Appendix 1

The BUC-63 Investigators

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Appendix 2. Interim analysis

The study was conducted using an adaptive two-stage group sequential test design within the $\Delta$-class of critical values according to Wang and Tsiatis (w1). The planned information rates were 0.4 and 1, i.e. the interim analysis was intended to take place after observation of 40% of the originally planned number of patients. These information rates fix the weights for combining the p-values using the weighted inverse normal method (w2). The critical values of the group sequential test design were calculated for the standardized (cumulative) test statistic for the design with boundary shape parameter $\Delta = 0.0$, i.e. O’Brien/Fleming type design.

<table>
<thead>
<tr>
<th>Stage</th>
<th>Critical value</th>
<th>Sign. level (one-sided)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3.110</td>
<td>0.0009</td>
</tr>
<tr>
<td>2 (final)</td>
<td>1.967</td>
<td>0.0246</td>
</tr>
</tbody>
</table>

The interim analysis was performed by an Independent Data Monitoring Committee (IDMC) after observation of 34 patients who were evaluable in the intention-to-treat (ITT) analysis. If the study continued without adaptation, the final analysis was to be performed after observation of a further 52 ITT evaluable patients.

From the 34 patients in the interim analysis, 16 patients (47.1%) were in the budesonide group and 18 patients (52.9%) in the placebo group. The proportion of patients in remission over 52 weeks was 56.3% (9/16 patients) in the budesonide group and 11.1% (2/18 patients) in the placebo group. The treatment difference with respect to remission over 52 weeks was 45.1% in favor of budesonide (95% repeated CI: [-5.0%, 78.2%]). The hypothesis test for treatment difference yielded a one-sided observed p-value of 0.0025 (overall one-sided p-value 0.0389) with a corresponding inverse test statistic of 2.808. This was below the pre-defined critical
value of 3.110 for the interim analysis. As a consequence the null hypothesis could not be rejected as the observed inverse test statistic did not exceed the critical level.

References
