

# List of major randomized clinical trials involving antiarrhythmic drugs and their effect on mortality and sudden arrhythmic death

| Drugs     | Study                    | Inclusion Criteria                           | Endpoints  | Drugs                                   | Control | Key Results   |
|-----------|--------------------------|--|--|---|---------|---|
| Class I   | CASH <sup>15</sup>       | Recent cardiac arrest not associated with MI | Total mortality Arrhythmic death                                   | Propafenone<br>Metoprolol<br>Amiodarone | ICD     | Sudden cardiac death mortality lowest in the ICD arm; increased mortality in the propafenone arm  |
|           | CAST <sup>16, 17</sup>   | Post-MI $\geq 6$ PVCs/hr LVEF $\leq 40\%$    | Arrhythmic death   | Flecainide<br>Encainide<br>Moricizine   | Placebo | Arrhythmic death increased in all treatment arms  |
|           | IMPACT <sup>18</sup>     | Post-MI                                      | Rate of PVCs and complex ventricular arrhythmias<br>Mortality      | Mexiletine                              | Placebo | Rate of PVCs and complex ventricular arrhythmias was lower in treatment arm at 4 months and a trend towards reduction was observed in treatment arm at 12 months; trend towards mortality increase in treatment arm |
| Class II  | BHAT <sup>19</sup>       | Post-MI                                      | Total mortality Sudden cardiac death                               | Propranolol                             | Placebo | Total mortality and sudden cardiac death decreased in treatment arm   |
|           | CAPRICORN <sup>20</sup>  | Post-MI LVEF $\leq 40\%$                     | Death or arrhythmias   | Carvedilol                              | Placebo | Death or arrhythmia decreased in carvedilol arms; ventricular arrhythmias also decreased in treatment arm   |
|           | CIBIS-II <sup>21</sup>   | NYHA Class III-IV LVEF $\leq 35\%$           | All-cause mortality  | Bisoprolol                              | Placebo | All-cause mortality was less in treatment arm; rate of sudden cardiac death less in treatment arm   |
|           | MERIT-HF <sup>22</sup>   | NYHA Class II-IV LVEF $\leq 40\%$            | All-cause death Sudden cardiac death                               | Metoprolol CR/XL                        | Placebo | All-cause death and sudden cardiac death lower in treatment arm   |
| Class III | ANDROMEDA <sup>23</sup>  | NYHA Class III-IV LVEF $\leq 35\%$           | Death from any cause or hospitalization for HF<br>Arrhythmic death | Dronedarone                             | Placebo | Increased mortality as well as arrhythmic death in treatment arm  |
|           | BASIS <sup>24</sup>      | Post-MI PVCs                                 | Total mortality Arrhythmic events                                  | Amiodarone                              | Placebo | Total mortality and arrhythmic events lower in treatment arm  |
|           | CAMIAT <sup>25</sup>     | Post-MI $\geq 10$ PVCs/hr or NSVT            | Arrhythmic death Total mortality                                   | Amiodarone                              | Placebo | Amiodarone reduced arrhythmic death but did not reduce total mortality  |
|           | CHF-STAT <sup>26</sup>   | CHF LVEF $\leq 40\%$ $\geq 10$ PVCs/hr       | Total mortality  | Amiodarone                              | Placebo | No effect in ischemic cardiomyopathy but there was a trend towards mortality reduction in nonischemic cardiomyopathy  |
|           | DIAMOND-MI <sup>27</sup> | Post-MI ( $\leq 7$ days) LVEF $\leq 35\%$    | All-cause mortality Arrhythmic death                               | Dofetilide                              | Placebo | No reduction of all-cause mortality or arrhythmic death in treatment arm  |
|           | EMIAT <sup>28</sup>      | Post-MI LVEF $\leq 40\%$                     | Total mortality Arrhythmic death                                   | Amiodarone                              | Placebo | Amiodarone reduced arrhythmic death but did not reduce total mortality  |

|                       |  |   |                                 |              |   |
|-----------------------|--|---|---------------------------------|--------------|---|
| GESICA <sup>29</sup>  | CHF LVEF ≤35%  | Total mortality   | Amiodarone                      | Best therapy | Amiodarone reduced total mortality; patients with NSVT had higher mortality                 |
| MUSTT <sup>30</sup>   | Post-MI LVEF ≤30%<br>NSVT                                  | Arrhythmic death or cardiac arrest                          | ICD Class I or class III agents | No therapy   | Improved survival in ICD group; no difference between antiarrhythmic therapy and no therapy |
| SCD-HeFT <sup>6</sup> | CHF LVEF ≤35% NYHA II-III                                  | Total mortality<br>Arrhythmic death<br>Cost Quality of life | ICD Amiodarone                  | Placebo      | Improved survival with ICD; no effect of amiodarone on survival                             |
| SWORD <sup>31</sup>   | Post-MI LVEF <40% <i>or</i><br>Remote MI NYHA Class II-III | Total mortality   | <i>d</i> -Sotalol               | Placebo      | Increased mortality in treatment arm  |

**MI: myocardial infarction; ICD: implantable cardioverter defibrillator; PVC: premature ventricular contraction; LVEF: left ventricular ejection fraction; NSVT: nonsustained ventricular tachycardia; CHF: congestive heart failure; NYHA Class: New York Heart Association heart failure class.**

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