Datacubed Health

ENSURING LONG-TERM PATIENT ENGAGEMENT IN AN ONCOLOGY TRIAL

EXECUTIVE BRIEF

Breast cancer is the most prevalent cancer and most frequent cause of cancer-related death and can be classified depending on hormone receptor expression.[1] Hormone receptor expression ultimately influences the course of treatment and prognosis. ER-positive breast cancers are associated with the overexpression of estrogen receptors, and may be treated with estrogen receptor ligands.[2] Human epidermal growth factor receptor 2 (HER2) is overexpressed in approximately 15% of breast cancers, and can be associated with more aggressive cancer progression.[3]

Datacubed Health worked with one top 20 pharmaceutical sponsor to evaluate an estrogen receptor ligand as a treatment for ER-positive, HER-2 negative breast cancers. The trial was conducted globally, with approximately 4,000 patients in 58 countries, and may last up to 10 years to assess invasive disease survival. This study follows patients for at least 5 years after one year of treatment. During year 1 of treatment, patients complete patient reported outcomes (PROs) every month. In year 2, patients complete PROs every 3 months. And in years 3 to 5, patients complete PROs every 6 months. During long-term follow-up, patients complete some PROs every 6 months for up to 10 years. Given the length of the study, any burdens associated with PRO completion must be reduced, and long-term patient engagement must be a priority to ensure data accuracy and comprehensiveness.

For the 5-year duration of follow-up, study staff gather information about concomitant medication use and initiation of new anti-cancer therapies every 6 months. In addition, physician's choice endocrine therapy can be expected to be highly variable on the patient level for the duration of the study. Collecting accurate information about treatment supports the evaluation of the study's primary endpoint; invasive disease-free survival following one year of treatment. Timely availability of medication information supports follow-up pursuant to potential adverse events.

SCIENTIFIC APPROACH & SOLUTION

In the past, data collection in oncology follow-up studies was straightforward as it was mostly limited to monitoring duration of response and overall survival – a time when patients' overall survival rates were unfortunately measured in months, not years. With patients living longer post-therapy, follow-up with many oncology participants can be more complex. To make follow-up successful, patient centricity is a must. Patient centricity can be achieved by understanding the issues patients and caregivers face and finding ways to minimize them.

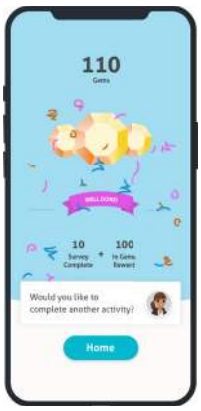
I REDUCING FRICTION

One of the central issues affecting post-treatment follow-up is increased participant attrition over time. There are several reasons for attrition in clinical trials, but in oncology studies attrition mainly occurs due to disease progression and death. Trials with patients whose disease has progressed may be more prone to attrition because they may not have the energy to respond to a PRO measure, especially if they have to boot up a computer and log onto a site web site. There is support, however, that many of these same patients with advanced cancers are willing to complete PRO measures to further research on their disease provided the process is easy for them.

Datacubed Health's Linkt app facilitates the easy completion of ePROs and ensures any data collected remotely is as accurate and complete as data collected in person. The Linkt app is patient centric, allows for ongoing communication with patients, and improves patient retention and compliance. Patients can access Linkt through their own device or through a provisioned device. Operationally, patients benefit from a Bring Your Own Device (BYOD) model, which increases compliance through the convenience and ease of ePRO completion, which is especially important for studies with a lengthy follow-up period.

II CREATING MOTIVATION FOR LONG-TERM PARTICIPANT ENGAGEMENT

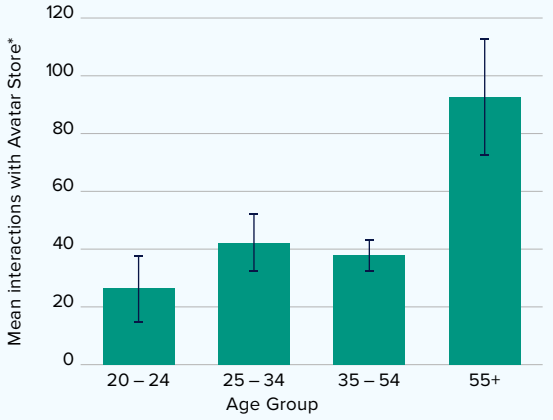
Linkt is specifically designed to maintain patient engagement and sustains high retention and compliance levels in longitudinal studies. Several classes of short, medium, and long-term (i.e., study-end) motivators are foundational to the design of the platform. For example, for short-term motivation, patients receive 'Gem' rewards for each ePRO completed, article read, or other task completed. Patients can immediately use these Gems to unlock in-app rewards in the Avatar Store. For medium to long-term motivation, patients gain access to the Treasure Chest Store at pre-determined intervals, when they can exchange Gems for a selection of out-of-app, real-world rewards (e.g., gift cards, merchandise, donation credits to disease-related charities, and digital minigames). These tiered motivational elements sustain engagement and feelings of patient involvement for the lengthy follow-up period, contributing to the collection of more complete, long-term ePRO data. Interestingly, patients aged 55 or older show particular interest and the most interactions with reward elements, of any age group, interacting with the Avatar Store four times as much as participants aged 20-24 (Figure 1).



