Explanation of the CRT Response Score

As opposed to a traditional Clinical Composite Score, the CRT response score is a hierarchical clinical endpoint that takes into account several parameters that have frequently been used in literature to assess response to CRT. As opposed to a more conventional time-to-event endpoint, the CRT response scores takes into account both the severity and frequency of endpoints.

In brief, physiological improvement is assessed at the 6 months follow-up visit, both in terms of *the extent of* reverse remodelling (i.e., LVESVi-reduction). Functional improvement in assessed using New York Heart Association (NYHA) classification. In addition, deaths and HF hospitalizations will be taken into account until 12 months after the initial CRT implantation procedure as hard clinical endpoints.

The CRT response score will be calculated as follows:

1. A patient who dies within 12 months after the initial implantation procedure will be assigned a score = 0.
2. All other patients will have a base score = 2, adapted with additive contributions for HF hospitalizations, relative LVESVi change, and (change in) NYHA class:
   a) For each HF hospitalization within 12 months after the initial implantation procedure, 2 is subtracted.
   b) Change in LVESVi at the 6 months visit compared to baseline will contribute:
      - +2 when there is ≥30% reduction (i.e., super-response),
      - +1 when reduced ≥15% but <30% (i.e., response),
      - +0 when LVESVi is reduced but <15% (i.e., non-response), or
      - -1 when LVESVi has increased (i.e., negative response).
   c) NYHA class at the 6 months visit will contribute +1 when the patient is in Class I or has improved by at least 1 class compared to baseline; +0 when NYHA class is unchanged; or -1 when NYHA class has worsened.
3. A negative score is replaced by 0.

The change score will be determined for all patients, also in case of partially missing data. A patient without any follow-up data will get the base score = 2. The maximal score will be 5, which is achieved by patients who survive through 12 months without HF hospitalization and have ≥30% reduction of LVESVi as well as improvement of NYHA class. The minimal score is 0, which can be achieved in several ways: including death, HF hospitalization and no improvement on LVESVi or NYHA class, multiple HF hospitalizations, or increase in LVESVi and NYHA class worsening.