Enabling Patient Centricity in Clinical Development Through At-Home Sample Collection

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Abstract

Traditional approaches for measurement of drug exposure in clinical trials involves having the patient travel to a clinical site for collection of venous blood. This puts a burden on the patient while also limiting the opportunities for assessment of drug exposure or other measurements to these clinical visits. The ability to collect samples at home would provide a more patient-centric approach. At-home collection would provide benefit for (1) disease areas associated with episodic events (eg, asthma, migraine, etc), (2) long half-life compounds, (3) assessment of adherence, (4) developing understanding of adherence patterns for new dosing regimens (ie, QWeekly, QMonthly), and (5) more frequent assessment of biomarkers of efficacy and toxicity.

At-home collection requires technology that is both convenient for the patient to use while providing a high quality sample for laboratory analysis and regulatory acceptance. Dried blood sampling has evolved from early use in neonatal screening programs to become a high-performance analytical tool capable of providing samples suitable for quantitative analysis in clinical development. Recent efforts have focused on volumetric approaches to sample collection coupled with single-use, integrated lancet devices that provide a convenient, easy-to-use collection experience. Addition of automated data collection for date and time of sampling as well as sample temperature during shipping will ensure accurate recording of sampling time and sample integrity. Data will be presented from clinical trials piloting the use of at-home sample collection technologies, highlighting the ability to collect pharmacokinetic data equivalent to data collected during traditional clinical visits.

DRIVERS FOR IMPLEMENTATION OF HOME SAMPLE COLLECTION

- Decreased patient burden and increased patient convenience
- Decreased blood volume requirements (µL vs mL quantities)
- Improved logistical feasibility (no need for centrifuges or shipment with dry ice) → potential for reduced cost
- Added flexibility in timing of sample collection for more informed PK and exposure-response analysis
- Enables collection of samples that may not have otherwise been feasible (eg, samples proximal to episodic events)

CURRENT STATE OF SELF-COLLECTION

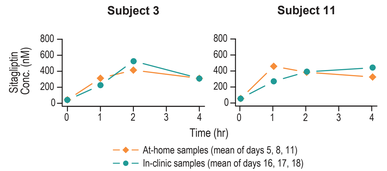
- Fingerstick sampling via lancets, blood spotted on dried blood spot (DBS) card, or transferred to polymer (Mitra®) tip (~10-20 µL/spot or tip)
- Sample barcode preassigned to each subject/nominal time
- Time/date recorded by subjects with eDiary or paper diary
- DBS cards or polymer tips returned to clinical site and shipped to lab for concentration analysis

AT-HOME vs IN-CLINIC COMPARISON

Study 1

- At-home and in-clinic fingerstick DBS samples collected for 16 healthy volunteers for analysis of sitagliptin concentrations
- Use of eDiary for capture of at-home sampling times

Figure 1. In-Clinic vs At-Home Representative Individual PK Profiles

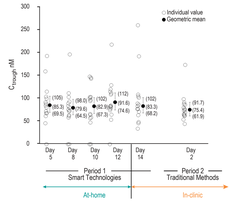


- Mean PK profiles were generally similar for at-home samples vs in-clinic samples
- PK and associated variability from in-clinic vs at-home samples were similar

Study 2

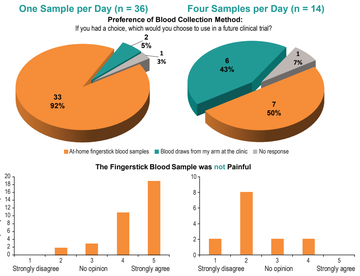
- Sparse at-home and in-clinic fingerstick DBS samples collected for 16 healthy volunteers for analysis of sitagliptin concentrations
- Use of eDiary for capture of at-home sampling times

Figure 2. Individual and Geometric Mean (95% CI) Fingerstick DBS Sitagliptin C_{trough} Values



- Sitagliptin concentrations from samples collected at home were generally similar to those collected in clinic
- Missing eDiary data in 2 subjects → highlights importance of adding automated date/time stamps

