Genetic Testing, Innovation, Prior Authorization, & the Individual Patient

October 25, 2019

J. David Liss
BioReference Laboratories, an OPKO Health Company
Without Genetic Testing, there is No Personalized Medicine

What is the connection between reimbursement policy and genetic innovation?
Some Basics

WHAT IS GENETIC TESTING?

• Genetic testing is a type of medical test that identifies changes in chromosomes, genes, or proteins. The results of a genetic test can confirm or rule out a suspected genetic condition, help determine a person’s chance of developing or passing on a genetic disorder, [determine the effectiveness of a medicine for an individual patient.] (HHS)

• More than 1,000 genetic tests are currently in use, and more are being developed. (HHS)
Some Basics

WHAT IS PRIOR AUTHORIZATION?

• Approval from a health plan that may be required before you get a service or fill a prescription in order for the service or prescription to be covered by your plan. (HealthCare.gov)

• Tool for controlling utilization

• Longstanding track record
Some Basics

HOW DOES PA WORK IN LABORATORIES?

• Lab receives specimen from physician/hospital
• Specimen must be processed when arrives to protect quality and provide timely results
• Processing is necessary whether or not PA is provided by physician
Changes in 2017 for Reimbursing Genetic Testing

Until 2017

• Laboratory could request PA, assume administrative burden
• Window of 30 days to request PA, in consideration of lab context

Since 2017

• Only ordering physician can request PA
• Window of as little as 48 hours
• Clinicians must use portals that are clunky, error-prone, and not loaded with the right information
Impact on Genetic Testing

- 60% of tests no longer being reimbursed
- Though clearly unsustainable, the industry has not yet ceased genetic testing from concern of patient impact.
- Expect innovation to slow. Academic centers may continue to perform research, but it is less likely that commercial labs will translate this research into patient interventions
- This has disrupted the innovation cycle and may limit the development of precision medicine
AMA 2018 Physician Survey on PA

• Patient Impact
  o 65% report PA approval wait time of at least 1 day, 26% at least 3 days
  o 91% reported PA-associated care delays
  o 28% reported PA led to serious adverse events
    ▪ 75% reported treatment abandonment
    ▪ 91% reported significant or serious negative impact on clinical outcomes

• Physician Impact
  o 86% report high or extremely high admin burden
  o Spend 2 days/week on PA
  o 36% physicians report having staff dealing exclusively with PA
Approaches

• There are consensus positions to address issues of PA between provider organizations and payor associations, including the AMA and AHIP that focus on payment policy

• Information Technology provides a promising direction
HIT Approach

• Just as the EHR can provide clinical decision support, it can be the locus for administrative decision support.
• PA rules would have to be standardized
• PA rules would have to be developed within existing technology standards
• In addition to improved patient/physician outcomes, 2018 CAQH Index estimates savings of as much as $7.28 per healthcare transaction if administrative processes were electronic.
HIT Approach

• H.R. 3107 seeks savings and improvements in Medicare Advantage by identifying the standards and methods to make prior authorization electronic, and to a large extent, automated.

• Automating PA can help support the innovation cycle by creating surety for appropriate reimbursement of genetic tests, restoring incentives to develop and commercialize foundational technology for precision medicine.

• We are hopeful Congress will rapidly move in this direction.
Chimeric Antigen Receptor T-cells in Adult Patients:
The Power of Innovation to Change the Lives of Cancer Patients

Elizabeth Budde, MD, PhD
Assistant Professor, Hematology/Hematopoietic Cell Transplantation

October 25, 2019
Diagnosed with Philadelphia chromosome positive ALL
Her leukemia proved refractory to all available treatments:
  • She underwent 6 lines of chemotherapy
  • Including 2 allogeneic blood stem cell transplants
The patient underwent treatment with CD19 CAR T-cells as they became available
  • At the time of treatment the patient had 70% leukemia cells in her bone marrow
  • Within 28 days of treatment her marrow showed no evidence of residual leukemia
  • Even with molecular testing
CD19-CAR T-cells Also Have Potent Activity Against Relapsed/Refractory Non-Hodgkin Lymphoma (NHL)

