FDA Companion Diagnostic Testing and Implications for Pharmacy and Medical Directors

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The Myriad Pharmacotherapy Outcomes Research Partnership
AGENDA

• Influence of biomarkers on clinical outcomes and treatment decisions
• AMCP member survey results on management of companion and complementary diagnostics
• Differences between diagnostic tests
• Payer considerations for diagnostic test reimbursement and access decisions
• Audience Q/A

NOVA Trial

Phase 3 NOVA Trial
High-Grade Serous Ovarian Cancer, Platinum Sensitive, Relapsed

Response to Last Platinum Treatment
N=553

Germline BRCA positive
n=203

Germline BRCA negative
n=350

2:1 Randomization

Niraparib 300mg

Placebo

Endpoint Assessment

Primary Endpoint PFS

Maintenance Therapy

Defined as:
• Complete response OR
• Partial response with residual disease <2 cm and CA-125 values either within the normal range, or a CA-125 decrease of >90% that was stable for ≥7 days

Niraparib 300mg Placebo Placebo

Endpoint Assessment

Primary Endpoint PFS

Maintenance Therapy


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NOVA Trial Results

<table>
<thead>
<tr>
<th>NOVA Companion Diagnostic</th>
<th>Prolonged PFS Benefit (Niraparib vs. Placebo)</th>
<th>Hazard Ratio (95% CI)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Germline BRCA Positive</td>
<td>15.5 months (21.0 vs. 5.5 months)</td>
<td>0.27 (0.17-0.41)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Germline BRCA Negative</td>
<td>9.1 months (12.9 vs. 3.8 months)</td>
<td>0.38 (0.24-0.59)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>myChoice HRD positive</td>
<td>3.1 months (6.9 vs. 3.8 months)</td>
<td>0.58 (0.36-0.92)</td>
<td>0.02</td>
</tr>
<tr>
<td>myChoice HRD negative</td>
<td></td>
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</tbody>
</table>


OlympiAD Trial Design

- Includes ER/PR+ and TNBC
- Metastatic Her2- Breast Cancer
- 1-2 prior lines of chemotherapy for adjuvant or metastatic disease
- Germline BRCA1/2 mutation (n=302)
- Identified with Myriad’s BRACAnalysis CDx
- Olaparib
- MD Choice Chemotherapy (Capecitabine, Vinorelbine, Eribulin)
- Primary Endpoint PFS
OlympiAD Trial Results - PFS


Summary of Trials

• NOVA data (Ovary): allcomers, no biomarker
• OlympiAD data (Breast): BRACAnalysis CDx (Companion Diagnostic)
• Breast vs Ovary
  • Differences in FDA biomarker labeling
  • Financial implications
Biomarkers: Gateway or Gatekeeper?

AMCP Survey Description Statistics

Data was collected by AMCP

Survey sent to 3,477 AMCP Members

1,090 opened

14% Response Rate
AMCP Survey Results

Does your plan provide coverage for BRCA testing now?

- Majority of respondents cover BRCA testing

What best describes management of requests for BRCA testing?

- Access is primarily managed through prior authorization

What best describes management of requests for access to PARPi?

- Majority of respondents require evidence of BRCA testing for access to PARPi

How important is it to you today that access to a PARPi (e.g. Olaparib, Lynparza®) requires a BRCA test?

- Although the majority find BRCA testing for PARPi access important, roughly a third of respondents thought BRCA testing was moderately to not important
• Whether the test is FDA approved or not did not influence response very much, with a slight increase in those who felt it was extremely important

• Majority do not treat PARP access differently for ovarian or breast, however a significant portion do, or do not know

• Over 70% of respondents recognize some likelihood that a patient may receive a PARP in the absence of a BRCA test

• Although similar, a few more respondents thought even more likely that patients may not receive the FDA approved test
Roughly 40% are considering a policy for an FDA approved BRCA test, and 25% of that group responded that the FDA approved test is preferred.

