SIMDAX® GIVES YOU TIME IN THE OPERATING THEATER
COMPARSED TO TRADITIONAL INOTROPES...

Current data suggest that SIMDAX® is superior to traditional inotropes when used in operative settings:

- Sustained hemodynamic improvement
- Less myocardial injury
- Less renal impairment
- Lower need for IABP
- Safe and efficacious even on patients with preoperative low ejection fraction

In case of hypotension, vasopressors should be used concomitantly.


SIMDAX® IS SAFE AND EFFECTIVE IN CARDIAC SURGERY

Taking all the available data into consideration, including the experience of three recent larger clinical trials1-3, a panel of experts reached the consensus that SIMDAX® is a safe and effective agent for the treatment of patients undergoing cardiac surgery and in need of inotropic support.4

In a recent meta-analysis (including the most recent data) the effects of SIMDAX® on mortality were confirmed. SIMDAX® reduces mortality in patients with preoperative severely reduced ejection fraction (<35%).5

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After operation, in a comparative study vs milrinone, the positive hemodynamic effects of 19 hours treatment with SIMDAX® lasted much longer than those from 83 hours treatment with milrinone.1

The positive inotropic effects of SIMDAX® are achieved without an increase in oxygen consumption either in healthy volunteers,1 heart failure patients,2 or in cardiac surgery settings.3

![Sustained effects of levosimendan when used in cardiac surgery](image)

Stroke volume index (SVI) at the start of surgery (base), 15 min after the end of cardiopulmonary bypass (CPB) (post-CPB), at the end of the operation (end surgery), at arrival in the intensive care unit (T0), and 6 (T6), 12 (T12), 24 (T24), and 48 (T48) hours later in both groups. Data are mean±sd. Levosimendan (orange) vs Milrinone (blue) *p<0.05.1

A significant increase in the oxygen consumption is induced by dobutamine while no difference is noticed during treatment with levosimendan.1

**References:**
In a study by Jørgensen et al., SIMDAX® not only improved contractility, but also decreased isovolumic relaxation time.1 SIMDAX® has beneficial acute systolic and diastolic functional effects in experimental chronic pulmonary hypertension and right ventricle afterload compared to dobutamine and milrinone.2

Current data suggest that SIMDAX® also diminished myocardial injury.1,2

**Effects of levosimendan on relaxation time**

- SIMDAX® does not disturb relaxation.
- SIMDAX® has beneficial acute systolic and diastolic functional effects in experimental chronic pulmonary hypertension and right ventricle afterload compared to dobutamine and milrinone.

**Current data suggest that SIMDAX® also diminished myocardial injury.**

**References:**

**Graphs:**
- Effects of levosimendan on relaxation time
- Effects of levosimendan on release of troponin T during cardiac surgery

**Graph Descriptions:**
- **Effects of levosimendan on relaxation time:**
  - SIMDAX® vs placebo on isovolumic relaxation time (IVRT) (mean±SEM) at maintained preload and afterload conditions after aortic valve replacement for aortic stenosis. *p<0.05.

- **Effects of levosimendan on release of troponin T during cardiac surgery:**
  - Troponin T levels up to 48 hours in cardiac surgery patients. Levosimendan (orange) vs placebo (grey). *p=0.032.

**References:**
In the recent Phase III trial (LEVO-CTS), SIMDAX®, despite not meeting the primary endpoint, decreased significantly post-surgical low cardiac output syndrome (LCOS). This was accompanied with increased cardiac index and lower need for secondary inotropes.

**Incidence of LCOS and secondary inotrope use in the LEVO-CTS trial (N=882)**

- **Levosimendan:** 25.7%
- **Placebo:** 42.4%

Odds ratio (95% CI): 0.62 (0.44-0.88)  
*p=0.007*

**Effects of levosimendan on weaning after cardiac surgery**

- 1st weaning attempt: 73% successful  
  53% successful  
  *Weaning failure leads to use of intra-aortic balloon pump.*

- 2nd weaning attempt: 33% successful  
  0% successful

**Weaning from cardiopulmonary bypass (CPB):** First weaning attempt with levosimendan and placebo. Epinephrine added to second weaning attempt.

References:
THE BENEFITS OF SIMDAX® FOR RENAL FUNCTION

SIMDAX® preserves GFR during operation\(^1\) and reduces the risk of renal replacement therapy.\(^2\)

**The benefits of SIMDAX® for renal function**

SIMDAX® preserves GFR during operation\(^1\) and reduces the risk of renal replacement therapy.\(^2\)

**Effects of levosimendan on glomerular filtration rate**

The comparison of preoperative (preop) and postoperative (postop) serum estimated glomerular filtration rate (eGFR) in renal disease equation. Levosimendan (orange) vs control (grey). *\(p<0.05\).

**Effects of SIMDAX® versus placebo on cardiac index (CI), renal blood flow (RBF), glomerular filtration rate (GFR), and renal vascular resistance (RVR).** *\(p<0.05\) **\(p<0.001\)

**References:**

...ARE MEDIATED BY A DIRECT EFFECT ON RENAL CIRCULATION

SIMDAX® selectively vasodilates the afferent renal arterioles\(^1\) thus inducing pre-glomerular vasodilation and leading to improved renal blood flow and glomerular filtration rate.\(^2\) The renal oxygen demand/supply relationship is not affected by SIMDAX®.\(^2\)

**Effects of levosimendan versus placebo on cardiac index (CI), renal blood flow (RBF), glomerular filtration rate (GFR), and renal vascular resistance (RVR).** *\(p<0.05\) **\(p<0.001\)

**References:**
EASING THE CHALLENGE OF TREATING THE FAILING HEART WITH A SUSTAINED HEMODYNAMIC STABILIZATION

SIMDAX® GIVES YOU TIME BY PROVIDING:

- Hemodynamic benefits¹,²
- Symptomatic benefits¹,²
- Sustained effects¹
- Protective effects on heart and other organs³,⁴
- Stabilizing the patient for operation¹