Bringing Precision/Personalized Oncology to the VA

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Quality of Care at the VA

- Preventive, acute, and chronic care: VA outperforms private sector.¹
- Cancer care: VA outperforms private sector.²
- Cancer screening: VA outperforms private sector.³
- Personalized medical oncology is already a reality at the VA:
  - Testing for validated genetic predictors of response (e.g. melanoma, lung cancer) are routinely performed at the VA.
  - Veterans have ready access to drugs (≤ $9.00/month for any drug).

Cancer at the VA

- VA is largest healthcare system in U.S.
  - 153 hospitals, 788 CBOCs.
- 8.8 million Veterans enrolled; 6.1 million Veterans routinely access VA for healthcare.
  - Median age at VA = 57 vs. 38 for U.S. population as a whole.
- 40,000 new cancer cases/year.
  - Median age = 66 (also 66 for U.S. population as a whole).
- Wait times for new patients: no more than 4 weeks, and as soon as same day.
Demographics of Cancer Patients

- White: 78%
- Black: 19%
- Other: 3%

- Male: 97%
- Female: 3%

- Prostate: 32%
- Lung: 41%
- Colorectal: 19%
- Other: 8%

Source: MILITARYMEDICINE, 177, 6:693, 2012
A Brief History of VA Research Accomplishments

- Radioimmunoassay to detect insulin (Yalow, Nobel laureate, 1977).
- Hormone therapy for breast and prostate cancer (Schally, Nobel laureate, 1977).
Research at the VA (cont’d)

- Technology for CT scanner (Oldendorf, Lasker Award, 1975).

**Others:**
- Link between smoking and lung cancer (1940s),
- Nicotine patch,
- Hepatitis C treatment,
- First successful liver transplant,
- Vaccine for shingles,
- Proton pump inhibitors,
- Aspirin for heart disease,
- TB treatment,
- MVP.
Precision/Personalized Medicine in Oncology at the West LA VA

- Molecular Pathology lab established in 2005.
  - Gene specific sequencing of validated molecular target for therapeutic intervention (e.g. lung cancer, melanoma, GIST).
  - Molecular analyses of MRD (e.g. CML, APML).
- Treatment decisions can be rapidly instituted without delays due to insurance authorization or drug affordability.
Precision/Personalized Medicine in Oncology at the West LA VA

- Prostate Cancer Stand Up 2 Cancer West Coast “Dream Team” site.
Precision/Personalized Medicine in Oncology at the West LA VA

- Prostate Cancer Stand Up 2 Cancer West Coast “Dream Team” site.
- Successfully performed biopsies of metastatic lesions in patients with advanced prostate cancer.
  - De-identified tumor tissue transferred to academic partners for next generation sequencing.
  - Treatment decisions can be made based on molecular data.
  - Clinical trials can be initiated to validate molecular biomarkers.
Precision/Personalized Medicine at the West LA VA – Lessons Learned

• Veterans gladly participate in research even if there is no immediate personal benefit.

• Acquisition of tissue for focused sequencing is feasible and is intramurally performed.

• More broad sequencing efforts, including unbiased next generation sequencing, is feasible with partnerships with academic, biopharmaceutical, and non-profit institutions.
Moving Forward and Conclusions

• Bridging the gap between Precision and Personalized Medicine:
  • *Multidisciplinary approach: clinician experts, bench researchers, human geneticists.*
  • “Virtual” Precision Medicine Tumor Boards.
• Establishing partnerships between VA and academia, biopharma and non-profits.
• Prostate cancer as a model for proof-of-principle of feasibility:
  • *High burden of prostate cancer amongst Veterans.*
  • *High proportion of African American Veterans with prostate cancer.*
  • *PCF-VA Initiative to bring Precision/Personalized Medicine*
Mark Simon
Partner, Torrey Partners
Background

- US specialty drug spending is increasing by from 15-25% included.
- This growth in spending clearly unsustainable.
- Another trend is the explosion of data (ie DNA, RNA, protein, etc.)
- Do patients (veterans) have access to the latest, high-end pharmaceuticals?
- Biologics will increase the silo of medicine cost 10-15 fold
- Are the right patients receiving the right drugs at the right time?
- How do the taxpayers ensure that the money is well spent?

Source: Torrey Partners.
A Potential Solution
Create a virtual center of excellence---use best human capital

- True KOLs, clinicians, nurses, geneticists for each disease area provides unbiased adjudication (initiation, continuation, or cessation of therapy)

- Each complex patient is its own clinical trial—leverages EMR and web portals

- Decision on care delivery in hands of true experts (not PBM, insurers, pharma, etc.)

