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Pioneering science delivers vital medicines™

Evidence to Support Erythropoiesis Stimulating Agents (ESAs) for Treatment of Anemia in Adults with Chronic Kidney Disease (CKD)

Key Points

- **Dialysis patients differ from CKD patients not on dialysis (NOD)**
  - Anemia in dialysis patients is nearly universal, severe, negatively impacts quality of life and necessitates intervention
  - CKD-NOD patients are heterogeneous; significant anemia can occur in a subset of CKD-NOD patients and these patients may benefit from intervention
- **Transfusions have multiple risks: *From the Circular Of Information For The Use Of Human Blood And Blood Components***

  "Contraindications: Red-cell-containing components should not be used to treat anemias that can be corrected with specific hematinic medications such as iron, vitamin B_{12}, folic acid, or erythropoietin."
- **Allosensitization, measured by panel reactive antibodies (PRA), is a uniquely important risk for CKD patients**
  - Negatively impacts transplant access and viability
  - Clinical practice guidelines caution against the use of transfusion in the management of potential transplant recipients
- **ESAs when used to raise Hb > 10 g/dL & maintain within ~10-12 g/dL range reduce transfusions & transfusion-related risks & improve physical function & exercise tolerance in dialysis patients**

Anemia is Severe in Dialysis Patients and Necessitates Intervention

Contributors to Anemia

- Annual blood loss estimated at 5-10 units annually
- Erythropoietin insufficiency
- Shortened RBC lifespan
- Increased bleeding tendency
- Co-morbid conditions

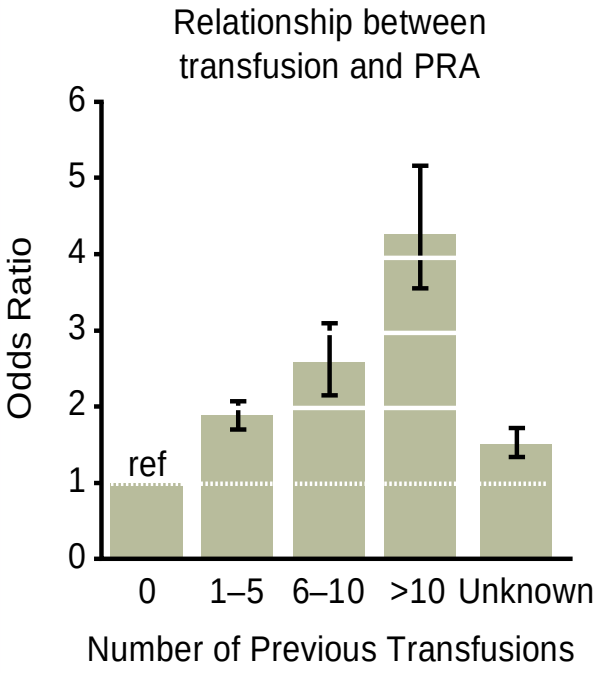
Transfusion-related Risks

- Allosensitization
  - Delays or precludes transplantation
  - Impacts transplant function and survival
- Transmission of infectious diseases
- Iron overload
- Volume and potassium overload

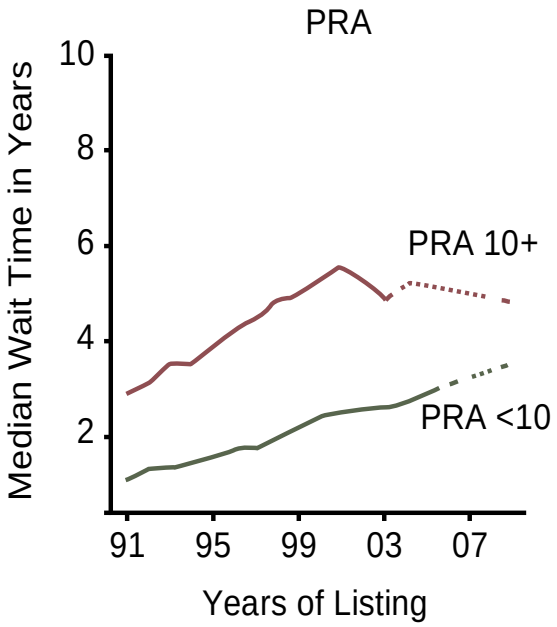
Eschbach and Adamson. *KI.* 1985. Beauregard and Blajchman. *Transf Med Rev*. 1994. Despotis et al. *Hematol Oncol Clin North Am*. 2007. Dodd. *Transfusion*. 2002. Simon and Bove. *Postgrad Med*. 1971 USRDS ADR. 2009. Hardy. Sensitization 2001, *Clin Transplant* 2001, UCLA. Sargent and Acchiardo. *Blood Purification*. 2004.

