

SCA 39

**EFFECTS OF COMPLEMENT INHIBITION BY PEXELIZUMAB ON MYOCARDIAL INFARCTION OR DEATH FOLLOWING CARDIAC SURGERY. A COMBINED ANALYSIS OF TWO MULTICENTER, PLACEBO-CONTROLLED, RANDOMIZED TRIALS.**

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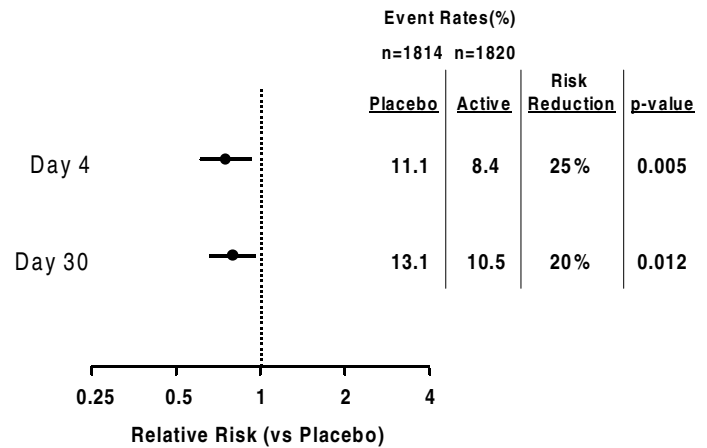
**Introduction:** During cardiac surgery requiring cardiopulmonary bypass (CPB), complement can be activated to produce inflammatory responses that potentially result in tissue injury. We examined the efficacy of Pexelizumab (Alexion Pharmaceuticals Inc., Cheshire, CT), a recombinant, single-chain, anti-C5 monoclonal antibody, on the attenuation of myocardial infarction (MI) or death in cardiac surgical patients undergoing CPB.

**Methods:** Pexelizumab was evaluated in 2 (Phase II and Phase III) randomized, double-blinded, placebo- controlled, multicenter trials involving 3634 patients undergoing cardiac surgery requiring CPB. Patients were prospectively stratified into CABG-only (n =3226) and CABG + valve surgery (N= 408) subpopulations, and subsequently randomized to receive placebo, or Pexelizumab administered intravenously immediately prior to the initiation of CPB as a bolus + infusion (2.0 mg/kg + 0.05 mg/kg/hr for 24 hours). A combined analysis including all patients enrolled in each trial was performed using Fischer's Exact test (significance at P=0.05) to determine the effect of Pexelizumab on the composite outcome of death or MI.

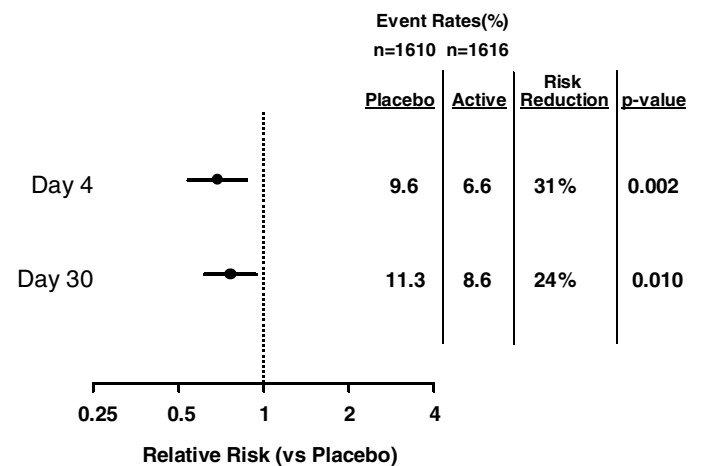
**Results:** Compared to placebo, Pexelizumab decreased the incidence of death or MI in the total population (CABG with or without valve surgery) through postoperative day (POD) 4 by 25% (8.4% vs 11.1%; P = 0.005), and through POD 30 by 20% (10.5% vs 13.1%; P = 0.012) (Fig 1). Pexelizumab administration was also associated with a reduction in the incidence of death or MI in the

CABG-only subpopulation through POD 4 by 31% (6.6% vs. 9.6%; P= 0.002) and through POD 30 by 24% (8.6% vs 11.3%; P=0.01) in the CABG-only subpopulation (Fig 2).

**Conclusions:** The results of this combined analysis indicate that in patients undergoing CABG with or without valve surgery, inhibiting perioperative complement activation with Pexelizumab can reduce perioperative MI or death, and represents a novel therapeutic approach in cardiac surgical patients requiring CPB.



**Figure 1.** Pexelizumab effect on death or myocardial infarction in pooled Phase II and Phase III studies: Combined population of coronary artery bypass graft with or without valve surgery patients



**Figure 2.** Pexelizumab effect on death or myocardial infarction in pooled Phase II and Phase III studies: Coronary artery bypass graft surgery-only subpopulation