any other liver-related complication was similar in the two groups at both 6 and 12 months.

“Abnormal bacterial translocation from the gut not only favours the development of bacterial infections, but also contributes to the chronic pro-inflammatory state that characterises advanced cirrhosis, which is responsible for multi-organ dysfunction and, ultimately, failure. Thus, long-term norfloxacin administration can be seen as treatment acting against a core pathophysiological mechanism. Indeed, until this antibiotic was administered, not only the incidence of bacterial infections, but also mortality was reduced. This favourable result, however, should be weighed against the risk of selecting antibiotic-resistant bacterial strains and studies devoted to his topic are warranted”, said Prof Mauro Bernardi, Department of Medical and Surgical Sciences, University of Bologna, Italy and member of the EASL Governing Board.

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About The International Liver Congress™

This annual congress is the biggest event in the EASL calendar, attracting scientific and medical experts from around the world to learn about the latest in liver research. Attending specialists present, share, debate and conclude on the latest science and research in hepatology, working to enhance the treatment and management of liver disease in clinical practice. This year, the congress is expected to attract approximately 10,000 delegates from all corners of the globe. The International Liver Congress™ 2017 will take place from April 19 – 23, at the RAI Amsterdam, Amsterdam, The Netherlands.

About The European Association for the Study of the Liver (EASL) (www.easl.eu)

Since its foundation in 1966, this not-for-profit organisation has grown to over 4,000 members from all over the world, including many of the leading hepatologists in Europe and beyond. EASL is the leading liver association in Europe, having evolved into a major European Association with international influence, with an impressive track record in promoting research in liver disease, supporting wider education and promoting changes in European liver policy.

Contact

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Onsite location reference

Session title: General session I and opening ceremony, Hall 5

Time and date of session: Thursday 20 April, 13:30 – 15:30

Presenter: Richard Moreau, France

Abstract: A randomized trial of 6-month norfloxacin therapy in patients with Child-Pugh class C cirrhosis (GS001), 13:50 – 14:05

Author disclosures

None.

References

1 NHS Specialists Pharmacy Service. What is the Child-Pugh score? Available from:

<https://www.sps.nhs.uk/articles/what-is-the-child-pugh-score/>. Last accessed: March 2017.

2 Franciscus, A & HCV Advocate. HCSP Fact Sheet – HCV Disease Progression. Available from: http://hcvadvocate.org/hepatitis/factsheets_pdf/cirrhosis.pdf. Last accessed: March 2017.

3 European Commission. Organ donation and transplantation: Facts and figures. Published November 2014. Available from:

http://ec.europa.eu/health/blood_tissues_organ/docs/ev_20141126_factsfigures_en.pdf.

Last accessed: March 2017.

4 Habka D, et al. Future Economics of Liver Transplantation: A 20-Year Cost Modeling Forecast and the Prospect of Bioengineering Autologous Liver Grafts. *PLoS One*. 2015; 10(7):e0131764.