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Amgen Presentation to MEDCAC

Erythropoiesis Stimulating Agents (ESA) in Anemia Related to Chronic Kidney Disease

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Key Points

- **Dialysis patients are distinctly different from non-dialysis patients**
 - Anemia is nearly universal in the absence of treatment
- **Transfusions have multiple risks including sensitization that can preclude or delay successful transplantation**
- **Hemoglobin (Hb) < 10 g/dL is strongly associated with transfusion risk as well as poor physical function and exercise tolerance**
- **Inherent Hb variability necessitates target range (10–12 g/dL)**

Reducing the need for transfusion is an important clinical outcome enabling regulatory approval in dialysis patients

Contributors to anemia in dialysis

- Annual blood loss estimated at 2.5-5.1 L (5-10 units) annually
- More severe erythropoietin deficiency
- Shortened RBC lifespan
- Increased bleeding tendency
- Co-morbid conditions

Risks of transfusion in dialysis

- Sensitization (measured as PRA)
 - Delays or precludes transplantation
 - Impacts transplant function and survival
- Volume and potassium overload
- Transfusion reactions
- Viral and other infectious agents

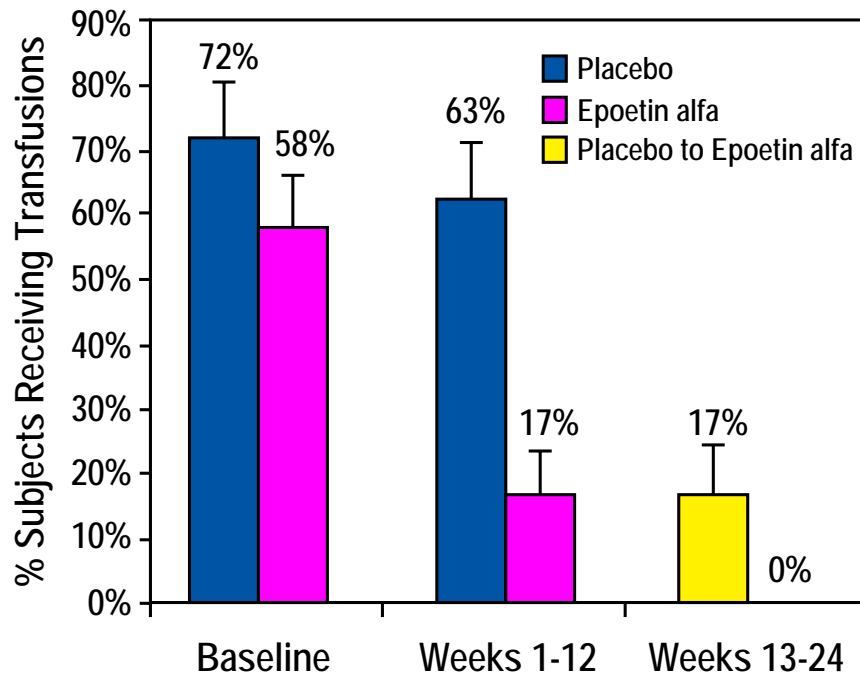
Sensitization is a uniquely important transfusion-related risk for CRF patients

¹ Eschbach and Adamson. *KI*. 1985. ² Beauregard and Blajchman. *Transf Med Rev*. 1994. ³ Despotis et al. *Hematol Oncol Clin North Am*. 2007. ⁴ Dodd. *Transfusion*. 2002. ⁵ Simon and Bove. *Postgrad Med*. 1971

⁶ USRDS ADR. 2009. ⁷ Hardy. Sensitization 2001, in PI, CJaT (ed): *Clin Transplant* 2001, UCLA. ⁸ USRDS ADR. 2004. ⁹ Sargent and Acchiardo. *Blood Purification*. 2004, ³⁰ Epogen PI

