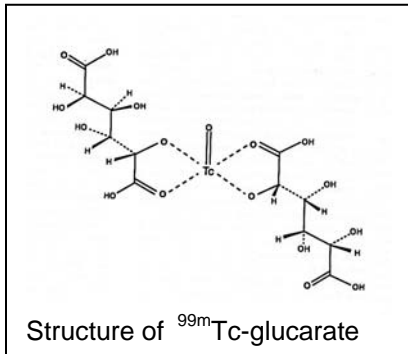




AMISCAN

Overview

AMISCAN (^{99m}Tc -glucarate) has been in development as a radiopharmaceutical diagnostic imaging agent for the diagnosis of acute myocardial infarct (AMI) for more than a decade. Previously the agent was thought to be specific for necrotic myocardium or MI.



However, more recent preclinical studies suggested that ^{99m}Tc -glucarate uptake is increased in the setting of ischemia, even in the absence of necrosis. This expanded specificity has led to the hypothesis that this imaging agent could be used to accurately assess the presence of ACS in the chest-pain patient with equivocal diagnosis. A multisite clinical study is being planned to extend the evaluation of ^{99m}Tc -glucarate imaging by studying its ability to detect ACS in chest pain patients with no signs of AMI

but with previous cardiovascular disease (CAD), in the setting of the emergency department (ED).

Introduction

Coronary artery disease is the leading cause of death in the US. Acute coronary syndrome (ACS) is an umbrella term used to cover any group of clinical symptoms compatible with acute myocardial ischemia. ACS thus covers a spectrum of clinical conditions ranging from unstable angina (UA) to non-Q-wave MI and Q-wave MI. These are life threatening disorders which are a major cause of emergency medical care and hospitalization in the US. Differentiating ACS from noncardiac chest pain is the primary diagnostic challenge for the ED physician. The majority of chest pain patients are admitted to the hospital or observation unit because the initial clinical evaluation and diagnostic tests were unable to eliminate the possibility of AMI or UA. Nonetheless, most of these patients prove not to have acute ischemia. Furthermore, among chest-pain patients discharged from the ED, a small percentage actually have acute ischemia, leading to unfavorable outcomes.

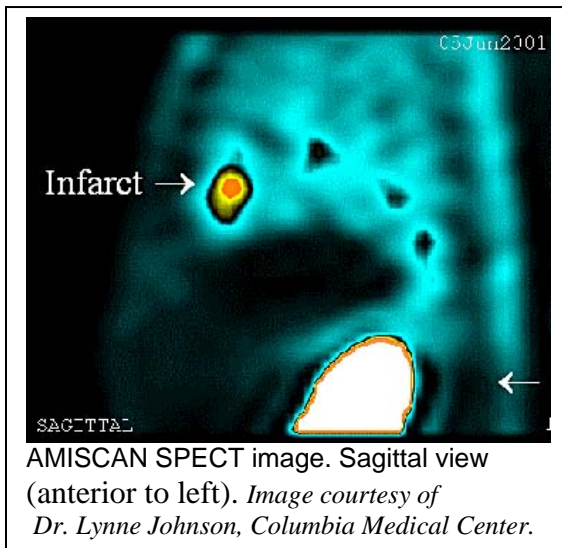
Differentiating acute coronary syndrome (ACS) from noncardiac chest pain is the primary diagnostic challenge for clinicians in the emergency department. Studies

of myocardial perfusion imaging have demonstrated important information for risk-stratifying stable post-ACS patients. However, this method is of limited value in patients with prior history of CAD, since these patients will often have abnormal resting perfusion patterns precluding the ability to differentiate old infarcts from new ischemic events. ^{99m}Tc -glucarate does not detect old heart attacks, and thus, should provide an advantage in the specificity for imaging suspected ACS patients with previous CAD.

Development Status

Our glucarate product is supplied as a lyophilized formulation in a 10 mL vial. It is labeled with ^{99m}Tc by sterilely adding ^{99m}Tc -pertechnetate, obtained from readily available generators in nuclear medicine labs. After 10 minutes at room temperature a rapid quality control test is done to confirm complete binding of the ^{99m}Tc and the agent is ready to be administered to the patient.

To date, five studies of AMISCAN (^{99m}Tc -glucarate) in a total of 223 patients have been carried out. No early or delayed adverse reactions of any type were reported in any of the studies. Studies evaluating dosimetry of ^{99m}Tc -glucarate showed all radiation dose estimates were at acceptable levels. Seminal clinical data were reported by Dr. Guiliano Mariani in the November 1999 issue of the *Journal of Nuclear Medicine*. Results suggested that ^{99m}Tc -glucarate localized in zones of acute myocardial necrosis when injected within nine hours of onset of chest pain.



A single photon emission computed tomography (SPECT) image of an AMI patient from a recent study is shown at the left. The uptake indicating the presence of an infarct is clearly seen in the anteroapical region of the left ventricle.

Currently the company is planning a study to assess the ability of ^{99m}Tc -glucarate to detect cardiac ischemia in chest pain patients. This study is a phase II, single-injection, open-label, non-randomized, single arm trial of ^{99m}Tc -glucarate in 100 chest pain patients suspected of ACS with no

obvious sign of MI and prior history of CAD. Patients will also be imaged with ^{201}Tl which will provide landmark images. ^{201}Tl was chosen over technetium-99m perfusion agents to avoid logistical difficulties due to radionuclide interference with the ^{99m}Tc -glucarate. We anticipate beginning this study in the second half of 2008.