Transfusions Increase Allosensitization (PRA) Impeding Transplantation

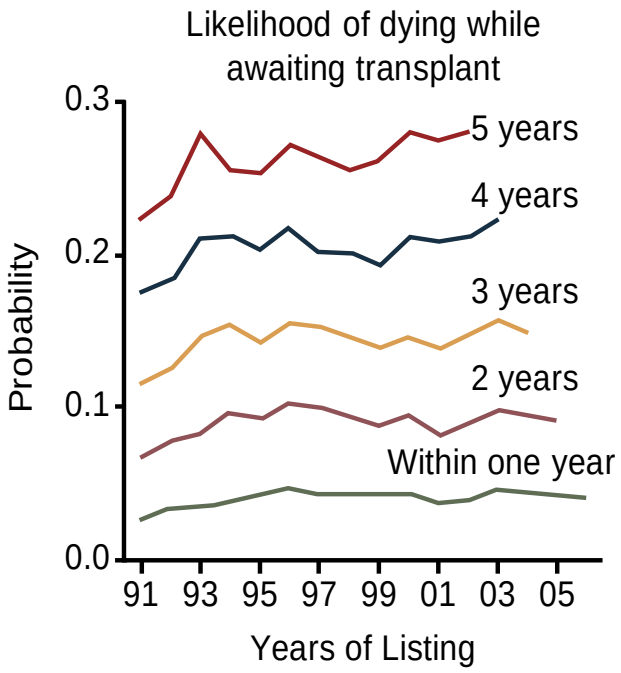
Risk of PRA > 50% with Cumulative Transfusion



Transplant Wait-time by PRA Level



Likelihood of Death by Time on Dialysis



The Risk of Allosensitization is Not Obviated by Modern Blood Banking Methods

USRDS Annual Data Report 2004.

USRDS Annual Data Report 2009.

USRDS Annual Data Report 2009.

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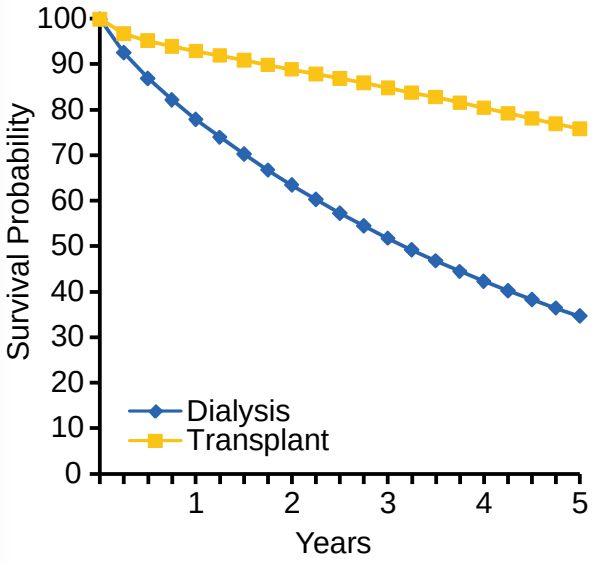
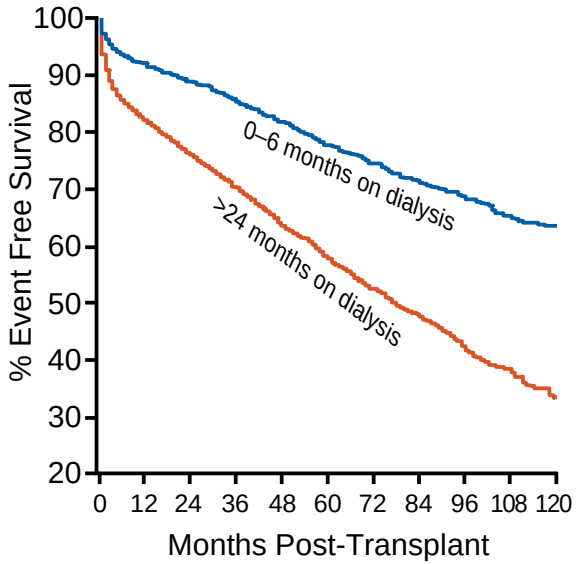
Transplantation Early and in Unsensitized Patients Yields Best Outcomes

