A randomized, double-blind, placebo-controlled phase IIIa study of bIAP, an anti-inflammatory moiety, in patients undergoing combined aortic valve replacement and coronary artery bypass grafting.

Published: 05-11-2009
Last updated: 06-05-2024

Primary Objective:The objective of this study is to determine the efficacy of bIAP as a prophylactic agent against inflammation-mediated complications from more invasive cardiac surgery, aortic valve surgery and CABG with cardiopulmonary-bypass time...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Cardiac therapeutic procedures
Study type	Interventional

Summary

ID

NL-OMON38040

Source
ToetsingOnline

Brief title
APPIRED II

Condition

- Cardiac therapeutic procedures

Synonym
whole body inflammatory respons

Research involving

Human

Sponsors and support

Primary sponsor: Alloksys Life Sciences B.V.
Source(s) of monetary or material Support: Alloksys Life Sciences B.V.

Intervention

Keyword: AVR/CABG, bIAP, cardiopulmonary bypass, Inflammatory respons

Outcome measures

Primary outcome

Main study primary endpoint is the reduction of post-surgical SIRS in bIAP* treated patients as compared to placebo*treated patients, that is the reduction of incidences of fulminate SIRS responses, indicated by pro-Inflammatory cytokines.

Secondary outcome

The incidence of new organ dysfunction within 14 days of surgery will be assessed, next to the duration of organ dysfunction, lengths of organ dysfunction-associated intensive care unit (ICU) and hospital stays, ventilation-assistance and renal failure-dialysis days, volume of blood and blood products infused within 24 hours of surgery, incidence of hospital readmission and 30-day all-cause mortality. Safety will be assessed by incidence and severity of adverse events, changes in physical examination, vital signs and changes in clinical laboratory measurements.

Study description

Background summary

It has been established that cardiac surgery is associated with a post surgical systemic inflammatory response (SIRS), the impact of which is subject to the immunological vigilance of the patient but also to surgical conditions. Thus it is generally accepted that the incidence of SIRS is correlated positively to the duration of perfusion time. In CABG, a relatively short-duration surgery, where perfusion time is limited to about one hour we have shown in the first APPIRED-I study that significant postsurgical inflammation is observed only in a specific relative small group of placebo-treated patients but not in patients treated with alkaline phosphatase. Specifically: solely in placebo-treated patients a significant subgroup was identified that responded in high post surgical TNF-*, whereas in alkaline phosphatase (AP) treated patients such a TNF-* response was not identified. Increased systemic TNF-* levels are reported to be associated with vascular injury and ischemic damage. On the basis of the APPIRED-I study outcome, where patients for elective CABG, with relatively low perfusion and cross clamp time were included, it is expected that in procedures with longer cross clamp and perfusion time, like combined aortic valve replacement and CABG, patients will benefit more from alkaline phosphatase treatment.

Study objective

Primary Objective:
The objective of this study is to determine the efficacy of bIAP as a prophylactic agent against inflammation-mediated complications from more invasive cardiac surgery, aortic valve surgery and CABG with cardiopulmonary-bypass time of longer than 1 hour.
Primary study endpoint is the postulated reduction of the number of post-surgical inflammatory response in the bIAP-treated patient group as compared to the placebo-treated group. Inflammatory response, in the sense of this study, is indicated by an increased TNF-* level of at least 10 pg/ml above the pre-surgical level, which is normally followed by an increase of IL-6 and IL-8.

Study design

Initially a mono-centre prospective, randomized, double-blind, placebo-controlled intervention trial involving a max of 50 patients. As of March 2012 ZOL-Genk (Belgium) participates in this study. From Q4, 2012 MUMC (Maastricht) likely will be participating as well (pending approval).
THe total study may involve up to 150 patients, of which first 50 patients and interim evaluation are expected ultimo Q4 2012.

Intervention

Patients receive intravenous as a bolus either placebo or bIAP (alkaline phosphatase, 1000 IU) just prior to surgery followed by a 40 IU/kg bIAP/placebo

infusion during 8 hours.

Study burden and risks

So far no identified risk is associated with the therapeutic use of intravenously or orally administered alkaline phosphatase. Burden to the patient is limited to disposing additional blood samples. Patients will be asked to allow blood sampling during a time interval of 5 days, most of which is during the time that intravenous lines are available during surgery and recuperation time at the ICU. A total of 12 samples will be collected, of which 5 samples are drawn by syringe. It is estimated that a total of 116 ml blood is required for the study, which does not constitute a health risk to the patients. Furthermore, the patients will be called for a follow-up visit at one month post-surgery, at which time data on concomitant medications and adverse events will be recorded.

Contacts

Public
Alloksys Life Sciences B.V.

Gildenring 74
Bunnik 3981JG
NL
Scientific
Alloksys Life Sciences B.V.

Gildenring 74
Bunnik 3981JG
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age

Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Patients planned for combined AVR and CABG surgery

Exclusion criteria

base alkaline phosphatase levels (>125 IU/L)
significant hepatic disease
renal insufficiency
scheduled to receive stress doses of glucocrticoids
vegetarians or intolerant for bovine products

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	21-04-2010
Enrollment:	50
Type:	Actual

Medical products/devices used

Product type:	Medicine

Brand name:	bIAP / bRESCAP
Generic name:	Alkaline phosphatase

Ethics review

Approved WMO Date:	05-11-2009
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	19-03-2010
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	31-07-2012
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2009-010191-19-NL

Register	ID
CCMO	NL26158.060.09