Emerging Value of the CorrectChemo® Apoptosis Assay in Oncology Care

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Staff Physician, City of Hope
Professor of Clinical Medicine, U Southern California Keck School of Medicine
Chairman of the Board, Medical Oncology Association of Southern California
Past President, Association of Community Cancer Centers
Past President, American Cancer Society California Division
Past Director, American Society of Clinical Oncology

DiaTech Oncology, LLC
Developer of CorrectChemo Assay®

• DiaTech Oncology, LLC is a privately held International Life Sciences company based in Franklin, Tennessee with laboratories located in the United States and Canada.

• DiaTech Oncology is an esoteric clinical pathology laboratory business whose primary focus involves the CorrectChemo technology which studies an individual’s live cancer cells to determine the most effective chemotherapeutic drug or combination of drugs to use in the course of treatment.

• DiaTech has exclusive and perpetual licensing rights for this technology, originally developed by scientists at Vanderbilt University. The company has filed five additional worldwide patents on improvements to the technology with an additional two patents that are in the final stages of review.
Treatment Regimens are Not Precise

Biomarker Technology / targeted therapies:
- lacks 100% response rates
- Many associated with only incremental improvement over chemotherapy
- Only a small number of tumor biomarkers have proven therapies

Result: For most cancers, non-targeted agents comprise the vast majority of recommended therapies.

“A large group practice instituted a pathways program ... we thought we had great savings ... when we did the multi-variant analysis, there was no cost-saving difference.”

“I am starting to wonder if we’re measuring the wrong thing as a payer. Instead of measuring physicians, perhaps we should be measuring chemotherapy.”

Lee Newcomer MD MHA  Senior VP Oncology, UHC  Presentation to ASCO Dec 2013

What is Needed

1. Chemo-responsive testing
2. Rapid results
3. Predictable, proactive method of:
   - Testing tumor / blood cells
   - Against a wide variety of chemotherapy agents

Result: the ability to predict the actual outcome in a specific patient and is accepted by oncologists.

“With the price of many cancer regimens reaching $10,000 a month, doctors need to communicate the medical implications of their care and, increasingly, the cost so patients can make the best decisions....”

“Cancer is one of the primary reasons families go bankrupt today. Often families are mortgaging their houses to pay for these expensive drugs.”

Dr. Gary Lyman, Fred Hutchinson Cancer Research Center, 4/17/14 @ ASCO Task Force
How does the CorrectChemo® Assay work?

A live tissue test that measures the morphologic changes of apoptosis.

Directly “counts” tumor cells killed of drug-induced apoptosis.

Measures tumor cells’ reaction to a chemotherapeutic agent

During a 48-hour period of cell-drug interaction, tumor cells are assessed for apoptosis 576 times (every five minutes). Whenever apoptosis occurs in the culture, it will be detected.

What is the CorrectChemo® Assay?

Also known as the Microculture Kinetic (MiCK) Assay®

Reveals which chemotherapeutic agent(s) will kill the cancer cells of a specific, individual patient

The only technology in the market that can measure apoptotic cancer cell death & predict chemotherapy treatment outcomes

Used successfully in over 50 different tumor types

Physician receives patient report within 72 hours of specimen receipt
Functional Response in Live Cells Encapsulates Pathway Biology

Protein Function
- Signaling
- Growth Differentiation
- Apoptosis

Proteins
- Proteomics
- Biomarkers

RNA
- mRNA
- siRNA

DNA
- Sequencing

Mutations

CorrectChemo
- Growth Factors
- Cytokines
- Chemotherapeutic Agent

Clinical: 60-year-old male with a diagnosis of lung adenocarcinoma since 10/2012, this is the first presentation, no previous chemotherapy

Recommendation: Based on the results of the MiCK® Assay, Cisplatin in combination with Docetaxel is the recommended chemotherapy regimen for the patient. Alimta with Paclitaxel is a reasonable alternative. (Note: Alimta alone is inactive, Alimta + Cisplatin is less active than Cisplatin alone. Alimta + Paclitaxel is more active than Paclitaxel alone.)
**Evidence for Clinical Utility of CorrectChemo**

- 17 published studies confirming MICK® assay measurement and validation
- Patient outcome studies peer reviewed by national journals and included multiple cancers, physician blinded, multi-institutional, prospective designs
  - 10 published studies in 471 patients confirming MICK® patient outcome results and cost savings
  - Study design oversight by UnitedHealthcare and HealthCore (WellPoint)
  - Patient outcome data statistically validated by independent research firm
- Longer survival is highly statistically significant when therapy based on MICK® is used
  - Multivariate analyses shows the MICK® assay is the most important element in longer survival
CorrectChemo Results