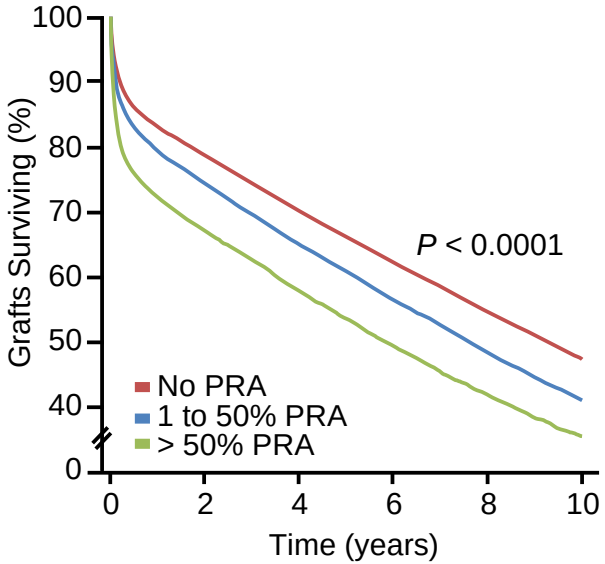
5-yr Survival Greater in Transplanted vs. Dialysis



Longer Time on Dialysis before Transplant Predicts Shorter Graft Survival



Higher PRA Predicts Shorter Graft Survival



Donated Kidneys Are Scarce; Transfusion-Related Allosensitization is a Modifiable Risk to Successful Transplantation

USRDS Annual Data Report 2010.

Mange et al., NEJM 2001;344:726-31.

Opelz et al., Lancet 2005;365:1570-76.

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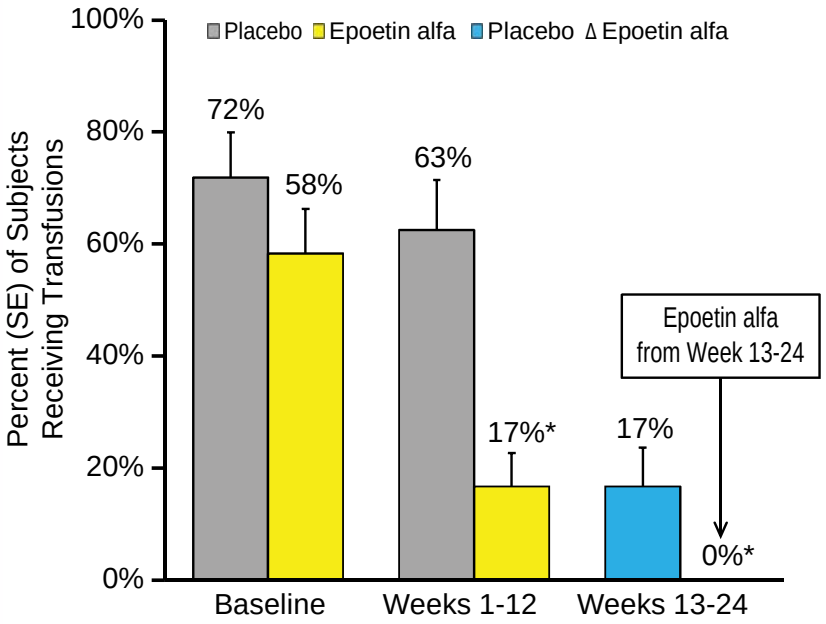
Transfusion Reduction with ESAs has been Demonstrated in Clinical Trials and Confirmed in Clinical Practice

