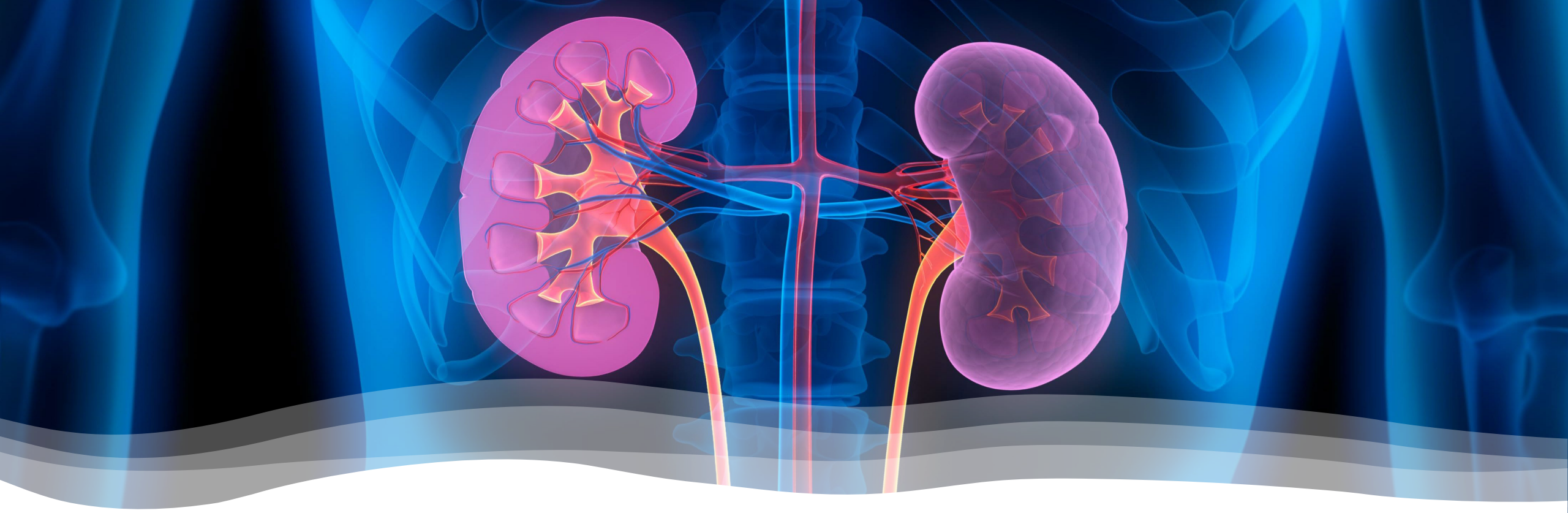

Hierarchical Composite Endpoints for Chronic Kidney Disease Trials

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Disclaimer: The views expressed are those of the presenter and not necessarily those of Bayer or Novo Nordisk.

Traditional and Modern Endpoints in Chronic Kidney Disease (CKD) Trials

- Traditional composite time-to-event endpoints in CKD trials include
  - Sustained* relative GFR† decline from baseline (typically ≥57%, ≥50% or ≥40%)
  - Sustained GFR <15 mL/min/1.73m^2
  - End-stage kidney disease (ESKD), i.e. initiation of dialysis or kidney transplantation
  - Death (typically renal and/or cardiovascular death)

- Recently, GFR slope (i.e. rate of GFR change over time) is becoming increasingly accepted in CKD trials
  - More efficient than traditional time-to-event endpoints
  - Handling of intercurrent events death and ESKD not straightforward