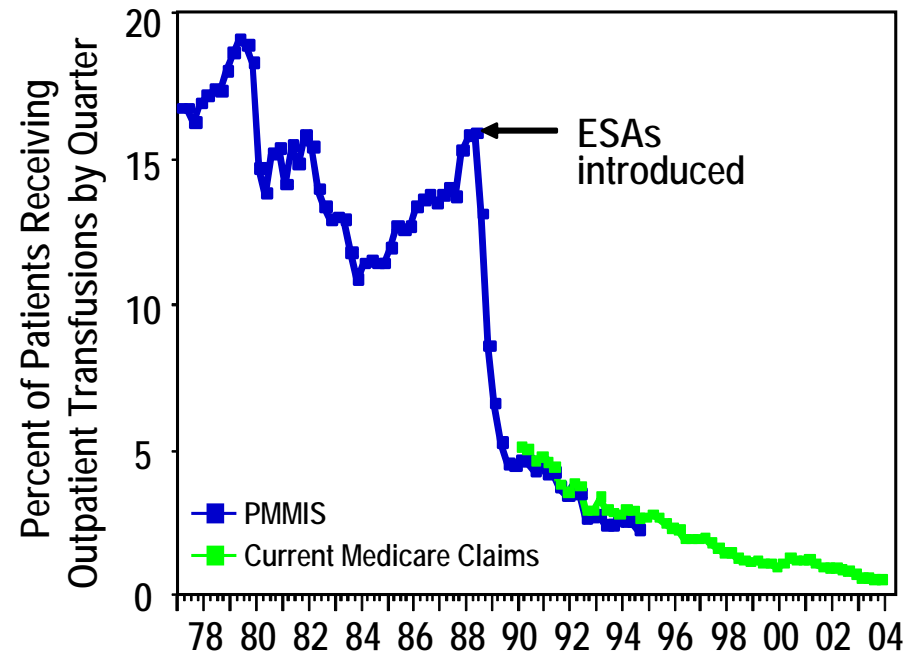
Transfusion reduction with ESAs has been demonstrated in clinical trials and confirmed in clinical practice

Reduction in transfusions in registrational program



Amgen data on file 8701

Reduction in outpatient transfusions in clinical practice



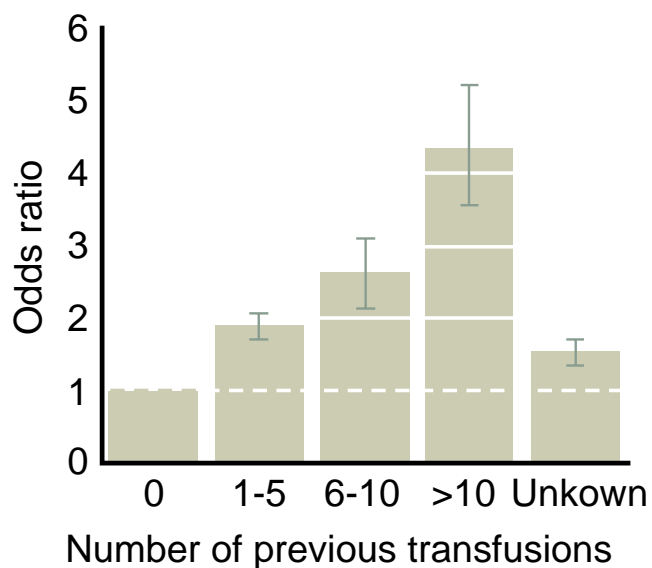
PMMIS = Healthcare Financing Administration Program Medical Management and Information Systems

