Bezafibrate Add-on Therapy in High-Risk Primary Biliary Cholangitis is Associated with an Improvement of FibroMeter and FibroMeter-VCTE, two High-Accuracy Non-Invasive Fibrosis Tests Extensively Validated in Frequent Chronic Liver Diseases

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1 INTRODUCTION

- Data from the BEZURSO trial [1] showed that 2 years of bezafibrate (BZF) therapy in addition to continued ursodeoxycholic acid (UDCA) improved the measures of vibration-controlled transient elastography (VCTE) and of enhanced liver fibrosis (ELF) score in patients with high-risk primary biliary cholangitis (PBC).
- The number of sequential liver biopsies, however, was too limited to show an effect on histological progression.

2 AIM

This post-hoc analysis aimed to assess the effect of BZF add-on therapy on the measures of FibroMeter and FibroMeter-VCTE, two high-accuracy non-invasive fibrosis tests [2, 3] and of Inflameter, a necro-inflammatory activity score.

3 METHOD

- The study population included 100 patients with a Paris-2 incomplete response to UDCA at baseline who were randomly assigned to bezafibrate 400 mg/d (n=50) or placebo (n=50), in addition to continued UDCA, for 24 months.
- FibroMeter^{2G}, FibroMeter^{2G}-VCTE, and InflaMeter (Echosens, France) were measured at baseline, 12 months, and end of study (EOS).
- Associations with histological fibrosis stage and hepatitis activity grade as defined by the METAVIR classification system were evaluated using the Kruskal-Wallis test.
- The performance for the diagnosis of cirrhosis was determined using the logistic C-statistic.
- Longitudinal changes in FibroMeter^{2G}, FibroMeter^{2G}-VCTE, and InflaMeter were analyzed in each treatment group using linear mixed models after log transformation.

4 RESULTS

- The parameters included in the calculation of FibroMeter^{2G}, FibroMeter^{2G}-VCTE, and InflaMeter are shown in **Table 1**.
- A total of 235, 210, and 235 measures of FibroMeter^{2G}, FibroMeter^{2G}-VCTE, and InflaMeter were analyzed in 82, 75, and 82 patients, respectively (**Table 2**).
- Concordance analysis was made based on 105 liver biopsies collected during the BEZURSO trial in 82 patients. Histological staging and grading was performed in each center according to local routine examination procedures.
- FibroMeter^{2G} and FibroMeter^{2G}-VCTE were significantly associated with histological fibrosis stage (p<0.001 for both; **Figure 1**). but not with hepatitis activity grade (data not shown).
- InflaMeter was associated with high hepatitis activity grade (p=0.07; data not shown).
- The diagnostic performance (95% CI) of FibroMeter^{2G} and FibroMeter^{2G}-VCTE for cirrhosis was 0.83 (0.67 – 0.96) and 0.92 (0.82 – 0.99), respectively.
- Longitudinal analysis showed a significant reduction in the slope of FibroMeter^{2G}, FibroMeter^{2G}-VCTE, and InflaMeter in the bezafibrate group as compared to the placebo group (p<0.001 for all, **Table 3**).
- The median differences (95% CI) between bezafibrate and placebo groups in percent changes from baseline to EOS in FibroMeter^{2G}, FibroMmeter^{2G}-VCTE, and InflaMeter were -42% (-69%; -14%), -37% (-83%; 8%), and -35% (-52%; -17%), respectively (**Figure 2**).

Table 1. Parameters included in the tests.

	FM^{2G}	FM^{2G}-VCTE	InflaMeter
Age	✓	✓	
Gender	✓	✓	
A2-macroglobulin	✓	✓	✓
Hyaluronic acid	✓	✓	
Platelet count	✓	✓	✓
Prothrombin index	✓	✓	✓
AST	✓	✓	
Urea	✓	✓	
Liver stiffness		✓	
ALT			✓

Table 2. Number of measurements.

	FM^{2G}	FM^{2G}-VCTE	InflaMeter
Baseline	82	75	82
Month 12	77	62	77
Month 24	76	73	76
Total	**235**	**210**	**235**

Figure 1. Associations of FM^{2G} (left panel) and FM^{2G}-VCTE (right panel) with severe histological fibrosis.

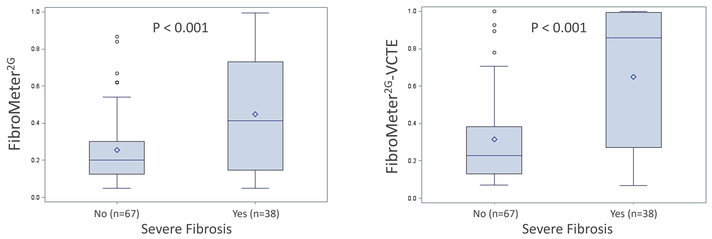
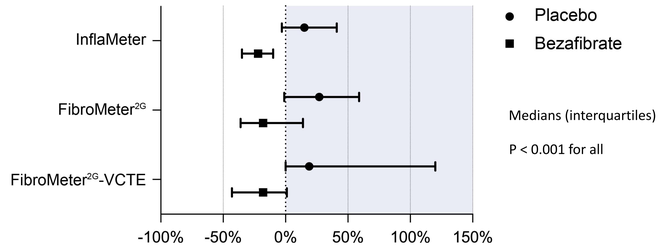


Table 3. Changes over time in FM^{2G}, FM^{2G}-VCTE, and InflaMeter as analyzed by linear mixed models.

	FibroMeter^{2G}			FibroMeter^{2G}-VCTE			InflaMeter		
	Estimate	SD	P	Estimate	SD	P	Estimate	SD	P
Intercept BZF - Placebo	0.1517	0.1669	0.3645	0.2720	0.2046	0.1852	0.2118	0.1118	0.0595
Slope (per year) Placebo	0.1560	0.03659	<.0001	0.1738	0.04640	0.0002	0.08747	0.02492	0.0005
Slope (per year) BZF	-0.04634	0.03643	0.2046	-0.1020	0.04763	0.0335	-0.1072	0.02484	<.0001
Slope (per year) BZF - Placebo	**-0.2023**	**0.05163**	**0.0001**	**-0.2758**	**0.06650**	**<.0001**	**-0.1947**	**0.03519**	**<.0001**

Figure 2. Percentage changes from baseline to EOS in InflaMeter, FM^{2G}, and FM^{2G}-VCTE.



5 CONCLUSIONS

- Two years of Bezafibrate add-on therapy in high-risk PBC is associated with a significant improvement of Inflameter, Fibrometer^{2G}, and Fibrometer^{2G}-VCTE, thus supporting a long-term beneficial effect on both hepatic inflammation and fibrosis.
- Long-term histological studies are required to confirm these results.

6 ACKNOWLEDGEMENTS

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7 REFERENCES

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