Variability in data selection between local sites and Blinded independent central review during a RECIST phase II trial: Association with rate of adjudication

Hubert Beaumont¹, Antoine Iannessi², Saerom Hong³, Sebastien Lavialle⁴, Mustapha Chadjaa⁴, Zsuzsanna Monostori⁵

¹ MEDIAN Technologies, Valbonne, France; ² Centre de Lutte Contre le Cancer, Antoine Lacassagne, Nice, France; ³ Yonsei University College of Medicine, Seoul, South Korea; ⁴ SANOFI, Vitry-Sur-Seine, France; ⁵ National Koranyi Institute of TB and Pulmonology, Budapest, Hungary

Background: In clinical trials, the double reading of images local investigator / central review (LI/CR) results in discordant evaluations. Some origins of disagreements have been investigated, as the limited precision of measurements or the mis-conformance to response criteria. However, other causes are less analysed as the variability in selecting target lesions (TL) or images in series. This study describes the LI/CR variability of data selection and its consequences on adjudication rate (AR).

Methods: We retrospectively analysed a RECIST 1.1 Randomized Phase II clinical trial of Cabazitaxel versus Topotecan. 179 relapsing adult patients were enrolled if meeting histological/cytological proven locally advanced or metastatic small cell lung cancer. Sixty-six LI sites, one CR and one adjudicator were involved. For each time point of LI/CR, we documented TLs location, non-Target Lesions (nTL) and new lesions (NL). TLs were labelled as equivocal when LI/CR had obvious different perception. Odd ratio measured the association between adjudication for progressive disease and differences in image, TL selection and NL detection.

Results: The average number of TL selected by patient differed for LI/CR (p=0.0012), respectively 2.93 and 3.37. LI/CR selected respectively 29.9% Vs 35.5%, 21.5% Vs 19.2% and 31.6% Vs 31.2% of pulmonary, hepatic and nodal lesions.

For 59% of patients, LI/CR evaluated different images at baseline and for 85% they did not select the same TLs. 18% of TLs were equivocal. AR was 36.7% (54/147). Disagreement was on NL (53%), tumoral burden assessment (18%), progressive nTL (11.2%) and 17.8% was a combination of causes.

NL declaration were nearly associated with adjudications (p=0.075). No association was found with small tumoral burden (p=0.16), equivocal lesion (p=0.47), different images (p=0.58) or progressive nTL (p=0.29). Near inverse association was found when selecting different TLs (p=0.06).

Conclusions: The distribution of direct causes of discordances were drawn. NL detection was the main factor of discordance. We observed a large variability in data selection; however, some of these variabilities had no impact on AR. Clinical trial information: NCT01500720