- **Ovarian study-** 68% increased survival
  - If CorrectChemo used survival increased to over 45 months
  - If CorrectChemo not used survival was 25 months
  - 80% CorrectChemo patients alive after 3.5 years
- **Acute Myeloid Leukemia study-** 257% increased overall Survival
  - If CorrectChemo used survival increased to 16.1 months
  - If CorrectChemo not used survival was 4.5 months
- **Breast study-** 236% increase in time to progression, 28% increase in survival
  - If CorrectChemo used time to progression increased to 7.4 months
  - If CorrectChemo not used time to progression was 2.2 months
- **All cancers-** 147% increase in overall survival
  - If CorrectChemo used survival increased to 10.1 months
  - If CorrectChemo not used survival was 4.1 months
Do Physicians Use CorrectChemo

Observational nonrandomized, multi-institutional prospective trial was conducted to determine how often physicians would use the results of the CorrectChemo assay when the physicians knew the results of the assay before planning and initiating chemotherapy:

- Oncologist used assay results 64% of the time.
- Original treatment plan changed 64% of the time based on assay results.
- Drug choice changed from proprietary to generic 38% of the time.


CorrectChemo Impact on Costs

“The treatment outcome for cancer patients could be significantly improved if oncologists could identify agents that are most effective against tumor cells of a specific patient in the first line of therapy and the cost savings impact could be dramatic.”

Frank Prendergast, M.D, Ph.D., Director of the Center for Individualized Medicine at Mayo Clinic

Reduces Total Costs & Co-Pays

- Increased use of Generics
- Single drugs in place of combinations
- Reduce administration costs and need for supportive drugs
- Reduce hospitalization, imaging, palliative drugs, consultative care
- Facilitate better informed decisions for hospice
Large Self Insured Employer Cost Savings Analysis

The Value of Personalized Treatment Planning: Cost Savings by the Microculture Kinetic (CorrectChemo ®) chemosensitivity assay, Evidence from a Large American Self-insured Company J Clin Oncol 27, 2009 (suppl; abstr e17541) ASCO

- 49,000 employees over 3.5 years
- Claims data for 196 cancer patients
- Total chemotherapy costs were $5,647,165
- 55 Patients Received Chemotherapy
- Savings Averaged 55%
- Savings from the 1st Patient paid for cost of over 150 patients
- Published June 2009 Journal of Clinical Oncology

(Only Chemotherapy Costs Were Evaluated - Total Savings Would Be Greater)

Cost Savings Based on Different Assumptions of Physician Drug Usage from CorrectChemo ® Assay

<table>
<thead>
<tr>
<th>Drugs Used</th>
<th>Duration of Chemotherapy</th>
<th>Average Total Cost Savings (Chemo + Admin + Support)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Single Best Drug</td>
<td>Time Drug Was Given</td>
<td>85%</td>
</tr>
<tr>
<td>Single Best Drug</td>
<td>100% of Time</td>
<td>26%</td>
</tr>
<tr>
<td>Single Best Drug</td>
<td>50% of Time with 50% as Holiday in Remission</td>
<td>63%</td>
</tr>
<tr>
<td>Single Best Drug + Biotherapy</td>
<td>50% of Time with 50% as Holiday in Remission</td>
<td>49%</td>
</tr>
</tbody>
</table>
Generic – Proprietary Substitution
Savings In Medicare Allowable Payment

<table>
<thead>
<tr>
<th>Disease</th>
<th>Cost Difference MSD vs SSD Per Patient</th>
<th>Fraction of Patients on MSD</th>
<th>Estimated Savings Per Patient</th>
<th>Net Savings Per Patient</th>
<th>Percent Savings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast CA</td>
<td>$13,593</td>
<td>98%</td>
<td>$13,321</td>
<td>$8,321</td>
<td>42.8%</td>
</tr>
<tr>
<td>Colon CA</td>
<td>$35,668</td>
<td>71%</td>
<td>$25,338</td>
<td>$20,338</td>
<td>54.0%</td>
</tr>
<tr>
<td>Lung CA NSCLC</td>
<td>$15,774</td>
<td>94%</td>
<td>$14,827</td>
<td>$9,827</td>
<td>47.0%</td>
</tr>
</tbody>
</table>

Data on chemo-sensitivity drawn from the DiaTech database on patients with recurrent breast cancer, colon cancer, and non-small cell lung cancer. Costs of chemotherapy based on current Medicare allowable payments for drugs and include only the costs of the drugs. Costs based on 6 cycles of chemotherapy. Estimated Savings formula: (SSD costs – MSD costs) * percent time MSD superior – costs of assay. Costs of supportive care drugs, chemo administration, subsequent hospital, not incorporated into estimates.