This patient is a 61-year-old man with relapse high-grade B cell lymphoma
- The patient had failed multiple prior therapies
- The patient had extensive lymphoma involvement throughout his chest and abdomen
- He received CD19 CAR T-cells as a salvage treatment
- By day +34 following treatment, he achieved a complete remission
CAR T-cells Complete Remission Rates May Result in Lasting Remissions For Patients with Non-Hodgkin Lymphoma

• **ZUMA-1** Trial
  • *Axicabtagene ciloleucel*
  • Phase 1/2 trial
  • 101 patients
  • Overall response rate 82%
  • Complete remission rate 54%

• **Juliet** Trial
  • *Tisagenlecleucel-T*
  • Phase 2a trial
  • 51 patients
  • Overall response rate 59%
  • Complete remission rate 43%
CAR T-cell Are Likely to Grow in Importance in the Care of Patients Whose Clinical Needs are Currently Unmet

A patient with relapsed glioblastoma

The CAR T-cell Pipeline is Growing

Clinical Trials in Progress
- Relapsed/refractory Glioblastoma
- Breast cancer with brain metastases
- Central nervous system lymphoma
- Acute myelogenous leukemia (AML) and BPDCN
- Relapsed/refractory multiple myeloma
- Prostate cancer

Brown et al. NEJM 2016 375(26): 2561-9
Why Are CAR T-cell Treatments So Expensive?

• **Very High Product Acquisition Costs**
  • $373,000-$475,000

• **Complex Clinical Care Pre/Post CAR T-cell Infusion**
  • CAR T-cell patients are clinically complex
    • Patients have advanced, frequently refractory leukemia and lymphoma
    • Patients may require additional chemotherapy prior to administration of CAR T-cells
    • Up to 20% of patients suffer disease progression between the time that their T-cells are collected and the CAR T-cell product is ready for infusion
  • Potent therapy, but associated with unique toxicities:
    – Cytokine Release Syndrome
    – CAR-Related Encephalopathy Syndrome
    – ICU Hospitalization of patients with severe CRS and CRES
    – Multi-departmental infrastructure management is critical
Current State of Reimbursement for CAR T-cell Therapeutics

• The very high cost of administering and caring for patients with CAR T-cell treatments has provoked significant concern amongst government and commercial payers, as well as, federal and state policymakers
  • Unprecedented in cost
  • Significant concerns about the precedent of a treatment technology that may cost over $1,000,000 per patient
  • Policymakers in federal government worry that these and other high-cost treatments may undermine the solvency of Medicare Trust Fund
• No consistency in reimbursement models
  • Some commercial payers are offering reimbursement for CAR T-cell Treatments based upon single patient agreements
  • Medicare outpatient payment for CAR T-cell treatments differs dramatically from the inpatient payment model
    • Inpatient payment model may lead to >$200,000 in losses on a per-patient basis
  • Uncertainty about reimbursement is likely leading to barriers to patient access to these potentially life-saving treatments
Uncertainty About Reimbursement Creates a Risk of Stifling Therapeutic Innovation

“I’m extremely worried that if we don’t adapt the approach to reimbursement soon, we may foreclose the therapeutic opportunities”

Scott Gottlieb, MD
Former FDA Commissioner
The Future of Hematology/Oncology Lies in Even Faster Integration of Innovative, Life-Saving Therapeutics Into Clinical Care

• New care solutions are now being identified for cancer patients at an unprecedented rate

• New anti-cancer therapeutics and immuno-oncological agents are changing the meaning of a cancer diagnoses for increasing numbers of patients
  • CAR T-cells are the first in a series of gene-modified and engineered therapeutics that may be produce better outcomes, and even cures, for patients who have failed standard treatment approaches

• These therapeutics come to market at prices that often exceed historic benchmarks