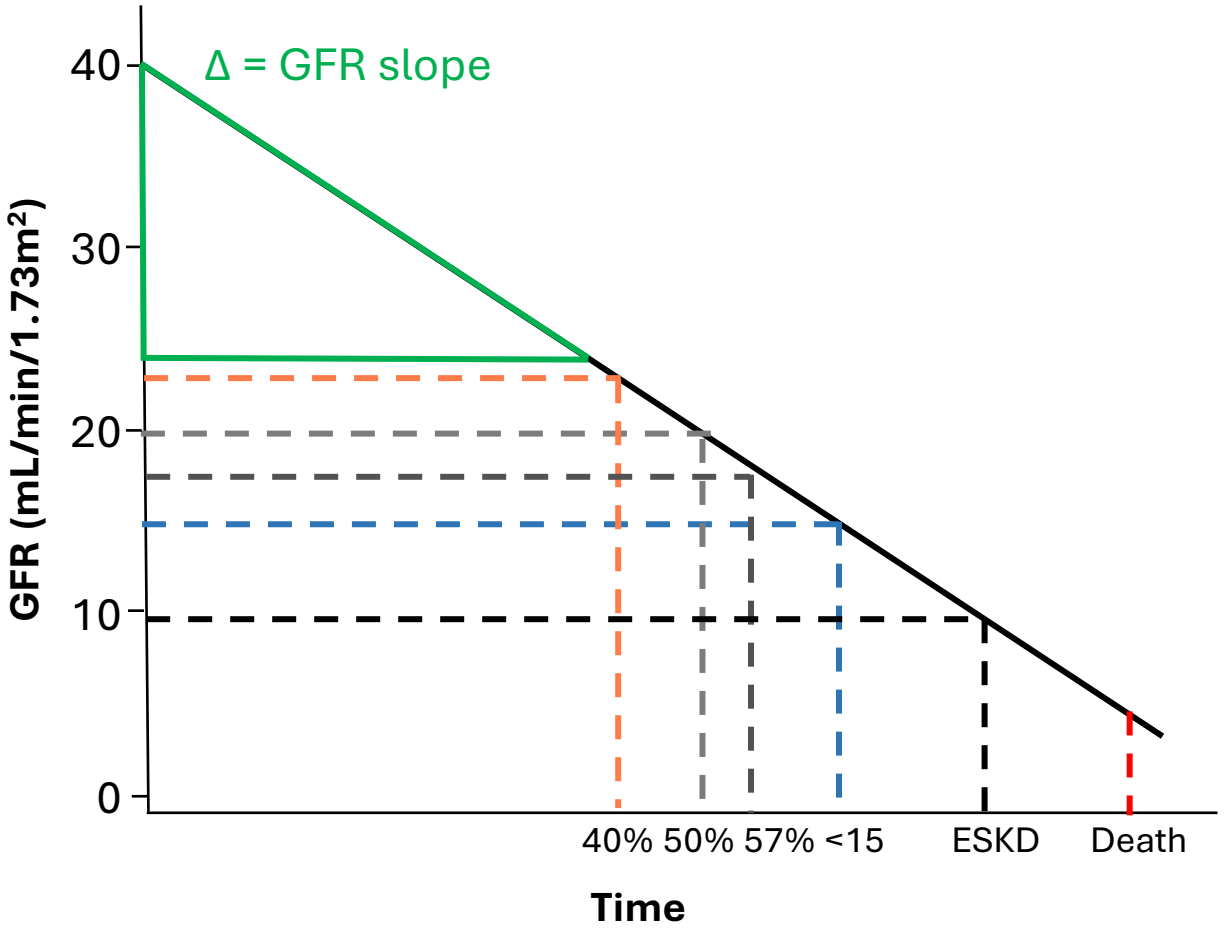
** Confirmed by a 2nd measurement ≥ 4 weeks later, † Glomerular Filtration Rate*

Combining Traditional and Modern The Kidney Hierarchical Composite Endpoint (HCE)

1. All-cause mortality
2. Dialysis/transplantation (ESKD)
3. Sustained GFR <15mL/min/1.73m^2
4. Sustained GFR decline from baseline of ≥57%
5. Sustained GFR decline from baseline of ≥50%
6. Sustained GFR decline from baseline of ≥40%
7. Total GFR slope

Variable: Time to the most severe of the first six components within t months. If none of the time-to-event components occurred within t months, total GFR slope at t months is considered.

Population-Level Summary: The odds that a subject has a better outcome when assigned to the intervention than when assigned to the control.



Questions

1. Given the increasing acceptance of GFR slope, what are your views on the application of the Kidney Hierarchical Composite Endpoint (HCE) in CKD trials?

2. How would you interpret the Kidney HCE?
   a) Holistic assessment of change in kidney function
   b) Assessment of GFR slope accounting for intercurrent events
   c) Something else