Table 1. Between-Group Comparison of Atrial Fibrillation Detection

	Repeat Holter (n=285)	30-Day Monitor (n=287)	p Value	Absolute Detection Difference (95% CI)	NNS
Primary Outcome					
AF ≥30 seconds (within 90 days)	3%	16%	<0.001	13% (9%, 18%)	8
AF ≥30 seconds (study monitors only)	2%	15%	<0.001	13% (9%, 18%)	8
Secondary Outcomes					
AF ≥2.5 minutes	2%	10%	<0.001	8% (4%, 12%)	13
Any AF	4%	20%	<0.001	16% (10%, 21%)	6

AF=atrial fibrillation; NNS=number needed to screen.

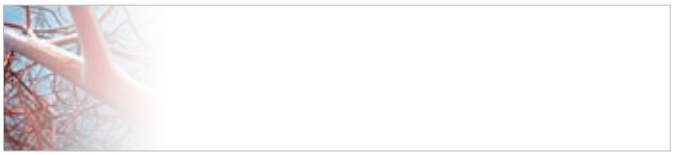
The absolute difference in AF detection between the 30-day and the repeat Holter groups was 13%, which translates into a number needed to screen of 8 patients (to identify one additional patient with AF). The prevalence of AF detected was similar whether the index event was an ischemic stroke or TIA; the yield was highest among patients aged >75 years.

Table 2. Anticoagulant Use

	Repeat Holter (n=285)	30-Day Monitor (n=287)	p Value	Absolute Treatment Difference (95% CI)
At index event	1%	1%		
At randomization	6%	5%		
At 90 days	10%	18%	0.01	8% (2%, 13%)
Switched from AP to AC	5%	13%	0.001	8% (3%, 13%)
Switched from AC to AP	1%	1%	0.997	0 (–2%, 2%)

AC=anticoagulant; AP=antiplatelet.

Dr. Gladstone noted that this study indicates that a substantial proportion of cryptogenic stroke or TIA patients have undiagnosed paroxysmal AF (1 in 6 patients aged ≥55 years; 1 in 5 patients aged >75 years), and it provides the strongest evidence to-date in support of prolonged cardiac monitoring in such patients. The findings of this trial have immediate implications for secondary stroke prevention.



DP-b99 Does Not Improve Recovery Following Acute Ischemic Stroke

Written by Phil Vinall

Despite encouraging preclinical and Phase 2 trial results [Angel I et al. *Drug Dev Res* 2002; Striem S et al. *Neural Plast* 2003; Rosenberg G et al. *Stroke* 2004; Diener HC et al. *Stroke* 2008; Barkalifa R et al. *Eur J Pharmacol* 2009], data presented by Kennedy R. Lees, MD, University of Glasgow, Glasgow, United Kingdom, showed that DP-b99, a lipophilic moderate-affinity chelator of zinc, did not improve outcome in patients with acute hemispheric ischemic stroke [Lees KR et al. *Stroke* 2013].

DP-b99 is a membrane-activated metal ion chelator that chelates ions such as zinc, a mineral that has been associated with cell signaling as well as some deleterious processes in ischemia. The rationale for the use of DP-b99 in ischemic stroke is that by chelating the zinc in the region of the membrane, there will be an improvement in ischemic damage. Although a small-scale Phase 2b study comparing DP-b99 with placebo in patients with acute ischemic stroke failed to reach its primary endpoint, its results suggested that patients with National Institutes of Health Stroke Scale (NIHSS) scores of 10 to 16 might realize some benefit from treatment with DP-b99 [Diener HC et al. *Stroke* 2008].

The Efficacy and Safety Study of DP-b99 in Treating Acute Ischemic Stroke trial [MACSI] was a Phase 3 study conducted to determine if intravenous administration of DP-b99 up to 9 hours following stroke onset and then for 3 additional days is effective in improving long-term outcomes. Patients with ischemic stroke untreated by tissue plasminogen activator (tPA), with a baseline NIHSS score of 10 to 16 and evidence of language dysfunction, visual field defect, and/or neglect were eligible. The primary study outcome was functional status measured by modified Rankin Scale (mRS) score at 90 days in the intention-to-treat population of patients with any post-treatment outcome, adjusted for initial severity. Functional and neurological recovery were secondary measures. Home time was an exploratory endpoint [Lees KR et al. *Stroke* 2013]. Planned follow-up was 3 months.

Enrollment was terminated at 446 patients after the planned interim analysis determined futility, but follow-up continued. On the primary endpoint, the mRS distributions were similar between the DP-b99 and placebo groups (p=0.10). Fewer patients in the DP-b99-treated group achieved mRS ≤1 (20.6%) compared with placebo (28.8%; p=0.05). Fewer patients in the DP-b99 group also attained NIHSS ≤1 (19.3% vs 25.6% with placebo; p=0.10; adjusted p=0.26). Mortality was similar between the DP-b99 and placebo groups (16.5% vs 15.1%, respectively; p=0.68). Home time was unchanged by treatment [Lees KR et al. *Stroke* 2013]. The outcomes were the same for all subgroups analyzed.