REVIEW ARTICLE

Update of ^{18}F-flurpiridaz

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Abstract

The novel positron emission tomography (PET) myocardial perfusion imaging tracer, ^{18}F-flurpiridaz (flurpiridaz), was discussed in 2023 at the Annals of Nuclear Cardiology. In a Phase III trial in 2020 by Maddahi et al., flurpiridaz demonstrated higher sensitivity (71.9%) than ^{99m}Tc-labeled single photon emission computed tomography (SPECT) (53.7%) for detecting ≥50% coronary artery stenosis but did not meet the non-inferiority criterion in specificity. This led to a second Phase III trial, the AURORA trial, which showed flurpiridaz PET to be more sensitive (80.3%) and not inferior (63.8%) in specificity compared to SPECT. The trial highlighted flurpiridaz's superior diagnostic accuracy, especially in women and obese patients. The tracer's ability to measure coronary blood flow reserve suggests its potential future use in clinical practice, possibly offering more accurate functional ischemia diagnostics and predicting cardiac events. The findings indicate that ^{18}F-flurpiridaz could be a significant advancement in coronary artery disease diagnosis.

Keywords: Flurpiridaz, Isotope, PET
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I have reported on the possibility of ^{18}F-flurpiridaz (flurpiridaz) at the Annals of Nuclear Cardiology in 2023 (1). Flurpiridaz is a novel positron emission tomography (PET) myocardial perfusion imaging tracer. A phase III prospective, open-label, multi-center study to assess the clinical utilities of flurpiridaz was documented by Maddahi et al. in patients with known or suspected coronary artery disease (CAD) in 2020 (2). In that first phase III trial, 795 participants with known or suspected CAD showed that sensitivity of flurpiridaz PET (for detection of ≥50% stenosis by invasive coronary angiography) was 71.9% (95% confidence interval [CI]: 67.0% to 76.3%), significantly ($p<0.001$) higher than ^{99m}Tc-labeled single photon emission computed tomography (SPECT) agent (53.7% [95% CI: 48.5% to 58.8%]), while specificity did not meet the prespecified noninferiority criterion (76.2% [95% CI: 71.8% to 80.1%] vs. 86.6% [95% CI: 83.2% to 89.8%], p=NS) (2).This trial showed that PET imaging was more sensitive than SPECT imaging, but failed to show non-inferiority in specificity, so a second phase III trial (AURORA trial) was conducted (3).

A total of 730 patients underwent 1-day rest/stress flurpiridaz PET and 1- or 2-day rest-stress ^{99m}Tc–labeled SPECT. 578 patients (age 63.7 ± 9.5 years, 32.5% were women, 52.3% had body mass index ≥30 kg/m^2, and 33.6% had diabetes) were evaluable. The results showed that flurpiridaz PET was more sensitive than SPECT (80.3% vs. 68.7%; P=0.0003) and specificity was not inferior to SPECT (63.8% vs. 61.7%; P = 0.0004). Area under the receiver-operating characteristic curves of Flurpiridaz PET were larger than that of SPECT in the overall population (0.80 vs 0.68; P < 0.001), women, and obese patients (P < 0.001 for both). The authors concluded that the diagnostic accuracy was higher than SPECT, especially in women and obese subjects. Of course, this deliverable new isotope can also measure coronary blood flow reserve, so it is expected to be introduced into clinical practice in the future.

When technetium tracers have been developed in the past, it has been superior to thallium, and the test in AURORA trial was to see if PET isotopes are superior to technetium tracers. In addition, myocardial blood flow tracers always evaluate anatomic coronary artery stenosis (4). However, coronary artery stenosis does not necessarily correlate with coronary flow reserve. Perhaps the new blood flow tracer is being evaluated for other diagnostics of functional ischemia (ex. fractional flow reserve or resting indices) or possible future cardiac events. This is because the predictive ability of

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myocardial perfusion imaging to predict cardiac events is universal across isotopes and modalities.

In conclusion, this new PET isotope is very promising, and will be a breakthrough in the diagnosis of CAD in the future. Finally, flurpidaz was approved by the U.S. Food and Drug Administration in September 2024 under the brand name FLYRCADO.

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Conflicts of interest

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References

1. Matsumoto N. Progress of ^{18}F-flurpiridaz in Clinical Trials. Ann Nucl Cardiol 2023; 9: 91–3.
2. Maddahi J, Lazewatsky J, Udelson JE, et al. Phase-III clinical trial of fluorine-18 flurpiridaz positron emission tomography for evaluation of coronary artery disease. J Am Coll Cardiol 2020; 76: 391–401.
3. Maddahi J, Agostini D, Bateman TM, et al. Flurpiridaz F-18 PET myocardial perfusion imaging in patients with suspected coronary artery disease. J Am Coll Cardiol 2023; 82: 1598–610.
4. Di Carli M, Czernin J, Hoh CK, et al. Relation among stenosis severity, myocardial blood flow, and flow reserve in patients with coronary artery disease. Circulation 1995; 91: 1944–51.