HIF Stabilizers: Will They Have a Place?

By Jay Wish

Hypoxia-inducible factor (HIF), a transcription factor that is stabilized under hypoxic conditions, plays a key role in the body’s response to oxygen deprivation. HIF stabilizers are a class of drugs that mimic the effects of hypoxia and stimulate erythropoiesis, the process of red blood cell production. These agents are designed to increase the production of erythropoietin (EPO), a hormone that stimulates the production of red blood cells, thereby improving anemia in patients with chronic kidney disease (CKD). The development of HIF stabilizers has been driven by the need for more efficacious, safer, and more convenient options for treating anemia in patients with CKD.

There are currently three HIF stabilizers under development: roxadustat, vadadustat, and daprodustat. These drugs work by stabilizing HIF, which leads to an increase in the expression of genes that are involved in erythropoiesis. This can lead to an increase in the production of red blood cells, which can help improve anemia.

The HIF stabilizers are administered orally, which can be an advantage over injectable ESAs, which require frequent injections. This can improve patient compliance and reduce the risk of infection and other complications associated with injections.

However, the development of HIF stabilizers has been slow, and there are still some concerns about their long-term safety and efficacy. The phase 3 trials of these agents have shown some promising results, but more data is needed to fully evaluate their safety and effectiveness in the long term.

References

Figure 1.

Intravenous Iron in Patients Undergoing Maintenance Hemodialysis.

Efficacy and Safety of Intravenous (IV) Iron in Patients Undergoing Maintenance Hemodialysis (MHD) or Peritoneal Dialysis (PD).

- **PROACTIVE**
  - Adults with ESKD
  - Ferritin < 400 µg/L
  - TAT 40%
  - Prophylaxis or dose adjustment

- **REACTIVE**
  - Adults with ESKD
  - Ferritin < 200 µg/L
  - TAT 20%
  - Prophylaxis or dose adjustment

- **On hemodialysis ≤ 12 months**
  - Ferritin 700 µg/L

- **Receiving ESA**
  - Ferritin 200 µg/L

- **Total iron content transfused**
  - 1093
  - 1048

- **Total iron content transfused**
  - 967
  - 1220

- **Total iron units transfused**
  - 79.75 µg
  - 38,805 µg

- **Nephrology**

- **Prophylaxis**
  - Prophylaxis or dose adjustment

- **Intravenous iron**
  - Intravenous iron in patients undergoing maintenance hemodialysis (MHD) or peritoneal dialysis (PD).

- **Cost**
  - Cost comparison: proactive vs. reactive approach.

- **Outcomes**
  - Efficacy and safety of intravenous iron in patients with CKD.

- **Conclusion**
  - Intravenous iron can be effective in the treatment of anemia in patients with CKD, but further study is needed to fully evaluate its long-term safety and efficacy.