CHRONIC KIDNEY DISEASE

Initial hemoglobin response to darbepoetin alfa determines outcome in patients with CKD and type 2 diabetes

A poor initial hematopoietic response to administration of darbepoetin alfa is associated with an increased risk of death and cardiovascular events, according to a new study. "These findings suggest that an individual's degree of responsiveness to an erythropoiesis-stimulating agent (ESA), and not the target range achieved, may be most important in determining risk", states lead researcher, Scott Solomon.

Findings from various trials, including the randomized, placebo-controlled TREAT trial, have questioned the safety of ESAs in patients with chronic kidney disease (CKD) and anemia. To better understand the factors that influence risk in this population, Solomon and colleagues used data from TREAT to assess how each patient's individual responsiveness to darbepoetin alfa related to that patient's risk of adverse outcomes.

The researchers divided patients who received treatment into quartiles according to their initial hemoglobin response to the first two weight-based doses of darbepoetin alfa. Patients in the lowest quartile were considered to be the poorest responders.

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Patients who had the poorest initial response to treatment had the lowest mean achieved hemoglobin level after 12 weeks despite receiving significantly higher doses of darbepoetin alfa. Poor responders also had a higher risk of cardiovascular events and death than patients with a better initial response to treatment. "Our finding that the poorest response group had the lowest achieved hemoglobin levels questions the notion that simply lowering the target hemoglobin range can mitigate any potential risks associated with the drug", explains Solomon. "In addition, we believe that future studies should incorporate an ESA 'test dose' to determine a patient's responsiveness before starting them on treatment, and that we should be cautious about escalating ESA doses to reach targets in less-responsive patients."

The researchers recognize that their study cannot determine whether the association between risk and initial hemoglobin response relates to illness severity or to the administration of greater amounts of drug. However, they will continue to investigate modifiers of risk in this population to better understand the factors that influence an individual's response to an ESA.

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