Carboplatin Dosing in Adults

Calvert Equation

- Carboplatin Dose (mg) = Target area under the curve (AUC mg/mL/min) x (GFR* + 25)

*GFR estimated by calculated creatinine clearance using Cockcroft-Gault Equation (see below).

Cockcroft-Gault Equation

\[
\text{CrCl (male; mL/min)} = \frac{(140 - \text{age}) \times \text{weight in kg}}{72 \times \text{serum creatinine (mg/dL)}}
\]

\[
\text{CrCl (female; mL/min)} = 0.85 \times \text{CrCl (male)}
\]

Maximum Carboplatin Dose Calculation

The FDA has recommended that physicians consider capping the dose of carboplatin for desired exposure (AUC) to avoid potential toxicity due to overdosing. The maximum dose is based on a GFR estimate that is capped at 125 mL/min for patients with normal renal function.

Based on the Calvert formula described in the carboplatin label, the maximum doses can be calculated as:

\[
\text{Maximum Carboplatin Dose (mg)} = \text{Target AUC (mg/mL/min)} \times (125 \text{ mL/min} + 25)
\]

For a target AUC = 6, the maximum dose is 6 x 150 = 900 mg
For a target AUC = 5, the maximum dose is 5 x 150 = 750 mg
For a target AUC = 4, the maximum dose is 4 x 150 = 600 mg

Additional Considerations

- Overweight or obese patients (BMI ≥ 25 kg/m²): Consider using an adjusted body weight.

\[
\text{Adjusted body weight (kg)} = \text{ideal body weight (IBW)} + 0.4 \times (\text{total body weight (TBW)} - \text{IBW})
\]

- Patients with abnormally low serum creatinine (Cr), including elderly or cachectic patients: Consider using a minimum Cr of 0.7 mg/dL to avoid overestimation of CrCl.

- Measured CrCl: Consider using ethylene diamine tetraacetic acid (EDTA) or a 24-hour urine to measure CrCl (not a serum creatinine-based mathematical equation) when dosing at an AUC greater than 6 or when using an un-capped CrCl.
Carboplatin Dosing in Pediatrics

- Several investigators have characterized carboplatin pharmacokinetics and pharmacodynamics in children, which led to the development of a variety of dosing formulas.

Modified Pediatric Calvert Equations

- Marina et al\textsuperscript{5}
  
  Carboplatin Dose (mg/m\textsuperscript{2})\textsuperscript{*} = Target area under the curve (AUC mg/mL/min) x [(0.93 x GFR*[mL/min/m\textsuperscript{2}]) + 15]

- Newell et al\textsuperscript{6}
  
  Carboplatin Dose (mg)\textsuperscript{*} = Target area under the curve (AUC mg/mL/min) x (GFR*[mL/min] + [0.36 x weight in kg])

- Pinkerton et al\textsuperscript{7}
  
  Carboplatin Dose (mg)\textsuperscript{*} = Target area under the curve (AUC mg/mL/min) x ([GFR*[mL/min] x 1.2] + 20)

- Mann et al\textsuperscript{8}
  
  Carboplatin Dose (mg)\textsuperscript{*} = Target area under the curve (AUC mg/mL/min) x [GFR*[mL/min] + (15 x BSA [m\textsuperscript{2}])] 

*Note appropriate units for carboplatin dose (i.e. mg/m\textsuperscript{2} or mg) and confirm units of measure for GFR (i.e. mL/min/m\textsuperscript{2} or mL/min) when performing calculations for the equations above.

Additional Considerations

- GFR Estimation: Use of Tc-99m labeled DTPA clearance, a 24-hour urine collection, or other validated methods to measure creatinine clearance are preferred for determining a carboplatin dose to achieve a desired AUC in children. If use of the aforementioned methods is not feasible, estimation by use of a serum creatinine-based mathematical equation may be considered, such as the Bedside Schwartz equation\textsuperscript{9} (GFR [mL/min/1.73m\textsuperscript{2}] = 0.413 x [(height in cm) ÷ serum creatinine (mg/dL)]) or another pediatric GFR equation as appropriate.

- Carboplatin dosing: Dose and frequency of carboplatin in pediatric patients varies. Carboplatin is not always dosed on AUC and is commonly regimen-specific in regards to dosing by AUC, mg/m\textsuperscript{2}, or mg/kg. Refer to the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines\textsuperscript{®}) for standard dosing recommendations based on regimen.
REFERENCES