Management of VEGF TKI-Induced HTN

**PROBLEM**

- Anti-vascular endothelial growth factor (VEGF) tyrosine kinase inhibitors (TKIs) (i.e., axitinib, cabozantinib, lenvatinib, pazopanib, regorafenib, sorafenib, sunitinib, and vandetanib) are associated with cardiotoxicity, leading to:
  - Hypertension (HTN) (up to 80%)
  - Left ventricular systolic dysfunction (3-15%)
  - Symptomatic heart failure (HF) (1-10%)
  - QTc prolongation (4.4%)
  - Myocardial ischemia (MI) (1.4-1.7%)
  - Thromboembolism (1-3%)

- HTN attributed to VEGF TKI is at least partially related to inhibition of nitric oxide, decrease in capillary density, and increased production of vasoconstrictors.

- The highest incidence of HTN is in initial stages of therapy (within hours to days).

**SOLUTION**

- **Initial evaluation**
  - Baseline blood pressure (BP), left ventricular ejection fraction (LVEF), electrocardiogram, and assessment of cardiac risk factors (i.e., pre-existing cardiac disease, diabetes mellitus, hyperlipidemia)

- **Monitoring**
  - HTN: Frequent BP monitoring (including ambulatory home BP) and adjustment of anti-hypertensive therapies with VEGF TKI initiation, dosage adjustments and discontinuation.
  - HF: LVEF assessment every 3-6 months, measurement of cardiac biomarkers at onset of new symptoms

- **Treatment**
  - HTN: As per treatment table
  - HF: Hold VEGF TKI when >10% drop in ejection fraction to a value below the lower limit of normal and initiate HF medications as per ACC guidelines

- Rule out secondary causes of HTN
- Educate patients on appropriate home BP-monitoring technique
- Monitor for hypotension upon discontinuation of VEGF TKIs

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**BEST PRACTICES:**

- Establish cardio-oncology clinic in collaboration with oncology
- Rule out secondary causes of HTN
- Educate patients on appropriate home BP-monitoring technique
- Monitor for hypotension upon discontinuation of VEGF TKIs

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