|  |  |
| --- | --- |
|  | **Fibulin-1, log μg/mL** |
|  | **Baseline** | **1 Year follow-up** | **4 year follow-up** |
|  |  | **Placebo** | **Treated** | **Placebo** | **Treated** |
| NT-proBNP, pg/mL | r=0.175; p=0.001 | r=0.222; p=0.002 | r=0.238; p=0.001 | r=0.354; p<0.0001 | r=0.262; p<0.0001 |
| suPAR, ng/mL | r=0.135; p=0.007 | r=0.302; p<0.0001 | r=0.204; p=0.004 | r=0.317; p<0.0001 | r=0.225; p=0.002 |
| Aortic valve area index, log cm2/m2 | r=–0.143; p=0.007 | r=–0.208; p=0.009 | r=–0.044; p=0.57 | r=–0.211; p=0.006 | r=–0.127; p=0.085 |
| Left ventricular mass index, log g/m2 | r=–0.072; p=0.18 | r=–0.055; p=0.48 | r=–0.044; p=0.57 | r=0.005; p=0.94 | r=–0.001; p=0.99 |
| Aortic regurgitation, cm | r=–0.023; p=0.68 | r=0.004; p=0.96 | r=–0.078; p=0.31 | r=–0.117; p=0.13 | r=–0.056; p=0.45 |
| Ejection fraction, % | r=–0.015; p=0.78 | r=–0.032; p=0.69 | r=–0.057; p=0.47 | r=–0.081; p=0.29 | r=–0.021; p=0.77 |

**Table S1.** Partial correlation coefficients of fibulin-1 with NT-proBNP, suPAR and aortic/cardiac measures at baseline and follow-up in patients with aortic stenosis stratified by treatment allocation

Adjustments applied for: age, body mass index and serum creatinine.

**Table S2.** Multiple regression analysis of fibulin-1 and NT-proBNP in patients with mild AS at baseline and after one and four years of treatment

|  |  |
| --- | --- |
|  | **Fibulin-1, μg/mL** |
|  | **BASELINE** | **1 YEAR FOLLOW-UP** | **4 YEARS FOLLOW-UP** |
| *R2* | 0.21 | 0.25 | 0.32 |
| *Adjusted R2* | 0.19 | 0.22 | 0.29 |
|  | **Standard β** | **p value** | **Standard β** | **p value** | **Standard β** | **p value** |
| NT-proBNP, pg/mL | 0.032 | 0.68 | 0.109 | 0.14 | 0.203 | 0.007 |
| suPAR, ng/mL | 0.076  | 0.31 | 0.153 | 0.040 | 0.158  | 0.036 |
| Age, years | 0.358  | <0.0001 | 0.308  | <0.0001 | 0.304 | <0.0001 |
| Gender | 0.194  | 0.092 | 0.130  | 0.061 | 0.160  | 0.020 |
| Aspartate aminotransferase, U/L | 0.132 | 0.058 | 0.115  | 0.12 | 0.067 | 0.33 |
| Treatment  | – | – | 0.063  | 0.37 | –0.002 | 0.98 |

Multivariate analysis was performed independently of age, gender, aspartate aminotransferase levels and treatment allocation.

**Table S3.** Multiple regression analysis of fibulin-1 and NT-proBNP in patients with moderate AS at baseline and also after one and four years of treatment

|  |  |
| --- | --- |
|  | **Fibulin-1, μg/mL** |
|  | **BASELINE** | **1 YEAR FOLLOW-UP** | **4 YEARS FOLLOW-UP** |
| *R2* | 0.17 | 0.26 | 0.29 |
| *Adjusted R2* | 0.15 | 0.24 | 0.26 |
|  | **Standard β** | **p value** | **Standard β** | **p value** | **Standard β** | **p value** |
| NT-proBNP, pg/mL | 0.250 | 0.001 | 0.213 | 0.003 | 0.223 | 0.004 |
| suPAR, ng/mL | 0.085  | 0.26 | 0.228 | 0.003 | 0.213  | 0.006 |
| Age, years | 0.117  | 0.142 | 0.037  | 0.63 | 0.124 | 0.12 |
| Gender | 0.178 | 0.014 | 0.218  | 0.002 | 0.214  | 0.002 |
| Aspartate aminotransferase, U/L | 0.168 | 0.022 | 0.228  | 0.001 | 0.194 | 0.006 |
| Treatment  | – | – | 0.054  | 0.41 | 0.013 | 0.85 |

Multivariate analysis was performed independently of age, gender, aspartate aminotransferase levels and treatment allocation.