• Our national leaders need to plan carefully for how we can ensure that these potentially life-saving treatments can reach those patients and families that reach them most quickly, efficiently, equitably, and sustainably
Why This Work is Never Complete
Digital Care Management

DR. ANDREA WILLIS
SVP and Chief Medical Officer
From Case Management to CARE MANAGEMENT

- Navigation throughout the continuum of care
- Integrated medical, behavioral, pharmacy, and social support
- Measurable impacts and outcomes
- Traditionally has been telephonic

Challenges
- Difficulty reaching members
- Challenges in sustaining relationships with members beyond a few conversations
- Limited time with members
MEMBER-CENTRIC DECISION MAKING: REACH THE RIGHT PERSON THE RIGHT WAY AT THE RIGHT TIME WITH THE RIGHT MESSAGE

- Consumer segmentation using demographics and psychographics
- Continuous monitoring of population health
- Personalized approach to consumer and provider outreach
- Centralization of all member touch points

Determining the uniqueness of each member — and what many in a subgroup have in common
Digital Care Management

Supports people outside of the walls of care delivery

80% of variance in health outcomes is due to non-clinical factors

- Technology that connects a member-facing, HIPAA-compliant mobile solution to a care management dashboard (Tech-Enabled, Data-Driven, Patient-Centric)
- Generates insights that enable early interventions
- Support the whole person
- Extend the reach of staff
- Tracks adherence and outcomes
Amplify the capacity of staff to engage more members, more effectively

Traditional model

- Onboarding Phone Call
- Phone Call
- Phone Call

6 MONTH SUMMARY
- 75 min / member
- 3 Touch Points
- Managing 100 Members

CARE TEAM IMPACT

Omni-channel model

- Onboarding Mobile App
- Sustained Mobile Messages, Reminders, Educational Content & Other Interactions

6 MONTH SUMMARY
- 35 min / member
- 100+ Touch Points
- Managing 300+ Members

POPULATION IMPACT

Onboarding Phone Call
- Only reaching highest risk, highest cost members

Moving down risk pyramid to drive engagement
Digital Member Interactions

Digital Member Checklist

- Reminders: important events, appointments, medications
- Educational activities and training opportunities articles and videos
- Physical activity tracking
- Behavioral and psychosocial surveys and questionnaires
- One on one messaging
- One to many messaging
- Links to telehealth
- Hand-offs to care team members
- Coming soon: video chatting
## The Digital Care Management Experience

For Members who opt in for digital interaction

| ✓ A multi-channel communication is set up to connect members, caregivers, and care teams (i.e. text, email, chat) |
| ✓ An Interactive Care Program is delivered to members via smartphone or tablet in the form of a health checklist |
| ✓ Checklist includes items such as education, reminders, and surveys |
| □ Care managers have dashboards which allow them to conduct one-on-one guidance |
| □ Alerts are surfaced to alert care managers to member issues needing immediate action |
| □ The Care Team can send secure messages to provide feedback, guidance, support and encouragement. When a new message is sent to the member, the member will receive a push notification about the new message on the app. |

✓ Reporting will be generated to identify process metrics:
  + Contact Rate
  + Engagement rate
  + Number of interactions (with staff and/or resources)
  + Case disposition
Measures of Success

- Increased engagement
- Engagement with self-service tools
- Decreased ER visits
- Decreased inpatient admissions
- More referrals to comprehensive care
- More referrals to community resources
- Care plan adherence
- Medication Adherence
- Medical cost savings
- Care manager productivity and satisfaction
- Improved ROI
THANK YOU
eliprio®: A machine learning approach to patient value

October 2019
Disclosures

To shed light on epilepsy’s impact and explore the possibility of working together on shared goals to improve outcomes for patients living with epilepsy

• UCB’s portfolio of predictive tools and solutions, including the drug resistant epilepsy (DRE) Risk Prediction Model discussed later in today’s presentation, is still under development.