SAVINGS WITH THE CORRECT CHEMO ASSAY BY DISEASE RECENT IPA DATA ASSESSMENT

<table>
<thead>
<tr>
<th>DISEASE</th>
<th>% PATIENTS</th>
<th>% COST</th>
<th>SAVINGS % OF COST PER DISEASE</th>
</tr>
</thead>
<tbody>
<tr>
<td>LYMPHOMA</td>
<td>17</td>
<td>33.1</td>
<td>13.5%</td>
</tr>
<tr>
<td>COLORECTAL</td>
<td>15</td>
<td>20.0</td>
<td>46.5%</td>
</tr>
<tr>
<td>LUNG</td>
<td>19</td>
<td>15.0</td>
<td>42.8%</td>
</tr>
<tr>
<td>BREAST</td>
<td>18</td>
<td>12.9</td>
<td>13.9%</td>
</tr>
<tr>
<td>LEUKEMIA</td>
<td>4</td>
<td>11.1</td>
<td>19.2%</td>
</tr>
<tr>
<td>OTHER</td>
<td>26</td>
<td>6.3</td>
<td>11.0%</td>
</tr>
<tr>
<td>TOTAL</td>
<td>100</td>
<td>25.0%</td>
<td></td>
</tr>
</tbody>
</table>
IMPACT OF CORRECTCHEMO ASSAY ON VALUE OF CANCER CHEMOTHERAPY

- META-ANALYSIS SHOWS SURVIVAL INCREASED 1.85X
- META-ANALYSIS SHOWS TTP INCREASED 2.0X
  - OUTCOMES INCREASED BY 1.93X
- COSTS OF CHEMO REDUCED BY 48%
  - NET COST OF CHEMO IS 0.52X
- VALUE = OUTCOMES/COST
  - VALUE INCREASE = 1.93/0.52 = 3.7X
  - USE OF CORRECTCHEMO INCREASES VALUE 3.7-FOLD

CorrectChemo® Assay Summary – Health Care Value

- Assay is easily understood by patients which drives utilization
- Personalized treatment – individual patient - precision medicine
- Significant cost savings - most effective on early presentation
- Mediate physician selection of proprietary vs generic drugs
- Leadership position in cancer care with patient centered focus
- Higher patient confidence in health plan treatment decision-making
- Clinical validation has been consistent across tumor histologies
- Clinical utility is high and learning curve is brief for clinical use
- Patient outcome correlations are robust
  .... response, time to progression, overall survival all significant
Q and A

EVERYONE AGREES TO HELP REDUCE HEALTH CARE COSTS!

I CAN'T AFFORD THAT DIAGNOSIS. DO YOU HAVE A CHEAPER ONE?

Appendix
DiaTech Medical Team

**Cary Presant, M.D., F.A.C.P.**, Chief Medical Officer

Dr. Presant has served as director of cancer programs at Washington University School of Medicine, the Jewish Hospital of St. Louis and the City of Hope National Medical Center in Los Angeles, California. He is currently Professor of Clinical Medicine at the University of Southern California School of Medicine, and is the Chairman of the Los Angeles Cancer Institute, St. Vincent Medical Center.

**Allan E. Hallquist, M.D., Medical Director**

Dr. Hallquist is Board Certified by the National Board of Medical Examiners, the American Board of Pathology and the Anatomic and Clinical Pathology. During his career, he has served as the President of the Cincinnati Society of Pathologists, and as President of the Northern Kentucky Medical Society. Dr. Hallquist directs all research and testing activity at the DiaTech Oncology Laboratory.

**Douglas Kingma, M.D. Director Molecular Pathology** - Dr. Kingma is Board certified in anatomic pathology, hematopathology, and molecular genetic pathology. He has served as a Medical Director and Chief Medical Officer of various companies and spent 13 years at the National Cancer Institute. Dr. Kingma has authored over 70 scientific studies published in peer reviewed journals, and has presented on numerous cancer research topics at major medical conferences around the world.

**Frank Prendergast, M.D, Ph.D., Advisor**

Dr. Prendergast is currently the Director for the Mayo Clinic Center for Individualized Medicine at the Mayo Clinic. Formerly, Dr. Prendergast was the Director of the Mayo Clinic Comprehensive Cancer Center; a Presidential Appointee to the National Cancer Advisory Board; and he was the Chair of Research of the Mayo Foundation. He is on the Board of the Eli Lilly Company; the Infectious Disease Research Institute.

