How New Telemetry Approaches Can Impact Clinical Trials of Drugs to Reduce Atrial Fibrillation (AF)

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Potential Rewards and Challenges of Mobile Telemetry in Drug Development

Benefits of mobile telemetry

• More complete assessment of patient disease state
• Safety monitoring of patients “in situ”
• Improves patient compliance

Challenges for mobile telemetry

• Large sensor-derived databases needed to inform clinical trial design and execution
• Manipulation, use and interpretation of these data not yet integrated into current practice
Atrial Fibrillation (AF)

AF is *uncoordinated atrial activation* that leads to irregular, often rapid heart beat

- Most common clinical arrhythmia (2.2 million people in the US)
- Palpitations, increased heart rate, and trouble breathing (dyspnea)
- $5 \times$ increased risk of stroke, $1.5-2 \times$ increased risk of death

**Stroke prevention**
- Antithrombotic medications

**Symptom control**
- Rhythm control medications
- Rate control medications
- Catheter ablation
- Pacemaker
“Time to first symptomatic recurrence” of AF

Hazard ratio, 0.75 (95% CI, 0.65 to 0.87)
P<0.001

No. at Risk
Placebo    Dronedarone
409        828
192        450
156        389
133        347
112        307
90         262

doi:10.1056/NEJMoa0803778
“Time to first symptomatic recurrence” of AF

Cumulative Incidence (%)

Days

0 60 120 180 270 360

Placebo
Dronedarone

Hazard ratio, 0.75 (95% CI, 0.65 to 0.87)
P < 0.001

No. at Risk

Placebo
409 192 156 133 112 90

Dronedarone
828 450 389 347 307 262

Many patients not contributing efficacy data

Large numbers of patients

Long study timelines

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“AF Burden” (percent time in AF) as a Study Endpoint in Pacemaker Patients

AF Burden (%)

Baseline 200 mg bid 400 mg bid 600 mg bid 800 mg bid Washout

Budiodarone Trial Period (2 w, sequential)

“AF Burden” (percent time in AF) as a Study Endpoint in Pacemaker Patients

All patients (symptomatic & asymptomatic) contributing efficacy data

Small numbers of patients

Short study timelines

AF Burden (%)

Baseline 200 mg bid 400 mg bid 600 mg bid 800 mg bid Washout

n=6 n=6 n=6 n=5 n=5 n=5

Budiodarone Trial Period (2 w, sequential)

The “burden” of measuring AF burden
Medtronic SEEQ patch
• Wear each patch up to one week
• Patches replaced by subjects at home
• Mobile base station transmits ECG data to cloud in real time
• Alerts if safety event detected or device not reapplied correctly

Holter monitor
• Wear up to two days
• Replaced by ECG technician at clinical site
• Base station stores data; needs to be docked
• No real time alerts

A Better Way to Monitor Arrhythmia
BMS-919373 Atrial Fibrillation Burden Study Schematic

- 80 subjects over 4 arms
- Continuous, real-time monitoring during treatment phase with individual baselines for efficacy and safety assessments

https://clinicaltrials.gov/show/NCT02156076
Mobile Telemetry in Drug Development
Key Insights & Opportunities

Novel technologies enable continuous remote monitoring

**Efficacy assessments:**
- Efficacy endpoint (AF burden) more reflective of true disease state
- Smaller sample size & shorter study duration required to show efficacy

**Safety screening:**
- Proactive assessment for potential compound pro-arrhythmic risk
- “Pre-screening” to assess arrhythmic risk in patients entering study

**Potential improvements in trial design & execution:**
- Current study based on “pre-SEEQ” data
- Beyond AF burden: patient stratification opportunities in AF
- Better data means better decisions