• The DRE Risk Prediction Model has only been tested retrospectively in claims data and has not yet undergone FDA review/approval; accordingly, it is not available for prospective use in a clinical setting.
What is Epilepsy?

[ep-u[h]-lep-see]

Noun – complex spectrum of disorders that is characterized by unpredictable seizures that differ in type, cause and severity

The International League Against Epilepsy defines epilepsy as any of the following:

- At least two unprovoked seizures occurring > 24 hours apart
- Diagnosis of an epilepsy syndrome
- One unprovoked seizure and a probability of further seizures*

*Similar to the general recurrence risk (at least 60%) after two unprovoked seizures, occurring over the next ten years

UCB leverages machine learning to predict the risk of DRE
To improve the quality of care and lower costs associated with DRE

DRE risk score may:
- Identify patients and patient populations most likely to benefit from interventions to proactively enable better care
- Define problems early
- Foster quality improvement through identification and closure of evidence-based gaps in patient care
- Effectively manage a provider network to identify opportunities for cost improvement, such as in the areas of pharmacy, imaging, and network leakage

Consider:
- Standard of care

- Rapid referral to specialist or epileptologist
- Review of diagnosis and classification of epilepsy
- More aggressive therapy
- Closer patient monitoring

Patients with epilepsy

Low risk for DRE

High risk for DRE

There is an opportunity to identify patients at risk for DRE to optimize care and improve outcomes
What are the key barriers?
Depends on what you’re building
Our Areas of Focus

- Neurology
- Immunology
- Bone

Everything we do starts with one question:

“How will this create value for people living with severe diseases?”

Our People

- 40+ countries
- 7.5K employees
- 3.3M patients use our medicines around the world
Thank you.
Focusing Innovation on the Individual Patient

Powering development of new therapies in the era of Precision Medicine

Rachael Fones
IQVIA - Formed by the merger of Quintiles and IMS Health

Where human science meets data science

Worldwide clinical trial and real world study experience informed by deep scientific expertise across every major therapy area

Leading healthcare “big data” and technologies fueled by commercial expertise to find unparalleled insights
Our role in context

Clinical trials

Basic research → Candidate selection → Clinical trials

Regulatory review → Product launch

7-10 years

Clinical phases

Phase I
- Safety studies in healthy humans
- 20-30 healthy participants
- Duration up to several months

Phase II
- Safety and immunogenicity studies in target population
- 100-300 participants
- Duration up to 1-2 years

Phase III
- Safety and efficacy studies in target population
- 10,000-30,000 patients
- Duration up to 4 years

Clinical trial steps:
1. Planning
2. Site start-up
3. Patient recruitment
4. Data collection & monitoring
5. Close-out & Reporting
Context: Understanding of human biology and clinical practice shifting from ‘one-size-fits-all’ to more targeted treatment decisions and therapies
“Before precision medicine can revolutionize the care delivery model, progress toward more effective and targeted drugs must be improved.”

Frost & Sullivan, “Global Precision Medicine Growth Opportunities, Forecast to 2025”, 2017
Good news: More new approvals are targeted therapies and meet needs of more specific patient populations

- FDA approvals in personalized medicines: 21% in 2014, 34% in 2017
- FDA approvals of novel mechanisms of action: 6 in 2007, 15 in 2017
- FDA approvals of rare or orphan drugs: 5 in 2007, 18 in 2017

The move away from the one-size-fits-all approach to precision medicine translates into medicines that target specific disease pathways to meet the needs of specific patient populations

Source: FDA
Challenge: New treatments are driving increased complexity in clinical development

Over a 10 year period, the number of distinct procedures in clinical trials has increased up to ~60%.

Effort for sites to administer required study procedures has increased up to 82%.

+$1B increase in cost to bring an asset to market vs 2013.

Up to 10 years to develop a new drug.

80% of time associated with drug development is in clinical trials.

