Discussion of Independent Review of PFS

EUROPEAN JOURNAL OF CANCER 47 (2011) 1772–1778

available at www.sciencedirect.com

journal homepage: www.ejconline.com

Blinded independent central review of progression in cancer clinical trials: Results from a meta-analysis ☆

O. Amit [a,*], F. Mannino [a], A.M. Stone [b], W. Bushnell [a], J. Denne [c], J. Helterbrand [d], H.U. Burger [e]

[a] GSK, Collegeville, PA, USA
[b] AstraZeneca, Macclesfield, UK
[c] Eli-Lilly, Indianapolis, IN, USA
[d] Genentech, South San Francisco, CA, USA
[e] Hoffman LaRoche, Basel, Switzerland

Conclusions

- The use of BICR increases trial complexity and cost and is an added burden to both investigators and sponsors. Based on the observations from our meta-analysis and simulations, the routine use of BICR in all randomised trials evaluating PFS as an end-point is not recommended.

European Journal of Cancer 2011(47), 1772-1778

Conclusions

- There are several situations in which a sample-based BICR might be useful. In non-blinded trials for example, a sample-based BICR in lieu of a 100% BICR would be desirable, particularly where the anticipated effect size on PFS is unknown. Alternatively, in situations where a large effect on PFS is observed or anticipated or where the trial is blinded, neither a sample-based or full BICR may be necessary.

European Journal of Cancer 2011(47), 1772-1778

Conclusions

- There are several logistical aspects of a sample-based BICR that need to be considered. All scans should be centrally managed, to allow maximum flexibility regarding management of the sample-based BICR, and to prevent significant delays and logistical hurdles associated with having to retrospectively retrieve the scans from the investigational centres.

European Journal of Cancer 2011(47), 1772-1778

Conclusions

- A typical approach would be to take a random sample of all subjects for the sample-based BICR including those who have progressed by LE and those who have not

- An alternative approach which reduces cost and complexity is to sample and centrally review only the LE events, however, this reduces the number of discordance measures that can be evaluated and may introduce bias if investigators know which scans will be subjected to a BICR

European Journal of Cancer 2011(47), 1772-1778

Our thoughts:

- There is no evidence/reference so far to indicate BICR is ‘better’
- For blinded randomized trials, or trials with large effect size, no independent review would be needed.