

# Blinded Independent Central Review – Some background

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- Topics
  - What is BICR?
  - Why use BICR?
  - What is blinded?
  - Operational aspects of BICR

## Background - What is BICR?

- Review of all tumour scans by a third-party organisation
- Timepoint by timepoint review of chronological radiology scans, labelled BL, TP1, TP2, ...
- Two assessors independently review a baseline scan and the scan from the current timepoint
- Use RECIST 1.1 to opine on tumour assessment for current timepoint (CR, PR, SD, NN, PD, NE, or ND)
- Once the review for a patient is complete the data are locked
- Any discordant timepoints are assessed by a third reviewer who chooses the set of assessments that they agree with the most. That set is used in the analysis.

## Background – Why use BICR?

- Tumour assessment by investigator may be biased
  - Evaluation time bias (systematic differences in evaluation times according to treatment arm)
  - Attrition bias (patient dropout varies by treatment arm)
  - Bias while reading and assessing the tumour scans
- BICR aims to reduce the third of these
- May also reduce variability in the measurement and assessment of scans
  - Uses pathology experts with experience in tumour assessment

...for large trials that are not adequately blinded a sample-based BICR may be recommended. A full BICR should be considered in the case of smaller trials or in situations in which there is a particular need to increase the confidence in the local results.

Stone et al, 2011

## Background - What is blinded?

- Reviewers do not know:
  - Name, initials, date of birth, treatment group, examination dates, visit names, total number of timepoints, reason for the scans, Investigator's lesion selection or tumour assessment
- Adjudicating reviewer does not know the identity of Assessor 1 or 2

# Operational aspects of BICR

- When is BICR performed?
  - In “real time” after each scan is assessed by Investigator?
    - Needs very regular transfer of scans, clear demarcation of decision-making role, may have legal implication
  - Once Investigator says patient has progressed?
    - May lead to informative censoring, can be improved by additional follow up scans, administratively challenging
- Which scans are assessed?
  - Often read in blocks eg the scans taken before a data cutoff
  - Several data cutoffs lead to several blocks of reading
  - Sponsor describes what they want; Central group operationalise that

# Operational aspects of BICR

- Use of the data influences how regularly the scans are transmitted to third-party
  - Program validation
    - Blocks of scans transmitted
  - Interim analysis, primary analysis
    - Blocks of scans transmitted
  - Event prediction leads to the need for regular, analysis-ready data and analysis datasets
    - Pushes assessment towards real-time
    - Requires regular data cleaning, dataset creation