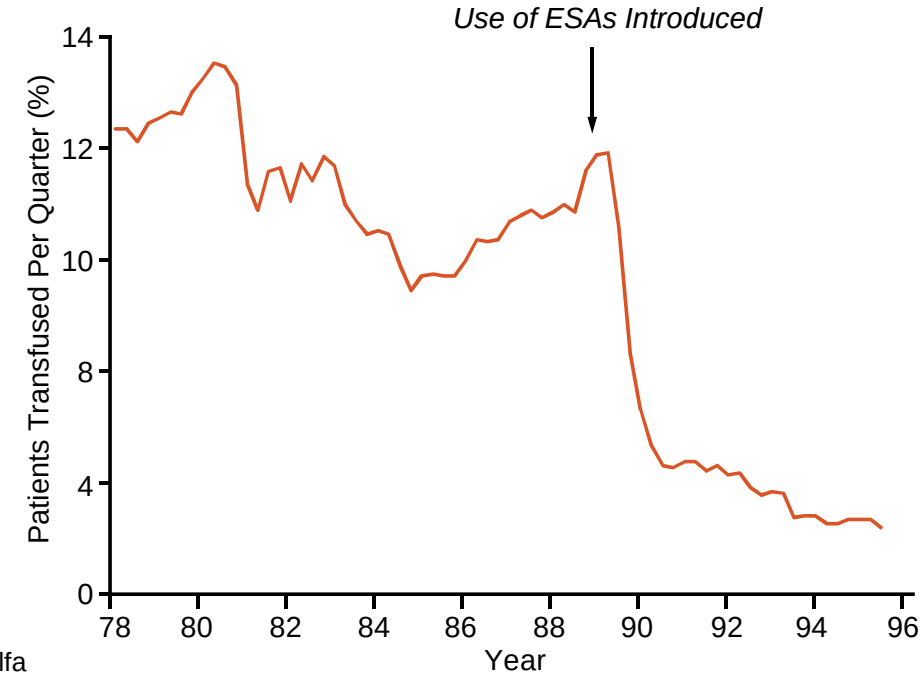
Significant Reduction in Transfusions in Clinical Trials



N = 32 (placebo); N = 36 (Epoetin alfa); *p < 0.05 placebo vs Epoetin alfa
Baseline rates are based on the 6 months before the start of the study.
Placebo Δ Epoetin alfa group: Transfusion requirements for subjects originally randomized to receive placebo in Study 8701 who began to receive Epoetin alfa after week 12.

Amgen data on file 8701.

