

The Detection of New Lesions as a Major Factor of Local Investigator-Central Review Discrepancy during a RECIST Phase II Trial

Beaumont H¹, Evans T.L², Hong S.R³, Chadjaa M⁴, Monostori Zs⁵

¹ Median Technologies, Valbonne, France; ² Hospital University of Pennsylvania-Perelman Center for Advanced Medicine, Philadelphia, PA, USA; ³ Gangnam Severance Hospital, Yonsei University College of Medicine, Seoul, Korea; ⁴ Sanofi, Vitry-sur-Seine, France; ⁵ National Koranyi Institute of Pulmonology, Budapest, Hungary

Dual readings of images by local investigators (LI) and central review (CR) can result in discordant interpretations. Variability of measurements and lack of conformance to response criteria were previously analyzed. Our study compares LI/CR sensitivity at detecting new lesions (NL) and the consequences on the discordances.

Methods

A RECIST 1.1 Randomized Phase II clinical trial of Cabazitaxel versus Topotecan enrolled 179 relapsing adult patients if meeting histological/cytological proven locally advanced or metastatic small cell lung cancer. Sixty-six LI and one CR were involved. When LI and CR disagreed on progressive disease, an additional reader (ADD) reviewed all patient images while blinded from other readers' assessments. New Lesions declared by LI, CR or ADD were retrospectively checked for presence/absence of lesions at current and previous time points.

Results

36.7% of patient follow-ups required ADD assessment. The majority of disagreements (53%) came from NL declaration.

CR detected 18.9% more NLs than did LI. CR reported four times more lung NLs, while LI reported 36% more nodal NLs. LI/CR reported similar numbers of NLs in the brain (38 vs. 33) and liver (36 vs. 39). 96.8% (30/31) of ADD reviewed patients with reported NL by LI/CR, displayed effectively what can be interpreted as NLs. LI, CR and ADD detected respectively 54.8 % [36.0; 72.7], 67.7% [48; 83.3] and 35.5% [19.2; 54.6] of these patients.

53% of nodal NL were debatable as having a shortest axial diameter (SAD) smaller than 15mm or larger than 10mm at the previous time point or a difference of SAD between time points smaller than 5mm. We also analyzed patients for which both LI and CR detected NLs. For 44.5% (4/9) of these patients, LI and CR detected NL at same time point. For 44.5% (4/9) patients, NLs were detected first by CR and, for 11.0% (1/9) patients, LI detected NL first.

Conclusions

The sensitivity of readers in the detection of NLs was the main cause of disagreement. LI had a lower sensitivity on new lung lesions than did CR.

Optimizing the criteria defining nodal NL would help reduce disagreements. CR anticipated the response due to a better sensitivity in detecting NLs. Blinding ADD from other readers' findings is questionable.