Digitizing the Patient: Objective Data that Complements Biobanks

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Disclosure:
I am disclosing that I hold patents related to digital tools for evaluating human performance, and ownership interest in Cansera, Inc.
Biomarkers

• Determinants of Prognosis
• Predictors
  • Response (linked to imaging)
  • Survival (linked to registry data)
• Associations
Molecular Drivers in Lung Cancer

64% of lung cancer patients have actionable driver mutations
**NIH Biomarker Definitions Group 1998:**

**Biomarker:** a *characteristic* that is objectively measured and evaluated as an indicator of normal biological processes, pathogenic processes, or pharmacologic responses to a therapeutic intervention.
With and without targeted therapy


<table>
<thead>
<tr>
<th>Group</th>
<th>N</th>
<th>Median survival (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Driver, no targeted therapy (A)</td>
<td>313</td>
<td>2.4 (1.81-2.93)</td>
</tr>
<tr>
<td>No driver (B)</td>
<td>361</td>
<td>2.1 (1.84-2.51)</td>
</tr>
<tr>
<td>Driver, targeted therapy (C)</td>
<td>264</td>
<td>3.5 (3.21-4.59)</td>
</tr>
</tbody>
</table>

P < .0001

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## Actionable mutation patients in USA

<table>
<thead>
<tr>
<th>Actionable Mutations *</th>
<th>No Actionable mutation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Young</td>
<td>Old</td>
</tr>
<tr>
<td>Non-smokers</td>
<td>Smokers</td>
</tr>
<tr>
<td>Female</td>
<td>Male</td>
</tr>
<tr>
<td>More Asians</td>
<td>More Blacks</td>
</tr>
</tbody>
</table>

*EGFR, ALK fusion, ROS1 fusion, BRAF, MET, NTRK fusion, ERBB2, (KRAS)*
My favorite biomarker

Table 1. Karnofsky Performance Scale Index (KPS)

<table>
<thead>
<tr>
<th>Score (category)</th>
<th>Karnofsky</th>
</tr>
</thead>
<tbody>
<tr>
<td>100</td>
<td>Normal; no complaints; no evidence of disease.</td>
</tr>
<tr>
<td>90</td>
<td>Able to carry on normal activity; minor signs or symptoms.</td>
</tr>
<tr>
<td>80</td>
<td>Normal activity with effort; some signs or symptoms of disease.</td>
</tr>
<tr>
<td>70</td>
<td>Care for self; unable to carry on normal activity or to do active work.</td>
</tr>
<tr>
<td>60</td>
<td>Requires occasional assistance but is able to care for most of his needs.</td>
</tr>
<tr>
<td>50</td>
<td>Requires considerable assistance and frequent medical care.</td>
</tr>
<tr>
<td>40</td>
<td>Disabled; requires special care and assistance.</td>
</tr>
<tr>
<td>30</td>
<td>Severely disabled; hospitalization necessary; active supportive treatment is necessary.</td>
</tr>
<tr>
<td>20</td>
<td>Very sick; hospitalization necessary; active supportive treatment is necessary.</td>
</tr>
<tr>
<td>10</td>
<td>Moribund; fatal processes progressing rapidly.</td>
</tr>
<tr>
<td>0</td>
<td>Dead.</td>
</tr>
</tbody>
</table>
Are these EGFR associated lung cancers the same?
The Cancer Genome Atlas
Lung Adenocarcinoma

• Outcome predictors – multivariate analysis
  • Stage*
  • Margin status at resection*
  • Non-smoker
  • Genomics
  • Gender
Biomarker Discovery

Veristrat Assay

British J Cancer 116,36-43 (2017)
Clinical Observation

A Kaplan-Meier survival curves according to performance status (PS)

- 0- normal
- 1- mild impairment
- 2- in bed <50% of waking hours
- 3- in bed >50% waking hours
- 4- bedridden

J Thoracic Oncol 2010 5(5) 620-630
Who knows more about prognosis?
Who knows more about prognosis?
Fitness Trackers
## Metabolic Equivalents

<table>
<thead>
<tr>
<th>Apple Watch Calories (kcals)</th>
<th>Indirect Calorimetry Calories (kcals)</th>
</tr>
</thead>
<tbody>
<tr>
<td>9.0 ± 2.6</td>
<td>10.2 ± 1.2</td>
</tr>
<tr>
<td>17.4 ± 4.7</td>
<td>22.4 ± 4.1</td>
</tr>
<tr>
<td>32.8 ± 8.3</td>
<td>29.6 ± 5.1</td>
</tr>
<tr>
<td>50.9 ± 11.8</td>
<td>46.3 ± 10.8</td>
</tr>
<tr>
<td>71.0 ± 29.5</td>
<td>62.4 ± 9.8</td>
</tr>
<tr>
<td>31.0 ± 17.5</td>
<td>25.0 ± 3.25</td>
</tr>
<tr>
<td>201.1 ± 41.5</td>
<td>195.8 ± 30.4</td>
</tr>
</tbody>
</table>