- Measurement of benefit can be inconsistent and often subjective—center determines

- A Foundation can lead here.

- Era of companion therapeutics

- Data is tracked, monitored, and de-identified, and shared goal of precision medicine

Source: Torreya Partners.

#MIGlobal
A Potential Solution

• Can be web-based with a tele-health component
• The system is fundamentally broken today.
• Delivery of optimal regimen, monitoring and adherence is flawed.
• Take concierge (personalized) medicine to wider audience that has complex diseases
• What are early indicators of bad outcomes?
• Absenteeism vs. presenteeism
• When does patient go from PCP to a specialist and vice-versa?
• Pharmacy cost cannot be the only driver of patient care
• We need a mature model of health care utilization and quality
VA Biotech Industry Considerations

- View VA as an insular, closed system—disconnected from research/clinical state of the art
- Full transparency and full accountability
- Do not fully appreciate the treasure trove of the VA data
- There is genomic, longitudinal, environmental, diet, lifestyle, etc. data that is unprecedented.
- This database can drive precision medicine
- VA’s image and messaging can improve
- Is the VA part of the problem or the solution?
- The access point for some biotechs is via an academic with a relationship with the VA
- Some are run by veterans—need rapid responses and high quality data collection

Source: Torreya Partners.
Ideas for Small Biotechs/VA

- A “Milken CDC” event with the VA---invite biotech companies for a “VA Day”
- Open-up the data –base (de-identified) for data mining, etc
- The recruitment of a new head of research at the VA with background in this area
- Easy wins that VA is “connected” to the state of the art research/clinical networks
- Closer NCI and FDA cooperation
- Clinical trials infrastructure/expertise raises quality of care
- Small biotechs—big challenges recruiting patients for all stage of clinical trials.
- Biotechs don’t appreciate that gov’t agencies do not conduct public affairs.

Source: Torreya Partners
“N-of-one Trials: Is This the Future of Oncology Drug Development?”

Mike Doherty

Head of strategic Innovation, Drug development, Genentech

Executive adviser- Foundation Medicine Inc.
The Evolution of Drug Development

- **Existing Paradigm**
  - OS: only endpoint for full approval
  - PFS with substantial clinical benefit, reproducible (x2)
  - Surrogates (used for accelerated approval) DFS, PFS, ORR, TTP

  **Challenges and transitions**
  - Single arm trials for approval
  - Small numbers/ rare tumors/rare genomic variants
  - Pan tumor approaches and Unknown primary

- **Future Paradigm: Precision Medicine**
  - Adaptive approach/adaptive design
  - Patient-centric approaches

Source: Mike Doherty, Roche
“N-of-one Trials: Is This the Future of Oncology Drug Development?”

- N=1 can impact safety (e.g. SJS, TENS, PML etc)
- N=1 with longitudinal monitoring could be evidence of target activity
- N=1 could be informative for dose selection for combo trials

- Patient-centric trial where the molecular information determines the individualized treatment using pre specified algorithms
  - Gradual build up of cohorts of treatment groups
  - Each patient considered individually

Source: Mike Doherty, Roche
### Veterans Mental Health Crisis

<table>
<thead>
<tr>
<th>Statistic</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;22</td>
<td>Veteran suicides per day</td>
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<tr>
<td>1 in 5</td>
<td>OEF/OIF Veterans diagnosed with PTSD</td>
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<tr>
<td>&gt;320,000</td>
<td>OEF/OIF Troops have suffered from TBI</td>
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<tr>
<td>20%</td>
<td>Also suffering from substance use disorders</td>
</tr>
<tr>
<td>0</td>
<td>Definitive diagnostic tests for PTSD and mild TBI</td>
</tr>
</tbody>
</table>

*Source: World Bank.*
From Reductionism to Complex Systems Modeling → Big Data
Step One: Reverse Engineering from Human Source: International Monetary Fund.
Cooperative Alliance Model(s)

Shared Disease Research Roadmap

Independent, trusted third party to manage diverse stakeholder interests.

Bilateral Contracts

Share costs, risk and rewards\(^1\) of respective projects. (\(^1\)incl. IP)

Further reduce cost and time to value by sharing experience, expertise and capabilities across projects.

Source: Milken Institute.
21st Century Mental Health for Veterans: Recommendations

1. Form National Alliance Coalition for PTSD & TBI (e.g. VA Brain Trust)

2. Expand Roadmap (Gap-driven, Top-down, Translational research focused)

3. Establish translational-research--friendly policies for data-sharing, IP, ICF

4. Embrace Disruption & Innovation – break down silos/utilize technology
Matthew Collier
U.S. Department of Veterans Affairs
Thank you!