Source: Therapeutic Innovation & Regulatory Science, Tufts Center for the Study of Drug Development.
Improving trials by increasing predictability and reducing friction

Applying domain expertise, data, technology and analytics yielding promising results

- **TRIAL DESIGN**
  - Strategic protocol assessment with real-world insights to reduce amendments

- **SITE SELECTION**
  - Predict the best-performing sites for your study

- **RECRUITMENT**
  - Empower CRAs with site-level enrollment forecasts based in real-world treatment dynamics

- **TRIAL EXECUTION**
  - Increase patient safety through early signal detection
  - Automate workflows based on end-to-end risk detection

Example actions by trial stage
Analytics drive better trials from the start

*Internal analysis: 68% included procedures or design features that increased patient burden*

- **Barriers to patient recruitment and retention**: Identified in study procedures and visit schedule
- **Design Consistency**: Audit for internal consistency to ensure that each objective has a matching endpoint with associated measurements
- **Extraneous and costly non-core procedures**: Identified and considered across study duration and compared to standard of care
- **Inclusion / exclusion criteria impact**: on potential patient volume and screen failure
- **Competitive intelligence**: on design and strategies for similar trials

**Patient & Site Burden**

**Study Procedures**

**Competitors**

**Eligibility Criteria**
Case Example: Insight to clinical practice reveals trial procedures that add additional cost and burden

Goal: Apply claims and EMR data to quantitatively assess and attempt to lower burden and trial cost

Is there a possibility to decrease the frequency or remove procedures, reducing cost and site/patient burden?

Example:

MRI should be familiar to many PD patients, but not at the protocol required frequency (US claims data)

- In a 5 year period, 49% of Parkinson's Disease patients may have had an MRI

- 51% Familiarity with procedure

- Occurrence in 5 year period

  - ≥1 MRI: 49%
  - No MRI: 51%

- Frequency in 60 week period

  - ≥1: 30%
  - ≥2: 21%
  - ≥3: 10%

However, the frequency within a 60 week period is not as high - Compare to protocol requirement of 3 during the treatment period and follow-up

Enabled by IQVIA E360 tool and datasets
Site Selection: How IQVIA is increasing predictability and reducing timelines

Predictive Machine Learning Algorithms

Quantify and Locate Sites with Potential Patients
- RWE Extraction
- Curation
- Validation
- Integration

Investigator Experience Data
- Quality
  - Protocol Deviations
  - Screen Failure Rate, SAEs & AEs
  - Overdue Actions
  - Query Rate
- Participation
  - Prior Trial Experience & Attributes
  - Practice Attributes
- Performance
  - Prior Trial Experience
  - Enrollment Measures

Action Ready Investigator and Site List

60% FEWER non-enrolling sites
30% FASTER average recruitment rate
Case Example: Finding the right sites with right patients speeds up clinical development

Traditional approach vs. New approach:
- **Site ID Completion Time (Days):**
  - Traditional: 112 days
  - New: 62 days
  - **45% faster**
- **Enrollment (Patients / Site / Month):**
  - Traditional: 0.58 p/s/m
  - New: 0.79 p/s/m
  - **36% faster**

Note: Case study for illustration purposes. Results may vary.
Engaging patients throughout the trial journey - and beyond

Patient Communities & Advocacy Networks

Longitudinal Insights & Personas

Deep Insights & Analytics
ML/AI Tools & Bots

eConsent & Health Records
Statistical monitoring: Better, faster identification of trial data quality and patient safety issues

Implementing machine learning models to identify patient outliers across several attributes

10,008 Records, running time 37 sec

>85% Accuracy in identification of outliers, with scale expect ~ 95%

88.9% Accuracy to detect the vital signs outliers effectively
Future is bright – Substantial runway for continued advances

New Applications for CORE in Development

Therapeutically Fit-for-Purpose Solutions

In Silico Trials
Cell & Gene Therapy, Oncology
AI/ML Site Solutions
Direct to Patient Solutions

Enable Faster, More Predictable Research and Development in the Era of Precision Medicine
Please feel free to contact us for more information

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