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To blind or not to blind? FDA guidance on placebos and blinding in oncology clinical trials

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FDA guidance on placebos and blinding
(released Aug-2019)

- Applicable for RCTs in oncology and hematologic malignancies
- Use of **placebo control might present ethical concerns**
  - Use of placebo if an active therapy exists is not acceptable
  - Only acceptable when surveillance represents SOC (e.g. adjuvant setting) or in add-on designs
- **Concerns of blinding the treatment**
  - Continued blinding at disease progression or at serious AEs is an ethical concern
  - Therefore, FDA recommends unblinding the patient and the investigator:
    a) at the time of disease progression
    b) when the patient has an AE suspected to be related to investigational drug
  - If sponsors intend to maintain patient-level blinding when disease progression / drug-related AE occurs the informed consent document should acknowledge the risks of this approach, and the protocol should include justification for the potential added risk

What is the European perspective?

Do European regulators share the same perspective as FDA?

- Should unblinding at disease progression / drug-related SAE be done systematically for all patients and recommended by study protocol
- Impact on the choice of endpoints?
  - Overall survival might be confounded by subsequent treatments if the blind is not maintained
  - Progression-free survival might be impacted for patients who get unblinded after discontinuing treatment due to drug-related AE and who remain in the tumor assessment follow up
  - How to interpret the results of more subjective endpoints like PRO assessments?
- What is the recommended approach?

Thank you