WIRELESS DETECTION OF DRUG INTAKE FOR MONITORING TREATMENT ADHERENCE IN RENAL TRANSPLANT PATIENTS

Proteus Raisin System for Adherence Monitoring

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Study Sponsor: Novartis Pharma AG, Basle, Switzerland
Blister Collection of 1-year Medication of a Renal Tx Recipient (>4000 pills)

Clinical risk implementation issues
>5% deviation

Nevins et al. Transplantation 2009;87:711–18
Ambühl Nephrol Dial Transplant 2005;20:1267–8
Measurement of medication adherence

**Indirect measures**
- Self-report
- Collateral report
- Pill-count
- Prescription refills
- Clinical outcome
- Electronic monitoring

**Direct measures**
- Observation
- Assay

Combination of methods shows highest sensitivity


Proteus Raisin System for Adherence Monitoring

FDA Approves the First Smart Pills That Track When You’ve Taken Your Meds

«Körper an Arzt, Körper an Arzt: Pille genommen»

De 'smart drug' is in aantocht

Vanaf september liggen de eerste zogenaamde 'smart drugs' in de apotheek. Dat schrijft Le Soir. In eerste instantie zullen de producten opduiken in het netwerk van het Engelse Lloydspharmacy, maar ze kunnen nadien vrij snel België bereiken.
Proteus Raisin System for Adherence Monitoring

- PRS is a novel technology for monitoring treatment adherence in transplant patients.
  - It uses a tiny ingestible micro-sensor (IEM) of 1x1x0.45 mm that can be combined with a drug.
  - The IEM consists of an integrated circuit coated with thin layers of Cu and Mg forming a biogalvanic battery in presence of water.
  - After ingestion the IEM becomes activated for a few minutes once in contact with gastric electrolytes and communicates within the body fluids to a battery-powered, unmedicated adhesive skin patch sensor (process similar to EKG).
Proteus Raisin System – Data Flow

- The adhesive skin patch sensor measures 11.4 x 5.4 x 1.3 cm and is worn on torso
  - The patch sensor is waterproof and may be worn continuously for 7 days.

- The data are then transmitted from the patch via a smartphone to a server for processing.
  - Information can then be sent back to patient and physician via SMS, smartphone displays and/or website

- In this study the IEM was combined with enteric-coated mycophenolate sodium 360 mg tablet (ECMPS) by means of over-encapsulation under Good Manufacturing Practice conditions.
Ingestible Event Marker (IEM) detection
Step count
Sleep time
Heart rate

Mobile telephony network

Patient
Adhesive Personal Monitor (APM)
Over-encapsulated enteric-coated mycophenolate sodium

Ingestible Event Marker (IEM)

Smartphone

Doctor

Phone and website displays

Proteus

SMS Messages

MEDS

Taken (wrong time): 2/26/11, 1:20 PM
Taken (wrong time): 2/26/11, 1:20 PM
Study PRO400A2201 – Objectives and Design

OBJECTIVES

- Pilot uncontrolled 12-week study to evaluate the accuracy, safety and usability of PRS combined with ECMPS 360 mg tablets in adult renal transplant recipients.

- Population – Stable maintenance kidney transplant patients
- IEM combined with enteric-coated mycophenolate sodium [IEM-ECMPS] 360 mg
- 12-week duration
- Endpoints: IEM detection accuracy, treatment adherence, safety
- N = 20 patients
- 5 sites, all in Switzerland

DOI

Directly Observed Ingestions
Patients Demographics and Disposition

DEMOGRAPHICS
- Mostly Caucasians (19/20) and males (15/20)
- Age range 35-68 years (mean 51.7)
- Average of 6.0 years after renal transplantation (range 1-19 years)
- Co-immunosuppression with CsA (7 patients), Tac (11), Srl (1), or Evl (1)

<table>
<thead>
<tr>
<th>DISPOSITION</th>
<th>ECMPS-IEM</th>
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<tbody>
<tr>
<td>N=20</td>
<td></td>
</tr>
<tr>
<td>Reason</td>
<td>n (%)</td>
</tr>
<tr>
<td>Screened</td>
<td>20</td>
</tr>
<tr>
<td>Enrolled</td>
<td>20 (100.0)</td>
</tr>
<tr>
<td>Completed</td>
<td>14 (70.0)</td>
</tr>
<tr>
<td>Prematurely discontinued study drug</td>
<td>8 (40.0)</td>
</tr>
</tbody>
</table>

- Four patients withdrew consent because of technical burden with using the system (limited access to mobile telephony network)
- Four patients discontinued due to AE
- No serious or severe adverse event
High Detection Accuracy of Drug Intake

- 100% detection of drug intake under DOI
- Taking adherence >99% over 2824 ingestions
- Accurate detection of two IEM-enabled capsules when taken at the same time

<table>
<thead>
<tr>
<th>% IEM Detection</th>
<th>Directly Observed Ingestion</th>
<th>Overall</th>
<th>One Capsule BID</th>
<th>Two Capsules BID</th>
</tr>
</thead>
<tbody>
<tr>
<td>n=34</td>
<td>100%</td>
<td>99.4%</td>
<td>100.0%</td>
<td>99.3%</td>
</tr>
<tr>
<td>n=2824</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n=448</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>n=2376</td>
<td></td>
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</tbody>
</table>

Data corrected for periods of patch impedance < 4000 Ω

Taking Adherence

____ p = NS ____
Automatic SMS reminders
Sent when timing adherence was <84% over the previous 72 hours, or APM required changing after 7-day wear or for battery depletion

- All patients received at least two SMS reminders for patch replacement
- 15/17 received more than 10 SMSs over the entire study duration
  - SMS triggered daily in case or early study discontinuation or phone connectivity issues even if patch was replaced
- Eight patients (47.1%) received SMS reminders for treatment adherence in the period from week 8 to week 12
  - Reminder sent if average timing adherence <84% over the last 72 hours
Usefulness of SMS Messages (Patients Questionnaires)

- Reminders were found useful by 85.7% of patients
- Missed medication alerts were found most useful

Number of Respondents

Patch replacement alert
- Not useful at all
- Somewhat useful
- Useful
- Very useful
- Not applicable

Missed medication alert
- Not useful at all
- Somewhat useful
- Useful
- Very useful
- Not applicable

Summary of adherence
- Not useful at all
- Somewhat useful
- Useful
- Very useful
- Not applicable

N=12 to 14 patients who completed this questionnaire
**Frequency of Reviewing the Information**
(Patients Questionnaires)

- Smartphone displays of adherence data were checked at least once a day by 64% of patients
- 57% read their weekly adherence summary as soon as it was received

*N=15 patients who completed this questionnaire*
Conclusions

- The Proteus Raisin System (PRS) is a new technology that provides direct and reliable confirmation of intake and timing of intake of drugs that are combined with the Ingestible Event Marker (IEM).

- Further studies are needed to evaluate general patient’s & health care worker’s acceptance for this system (e.g. usability).

- The PRS’ potential to improve adherence to treatment will depend on how it can be successful integrated in chronic illness management strategies of transplant centers (multilevel approach).
Lloyds Pharmacies to sell Proteus smart pills, sensors (UK)

By: Brian Dolan | Jan 13, 2012

UK-based retail pharmacy chain Lloydspharmacy has inked an exclusive deal with Proteus Biomedical to launch Proteus’ first commercial product, Helius, an offering that includes sensor-enabled pills, a peel-and-stick sensor patch worn on the body, and a mobile health app. The patch records when a pill is ingested, tracks sleep patterns, and records physical activity.