Subject Feedback



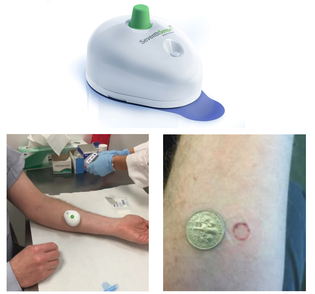
- One at-home fingerstick sample a day was favored over clinic-based venous sampling and generally not perceived to be painful
- When four fingerstick samples were collected per day, there was not a strong preference among subjects between at-home fingerstick and in-clinic venous sampling and many subjects indicated some pain with the fingerstick sampling

CHALLENGES WITH SELF-COLLECTION

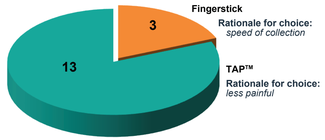
- Painful to use a lancet for repeated blood collection for some subjects → need for less-painful sampling technologies
- Accurate time of sample collection required for PK studies → need for automated time and date collection
- Sample quality directly impacts data quality → need for sampling devices that are easy to use

RECENT DEVELOPMENTS IN SAMPLE COLLECTION TECHNOLOGIES

Figure 3. Seventh Sense Biosystems TAP® Device



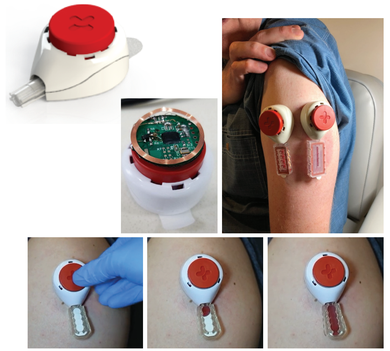
Subject Feedback



- Painless blood collection
- Requires about 2 minutes to collect the sample
- Current version collections 100 µL of blood inside of the device; however, more work is needed for at-home sampling with this device to enable at-home transfer of blood from device to collection matrix (eg, DBS cards or Mitra® tips)

Tasso HemoLink™ Device

- Painless blood sample collection
- Integrated with Mitra® tips and DBS cards for simplified dried sample collection
- Date and time collection being built into the device



Pilot Trial

- 32 subjects administered acetaminophen and caffeine
- Dried sampling by HemoLink, fingerstick, and venous sampling in-clinic on Mitra® tips 1 and 2 hours postdose
- Comparisons of drug concentrations for different sampling methods
- **Results:** Similar concentrations among different sampling methods

Figure 4A. Acetaminophen Concentration Comparison

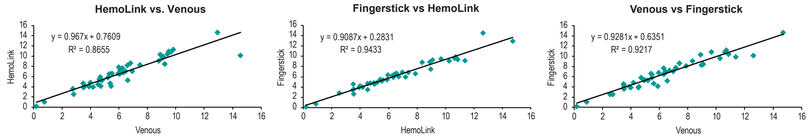
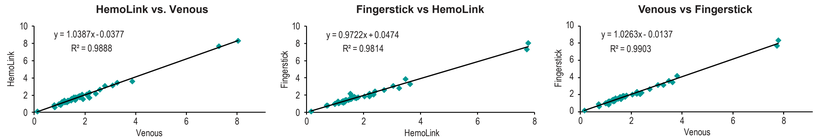


Figure 4B. Caffeine Concentration Comparison



CONCLUSIONS AND FUTURE DIRECTIONS

- Patient-centric sample collection appears to be feasible from a technology and bioanalytical perspective
- Pilot studies have demonstrated it is feasible to get similar PK results at home compared to in-clinic results
- Logistical implementation issues need to be addressed:
  - Training for sites and patients
  - Shipping within a country and country to country logistics in different countries
  - Date and time collection and data management of this information
- Future directions include shifting toward less painful, more automated sample collection with automated date/time stamps for at-home sample collection and using at-home samples for measurement of biomarkers and pharmacodynamic endpoints

Presented at the 4th FDA/PQRI Conference on Advancing Product Quality; Rockville, MD, USA; April 9-11, 2019.