STIFFNESS? AN EXPLORATORY STUDY

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Background: Systemic sclerosis (SSc)-related vasculopathy is generally thought to occur on a microvascular level. However, some observations also suggest involvement of arterial vessels. Macrovascular involvement (e.g., aorta or upper extremity) can be non-invasively assessed by measuring pulse wave velocity (PWV). Although, several studies have assessed aortic and upper extremity PWV in SSc, studies have not reached a consensus regarding this matter. Furthermore, we hypothesized that the endothelin antagonist bosentan may improve arterial stiffness by its direct endothelial and potential anti-fibrotic effects.

Objectives: The aim of this exploratory study was two-fold. First, we aimed to compare arterial stiffness in patients with SSc and age and sex-matched healthy controls (HC). Secondly, we will investigate the effect of bosentan on both short-term (three month) and long-term (one year) PWV.

Methods: Baseline differences between HC and SSc patients were studied in a case-control design. The follow-up of SSc patients was a randomized, prospective, 2-arm parallel group, open-label, blinded endpoint, intervention study. PWV (Sphygmocor) in meters/second was measured to assess arterial stiffness in the aorta (carotid-femoral PWV), upper arm (carotid-brachial PWV), and forearm (brachial-radial PWV), adjusted for mean arterial pressure.

Results: Baseline characteristics are shown in table 1. No significant differences were observed in PWV (at all sites) between HC and SSc patients. No effect of bosentan on aortic, and upper arm PWV was found. The change in forearm PWV was different between the groups, with a decrease (e.g. lowering arterial stiffness) in the bosentan group (figure 1).

Table 1. Baseline characteristics

<table>
<thead>
<tr>
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<th>Healthy controls (n=19)</th>
<th>Systemic sclerosis patients (n=19)</th>
<th>Bosentan group (n=9)</th>
<th>Usual care group (n=10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female, n (%)</td>
<td>13 (69)</td>
<td>13 (69)</td>
<td>6 (67)</td>
<td>6 (60)</td>
</tr>
<tr>
<td>Age in years, median (IQR)</td>
<td>53 (47–63)</td>
<td>50 (44–54)</td>
<td>52 (49–60)</td>
<td>54 (43–66)</td>
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<tr>
<td>Pack years, median (IQR)</td>
<td>0 (0–7.5)</td>
<td>2.5 (0–30.6)</td>
<td>17.3 (0.7–34.1)</td>
<td>0.8 (0–2.75)</td>
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Conclusion: This small study shows that aortic, upper arm, and forearm arterial stiffness does not appear to increase in patients with SSc, as compared to age- and sex-matched healthy controls. To the best of our knowledge, this is the first study to investigate the concept of potential effects of an endothelin receptor antagonist on macrovascular involvement in SSc. Although the results demonstrate no effects on aorta and upper arm arterial stiffness, they may indicate a beneficial effect on the stiffness of the smaller arteries of the forearm. Future studies are needed to further investigate the potential effect of bosentan on these smaller arteries.

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SAFETY AND EFFICACY OF LENABASUM IN AN OPEN-LABEL EXTENSION OF A PHASE 2 STUDY OF LENABASUM IN RefRactory Skin-Predominant DERMATOMYOSITIS (DM) SUBJECTS

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Background: Lenabasum is a synthetic, non-immunosuppressive, selective cannabinoid receptor type 2 agonist that activates resolution of innate immune responses. Lenabasum had acceptable safety and tolerability and improved efficacy outcomes in the initial 16-week double-blinded, randomized, placebo-controlled Part A of Phase 2 trial JBT101-DM-001 (NCT02466243) in dermatomyositis (DM) subjects with refractory, skin-predominant involvement.

Objectives: To provide long-term safety and efficacy data in DM subjects in this study.

Methods: Subjects who completed Part A were eligible to receive oral lenabasum 20 mg BID in an open-label extension (OLE) that assessed safety and efficacy at 4 weeks, then every 8 weeks.

Results: 20/22 (90.9%) eligible subjects received open-label lenabasum, following a mean interval of 31 weeks from end of Part A, during which when they received only standard-of-care, to start of OLE during which lenabasum 20 mg BID was added. 17/20 (85.0%) subjects were on stable baseline

Figure 1. The mean (IQR) of the brachial-radial pulse wave velocity over time of the bosentan and usual care group