**Roy Herbst, M.D, Ph.D., Advisor**

Dr. Herbst is the Medical Director at Smilow Cancer Hospital at Yale-New Haven and was previously at University of Texas MD Anderson Cancer Center. Dr. Herbst received his medical degree from Cornell University Medical College and earned a Ph.D. in molecular cell biology from Rockefeller University. He completed his medical oncology fellowship at Dana Farber Cancer Institute and Brigham and Women’s Hospital in Boston.

**Marty Fleisher, Ph.D., Advisor**

Dr. Fleisher is the Chairman of the Department of Clinical Laboratories and Chief of the Clinical Chemistry Service at the Memorial Sloan-Kettering Cancer Center in New York City. He has over thirty years experience in discovery and application of new tumor markers and biomarkers for the early detection of cancer.

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CorrectChemo® Assay comparison with Genomic Biomarker Assays

<table>
<thead>
<tr>
<th>CorrectChemo® Assay</th>
<th>Genomic Biomarker Assays</th>
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</thead>
<tbody>
<tr>
<td>Purified viable cells</td>
<td>Fixed tissue mixed cells with selection</td>
</tr>
<tr>
<td>No interval therapy</td>
<td>Usual interval therapy</td>
</tr>
<tr>
<td>No interval drugs changes</td>
<td>Usually has interval drug induced changes</td>
</tr>
<tr>
<td>Measures actual apoptosis</td>
<td>Identifies possible target</td>
</tr>
<tr>
<td>Accounts for salvage pathways</td>
<td>Salvage pathways may not be identified</td>
</tr>
<tr>
<td>Accounts for epigenetic changes</td>
<td>Usually does not identify epigenetic changes</td>
</tr>
<tr>
<td>Not dependent on number of mutations</td>
<td>Integration of mutations per cell not feasible</td>
</tr>
<tr>
<td>Response rates 50-80%</td>
<td>Response rates 5-30% (except bcr/abl)</td>
</tr>
<tr>
<td>Correlates with time to progression &amp; survival</td>
<td>Variable correlation with time to progression &amp; survival</td>
</tr>
<tr>
<td>Fast patient reporting</td>
<td>Single chip quick, whole genome slow</td>
</tr>
<tr>
<td>Cost Range $9200</td>
<td>Cost Range $10000 - $100000</td>
</tr>
</tbody>
</table>

It is the only laboratory test that measures apoptosis directly and can tell a physician which chemotherapy agent will kill a patient’s cancer cells.
Discovery and Preclinical Development

The CorrectChemo® assay can be an effective tool for complementing other platform technologies

- Screening compound libraries for functional profiling for target selection and validation
- Confirmation of drug mechanism via programmed cell death
- Identification of the range of cancer types where a compound may have effect
  - Assay on xenografts of various tumor types
  - Assay on primary human tumor cells
- Comparison of potency and selectivity with multiple drug and drug combinations
- Correlation of CorrectChemo Assay with gene sequencing results
- Validation of Biomarker impact for targeting diseases

Clinical Development

CorrectChemo® assay can provide key information at critical decision points

- Patient selection: For trials of new chemotherapeutic agents or targeted compounds linked with drugs, or used in combination with adjuvant chemotherapy, the assay can identify patients for which the chemotherapeutic agent will be most effective.
- Companion diagnostic development: for potential new chemotherapeutics, or targeted agents intended to be administered with adjuvant chemotherapy, the assay can used as a companion diagnostic for patient selection post approval.
- Indication selection: By identifying apoptotic activity of compounds in tumor types not currently indicated, assay data can enable additional indication selection of candidate compounds as well data for line extension for currently approved therapeutics.
How do Doctors choose chemotherapy?

Although doctors use the latest chemotherapy research to select the best treatment protocols for their patients … it is impossible to predict the outcome of therapy for any individual.

The Scott Hamilton CARES Initiative chemocare.com Feb 2013

On Average ….. A cancer patient has about a 20-25% chance of getting the right chemo the first time

“To me it’s a little troubling that so many drugs are given in areas where there is not a lot of data to back it up,” said Dr. Nancy Keating, a cancer researcher from Harvard Medical School and Brigham Women’s Hospital

Cancer Chemotherapy NEW YORK (Reuters Health) Feb 2013

Cancer Drug Costs - Challenging - Unsustainable

“Look at the complexity of trying to manage cancer drug spending. We have more than 100 diseases included within cancer. We have over 200 drugs .... approximately 30% of these drugs are used off label .... 75% of drug spending still falls under the medical benefit. Oncology is about 50% of that drug spending.”

“This will become more challenging, as 25 new oncology drugs have been approved in just the past 2 years, and more than 300 oncology compounds are in development”

Kirby J. Eng, Director of Oncology Medical Pharmacy, CVS Caremark
Third Annual Conference of the Association for Value-Based Cancer Care
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