USRDS ADR 2009

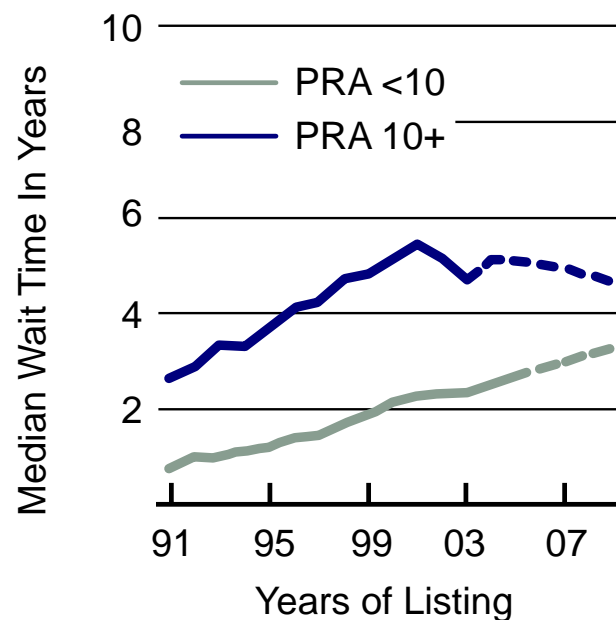


Transplantation is the treatment of choice for ESRD

Risk of PRA > 50% with cumulative transfusion



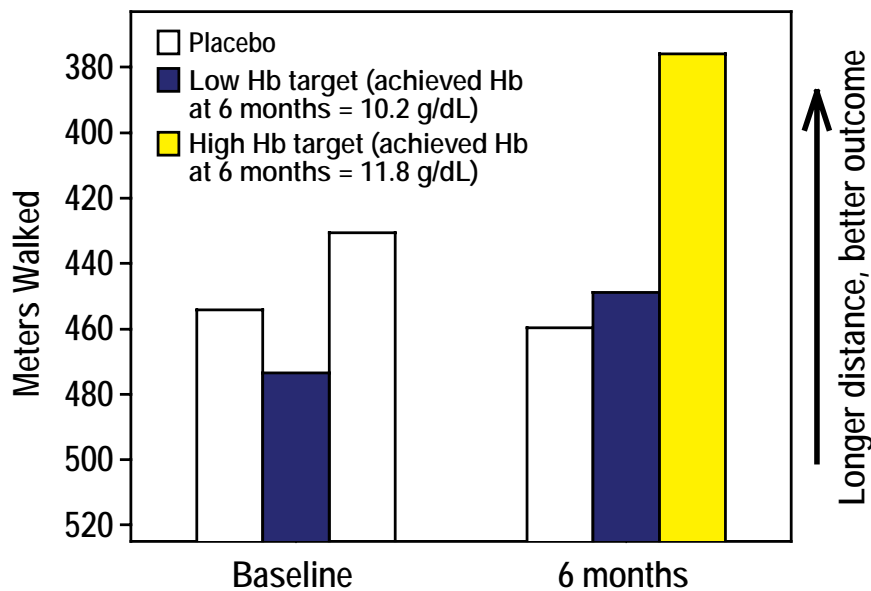
Transplant wait-time by PRA level



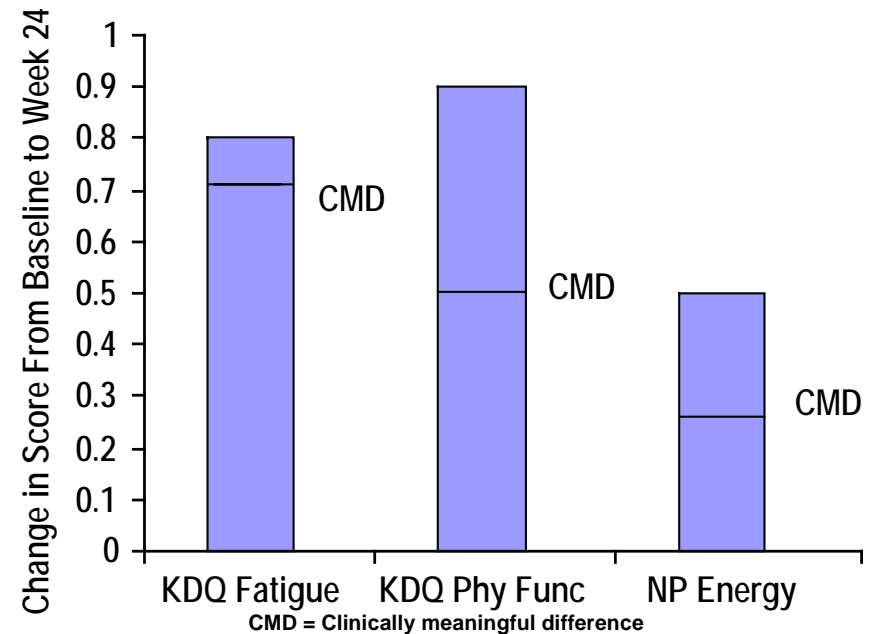
Transfusions can delay or preclude kidney transplantation due to sensitization

Robust evidence demonstrates that ESA therapy in dialysis patients improves anemia symptoms, physical function and exercise tolerance

