Safety, tolerability and diagnostic ability of a novel 18F-labelled tracer, [18F]SYN2, for PET myocardial perfusion imaging (SAFER) in patients with suspected coronary artery disease - phase II trial

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[18F]SYN2 is a novel radiotracer for PET myocardial perfusion imaging MPI that showed promising results in the phase I SAFER trial.

Aim: To assess safety and tolerability of [18F]SYN2 in phase 2 trial in patients with suspected CAD and referred to invasive coronary angiography (ICA). To test diagnostic ability of [18F]SYN2 PET perfusion in the detection of CAD using ICA or ICA with fractional flow reserve (FFR) in patients with coronary stenoses as the reference standard.

Method: The study was performed in 7 centers, and 40 subjects were enrolled. Patients were screened within 28 days prior to first dosing day. The patients were asked to admit to investigational site 2-3 hours before the first dosing and PET scan (resting baseline). The second dosing and stress PET scan (during regadenosone vasodilation) was performed 1 day – 7 days after the first. All patients returned to the investigational site 5 ± 2 days after the last dosing for a follow-up safety visit. During the follow-up period the ICA was performed for all patients at dedicated sites. All subjects also received an additional follow-up telephone call 30 ± 7 days after the last PET examination.

Results: Out of 34 reported adverse events (AE), 27 (79%) were not related to [18F]SYN2, 3 (9%) (chest pain, peripheral edema, musculoskeletal pain) were unlikely related and 4 (12%) were possibly related (diarrhea, musculoskeletal pain, palpitations). AEs of the highest incidence were general disorders and administration site conditions (5 cases in 5 (12.5%) patients), cardiac disorders (6 cases in 4 (10.0%) patients), and nervous system disorders (6 cases in 4 (10.0%) patients). The most common AE was headache (n = 4, 12%). The sensitivity, specificity, accuracy, positive predictive value and negative predictive value of SYN2 PET/CT MPI (results provided by independent panel of cardiologists) in comparison to ICA or ICA/FFR in diagnosis of CAD were 80%, 75%, 77%, 62% and 88%, respectively. The inter-rater agreement (results provided by each of the experts included in the independent panel of cardiologists and by local laboratory were taken in the analysis) for [18F]SYN2 PET/CT MPI was almost perfect in terms of inter-rater agreement in diagnosis of CAD and diagnosis of fixed defect (Fleiss’ kappas = 1.000), and moderate in terms of agreement in diagnosis on reversible defect (Fleiss’ kappa = 0.593), which corresponds to the almost perfect agreement in SSS and SDS (ICC of 0.900 and 0.903 respectively), and good agreement in SRS (ICC of 0.784).

Conclusion: [18F]SYN2 tracer administration for PET/CT myocardial perfusion imaging in subjects with suspected coronary artery disease was feasible and safe and shows reproducible diagnostic results to be confirmed in larger population.