Receiving periodic updates about disease progression and treatment can help patients feel more engaged and support long-term participation in clinical trials, particularly in older adults with cancer.[4] In a pilot study, over 70% of respondents with cancer, and their family members, showed high rates of interest in educational content and 81% believed such content would be valuable to others with cancer.[5]

Figure 1

LINKT ENGAGEMENT INCREASES WITH AGE



*In Linkt, participants receive rewards for viewing educational content or completing tasks (e.g., compliance diary). They can then use these rewards to purchase customizations for their **Avatar** in the **Avatar Store**.

Datacubed Health's Linkt platform allows researchers to deploy patient engagement content (e.g., Articles, Announcements) to patients' own devices. Participants can receive a configurable, in-app reward for viewing engagement content deployed in Linkt. Such engagement content includes weekly updates about study progress and planned activities for the upcoming week or month. Tailored announcements around study milestones also let participants know when they transition into a new period of the study (e.g., the transition from active treatment to short-term follow-up). Study-specific engagement content includes relevant educational materials about the study indication and patient-facing, aggregate data summaries presented in easily digestible infographics, delivered on a monthly or quarterly basis. This enables more frequent engagement touch points with participants outside of clinical visits and endpoint activities alone. Delivering engagement content via Linkt can keep participants feeling less like study subjects and more like study partners who are involved, motivated, and even rewarded for continued participation in a longitudinal clinical study.

III ENSURE DOSING COMPLIANCE

Datacubed Health's Medication Adherence module can be used to gather information about medications and long-term concomitant medications or initiation of anti-cancer therapy. Through the Linkt app, patients track medication use in a central, easy-to-use module designed to encourage compliance. The data is immediately available to study staff, facilitating follow-up relevant to compliance. Patients can be given the option to report symptoms directly within the Linkt app, which may be used by study staff to inform and supplement follow-up related to treatment tolerance and adverse events. This minimizes the need for data reconciliation and supports safety reviews of patient data, reducing burden for patients and study staff during treatment and long-term follow-up.

IV MONITORING ADVERSE EVENTS

Linkt's study-staff facing component, the **Admin Panel**, provides study administrators a convenient suite of tools through which to communicate with patients, monitor compliance, and to investigate potential adverse events. Patient data from Linkt (e.g., compliance diary, alerts, self-reported symptoms) are directly and immediately visible to administrators. Several different user roles with different levels of data access exist within Admin Panel, ensuring that PII/PHI access is limited and secure. Through the Admin Panel, study staff can automate reminders to patients to complete reoccurring measures, such as a medication diary. In studies with a long-term safety follow-up period, several Linkt features can assist study staff in identifying and responding to potential adverse events. A button to report symptoms can be made persistently or intermittently available to participants in Linkt. Linkt geofencing can also be configured, such that study administrators receive an alert when participants' phones enter a designated boundary, such as an area around a hospital.

V PASSIVE DATA COLLECTION

Linkt easily integrates with sensors and wearables for safety and quality of life monitoring to proactively identify any drug- or disease-related changes in vitals, cardiac functioning or activity, for example.

VI SIMPLIFY DATA REVIEW

Study data collected through the Linkt system can be downloaded from the Admin Panel by users with the right access. Study data can also be pushed directly into an electronic data capture (EDC) system through API integration. Alternatively, a Data Transfer Specification (DTS) document can be completed during Study-Start up when specific data formats are required (e.g., for

FDA submissions). This document outlines the contents, frequency, recipients, and process of data transfers during the study. Advanced user behavior metrics beyond those available in the Admin Panel can also be provided and included as metrics transfers, upon request. All data and subsequent data corrections, as needed, as well as any metrics undergo a rigorous quality assurance review before transfer to sponsors.

Once the last patient last visit (LPLV) milestone is reached, and no data corrections remain to be processed, the study enters a **Locked State** for 60 days unless otherwise specified. In this period, all study participants are force logged out of Linkt, and collection of any passive data (e.g., step counting) is ceased. During this period, study staff users retain read-only access to data in the Admin Panel, with the ability to download but not modify participant lists, consent forms, and participant data (e.g., survey answers, geofencing data). After 60 days, the study enters the 6-month **Archival State**, during which users can no longer log into the Admin Panel and the study is deleted from the Admin Panel. Data remain archived in AWS and can be retrieved on written request from the client. Following the **Archival State**, archived study data are deleted from AWS (except metadata, which will remain archived).

CONCLUSIONS

From study start-up to closeout, Datacubed Health offers a seamless, integrated platform through which study staff may monitor participant retention and compliance, deploy patient engagement materials, and collect participant data as needed. The participant-facing component, Linkt, is particularly well tolerated by older adults, and individuals in cancer treatment studies respond well to patient engagement materials delivered in this manner. Each step of the data transfer, correction, and archiving process is securely handled with the support of Datacubed Health scientists, to the ultimate end of maximizing patient retention, compliance and satisfaction while limiting operational costs and burdens.

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