Registrational: Increased exercise tolerance and physical functioning



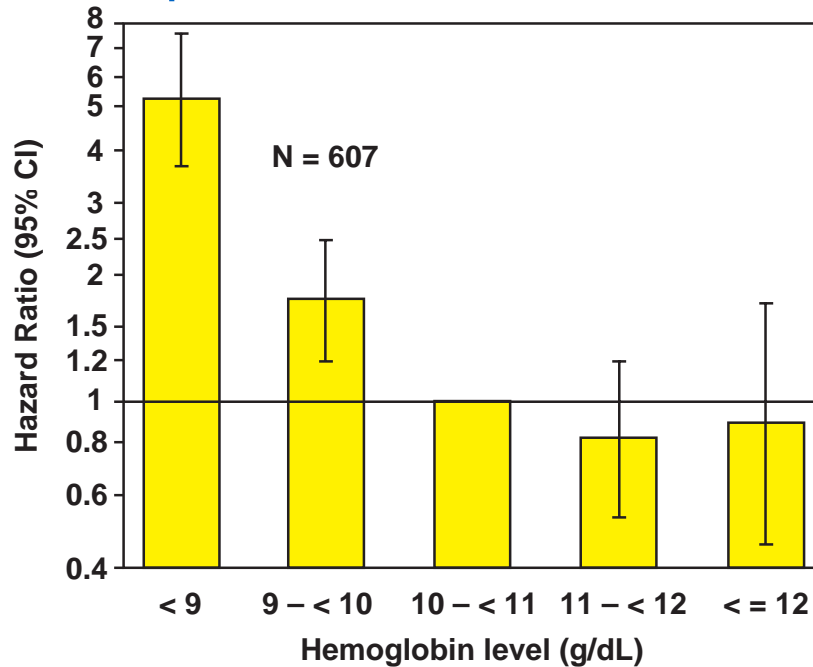
Clinical practice: Consistently demonstrates increased exercise, physical functioning and energy



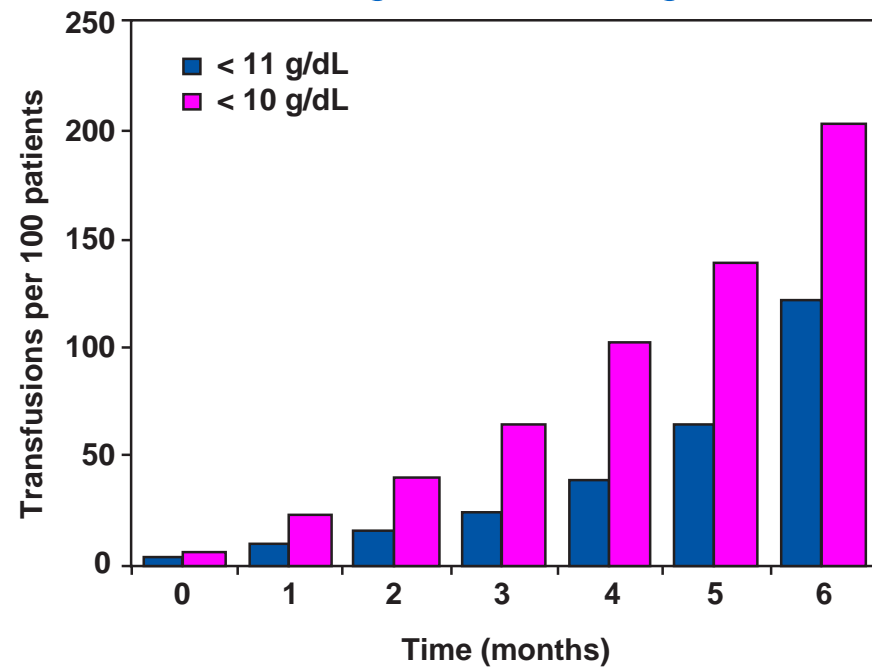
Treatment with ESAs improves anemia related symptoms and functioning

Treating to maintain Hb above 10 g/dL is necessary to reduce the risk of transfusion

The risk of transfusion by the previous month's Hb level



The risk of transfusion by time with Hb < 10 g/dL and < 11 g/dL



Medicare data show strong association between Hb < 10 g/dL with increased transfusion risk