**AT HOME ACTIVITIES**

- **Sweeping carpet**: 3.3 kcal/min (99-124 kcal / 30 min)
- **Gardening**: 4.0 kcal/min (120-150 kcal)
- **Playing with dog (moderate)**: 4.0 kcal/min (120-150 kcal)
- **Wash & wax car**: 4.5 kcal/min (135-168 kcal)
- **Playing with Kids (vigorous)**: 5.0 kcal/min (150-188 kcal)

Ferrara et al J Exercise physiol 2017
Activity Trackers – Noisy Data

Physical Activity of Patients in Each Activity Level Group

- Activity Level
  - Active < 10 Hrs
  - Active ≥ 10 Hrs

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Activity Trackers – Noisy Data

Physical Activity of Patients in Each Activity Level Group

- Activity Level
  - Active < 10 Hrs
  - Active ≥ 10 Hrs

Study Timeline Daytime Hour
Chemotherapy Complications

**Unexpected Healthcare Encounters**

- Hospitalization
- Emergency Room Visits
- Trips to Infusion Center (not for scheduled chemotherapy)
- MD visits that were not scheduled at the time of last MD appointment
Outpatient Activity and Unexpected Healthcare Encounters

Unplanned Healthcare Events

- UHE Types
  - Urgent Office Visits
  - ER Visits
  - Urgent Hospitalizations

- Unplanned Day Hospital Visits
- Standard Deviation

(Only the positive part is shown)

Daytime Non-sedentary Hours during 60-day Period

- $x < 5$ (n=8)
- $5 \leq x < 10$ (n=8)
- $10 \leq x < 20$ (n=9)
- $20 \leq x < 40$ (n=8)
- $x \geq 40$ (n=6)
Impact of Objective Enrollment on Clinical Trials

2019 NCI-Designated Cancer Centers¹

2018 Community Oncology Clinics Impacted²

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Increasing Scale
QCPPS Digital Measure:

DATA RECORDING IS RUNNING

1. Please sit on a chair
2. Press "START TASK"
3. Stand up from the chair walk around for 30 seconds without any support
4. Task will finish automatically after 30 seconds, if you are unable to walk for that long, please sit down and rest

Remaining time: 27

TASK FINISHED
Impact of Performance Status Discordance

- Lower by 3
- Lower by 2
- Lower by 1
- Agreement: 16% better outcomes
- Higher by 1
- Higher by 2
- Higher by 3

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Incentives to assign higher performance status

- Patients get access to exciting new clinical trial drugs
- Physicians are credited with clinical trial accruals
- Large institutional payments for each clinical trial accrual
- Less insurance company scrutiny with regard to payments for high cost drugs
- Avoidance of arguments with patients who are “too sick” to be treated for cancer
Kinect One Data Collection

Used to sense movement of human body through skeleton data (25 nodes)

Second version of Kinect Sensor

Time of flight sensor

Using Kinect SDK to validate/process

Looking at Facial Modeling & Tracking (military trial)
De-identified Performance Status Assessment via Kinect movement tracker
Unplanned Healthcare Encounters

Quantitative CPPS study

- Prospective clinical trial with kinematic data on 35 patients
- USC/MD Anderson
- Treated with highly emetogenic chemotherapy
- Unexpected Healthcare Encounters include:
  - ER visits
  - Hospitalization
  - Unplanned Day Hospital treatments (usually hydration and anti-emetics)
  - Unplanned MD visits for toxicity management
Patient Consent & screening for EDT trial

Pre-treatment + 180 days
- Daily weight
- Daily smartphone based PRO diary
- Movement tracking with Fitbit Alta HR

Up to 30 days
- Pre-treatment
- Before C1D1
  - Screening visit/Baseline
  - Kinect assessment #1

180 days
- Treatment on EDT
- C1D1 of EDT
  - Kinect assessment #2
- • Trial enrolls patients across all phase 1 and EDT studies at Norris
- • A companion trial that exists as an add-on to other studies
- • Data collected by separate research team prior to data entering sponsor specific databases

Precision PS:

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The patient vs the tumor

- The outcome for patients with cancer is dependent on both tumor and patient factors
- Technological tools are now available for quantification of the global health of the patient
- Linking patient information about performance to tumor data has the potential to improve understanding of prognostic features obtained from biobanks