Significant Reduction in Outpatient Transfusions in Clinical Practice

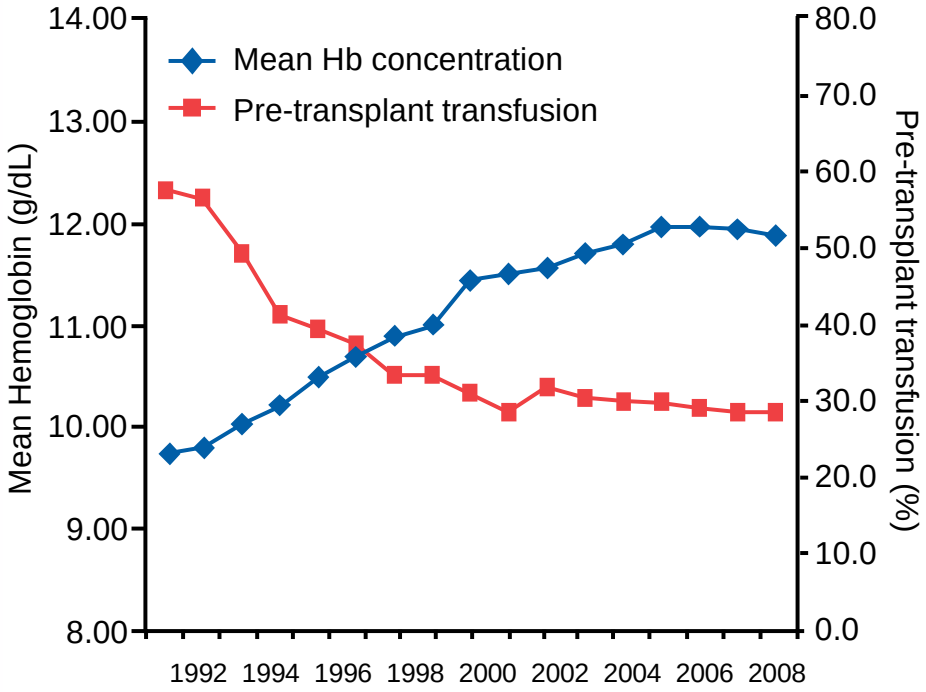


PMMIS = Healthcare Financing Administration Program Medical Management and Information Systems

USRDS Annual Data Report 2009.

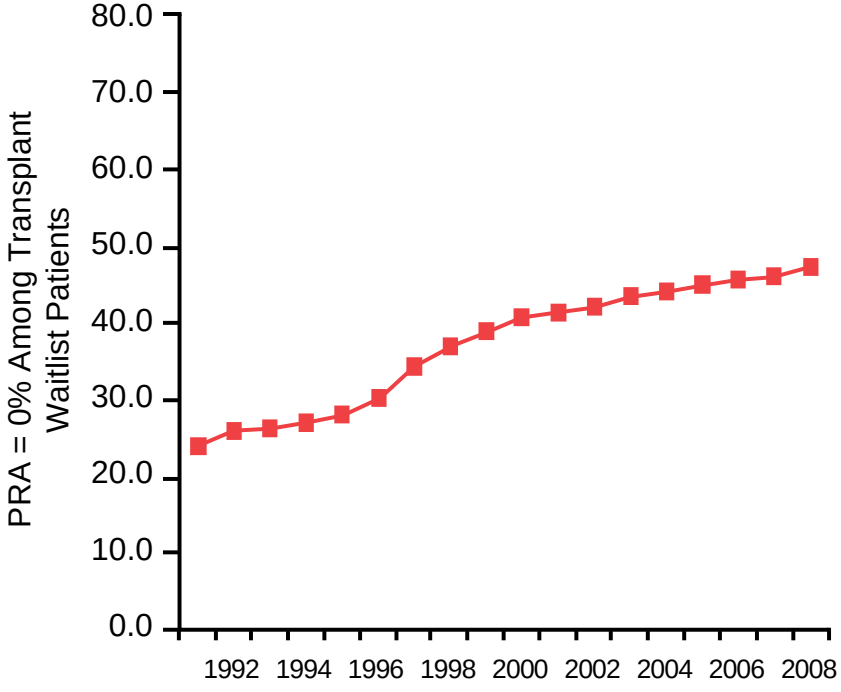
With the Introduction of ESAs, Transfusions Decreased, and Proportion of Unsensitized Patients Increased

Mean Hb Increased > 10 g/dL, Transfusions Declined



USRDS 2010 Annual Data Report.

Increase in Proportion of Unsensitized Wait-listed Patients



USRDS 2010 Annual Data Report.

ESAs used to Maintain Hb > 10 and ~10-12 g/dL, Reduce Transfusion-Related Risks and Improve Physical Function and Exercise Tolerance in Dialysis Patients