AMCP Survey Results Summary

- Majority of respondents cover BRCA testing and access is primarily managed through prior authorization.
- Majority found BRCA testing for PARPi access important and require evidence of BRCA testing for access to PARPi.
- Roughly half treat access to PARPi the same for ovarian and MBC; others treat differently or do not know.
- However, the majority of respondents stated that it is likely that patients would receive a PARPi in the absence of a BRCA test, which is a concern for both payers and patients.
- Opportunity exists to align BRCA testing to PARPi access.
"A bad tumor biomarker test is as bad as a bad drug."

Daniel F. Hayes, MD, FACP, FASCO
2017 ASCO Presidential Address

Why does it matter which diagnostic I cover?
FDA vs. CLIA Approval

The Clinical Laboratory Improvement Amendments (CLIA) program regulates laboratories to ensure **accurate and reliable** test results when laboratories perform testing on patient specimens.

The FDA regulates manufacturers and devices under the Federal Food, Drug, and Cosmetic Act (FFDCA) to ensure that devices, including those intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, are reasonably **safe and effective**. Analytic and Clinical validity

https://search.cms.gov/search?utf8=%C3%A2%C5%93%E2%80%9C&affiliate=cms-new&dc=&query=ldt+and+clia+lab+faq&commit=Search
Why does it matter which diagnostic I cover?
Companion vs: Complementary Diagnostic

A *companion* diagnostic is an *in vitro* diagnostic that is required for the **safe and effective** use of a corresponding therapeutic product.

A *complementary* diagnostic is an *in vitro* diagnostic that identifies a biomarker-defined subset of patients that respond particularly well to a drug and aids **risk/benefit assessments** for individual patients, but that is not a prerequisite for receiving the therapeutic product. (Draft FDA Definition)

The Promise of Companion Diagnostics: Payer Perspective

- Pay for drug only in patients who are likely to respond
- Avoid outcomes and costs of side effects from treatment that would not benefit patient
Companion vs. Complementary Dx Test
Use in Metastatic NSCLC

**Figure 2**: Impact of companion and complementary diagnostic status on (a) use of diagnostic test and (b) use of drug in advanced NSCLC. Data from Flatiron Health database 31 July 2016.


Fast Forward to 2017
Drug Utilization in Front-line NSCLC

Indicators of Economic Value

- Incremental cost per diagnosis
- Treatment modification
- Events avoided
- Life-years saved
- Quality-adjusted life-years gained
- Drug costs in one patient with no response, can cover diagnostic testing in 75 patients

Robust data are needed to demonstrate the added value diagnostic testing brings

What are Payers Looking for?

1. Technology must have final approval from the appropriate governmental regulatory bodies

2. Scientific evidence must permit conclusions concerning the effect of the technology on health outcomes

The Pharmacy vs. Medical Benefit Challenge

- Oral Oncology agents
- Oncology support agents
- Patient self-diagnostics
- Home infusion agents
- Genetic testing
- Companion Diagnostics
- Complex infusions
- Agents with REM program
- Requirement and physician oversight


The Pharmacy vs. Medical Benefit for Companion Diagnostics

- Scenarios for CDx associated drug products
  - Ideally drug is covered by pharmacy, therefore the companion diagnostic is covered to assure drug used ONLY in those who will benefit
  - CDx has been reviewed and approved by medical but drug has not yet been reviewed by pharmacy; leads to no access to drug despite coverage for the test
  - Drug has been reviewed by formulary committee however medical benefit has not yet reviewed the test. Often pharmacy benefit will not cover without the test
  - Non coordinated copayments between test and drug can lead to above scenarios despite coverage

Coverage and access to both CDx and drug needs to be coordinated across the medical and pharmacy benefits for a health plan
The Pharmacy vs. Medical Benefit Challenges

• When health plan has authority over both medical and pharmacy benefit integration is seen most often
• Employer with different suppliers of medical and pharmacy benefits do not see efficiency in coverage and access
• Where there is coordination between manufacturer of drug and CDx reimbursement negotiations can happen in tandem
• When drug and CDx manufacturers negotiate independently health plans have less negotiating power and employers and patients pay higher premiums

Summarized Points

• Companion diagnostics clearly indicate patients who will benefit from therapy vs. those who will not
• However even in these cases PA policies intended to manage access to only those tested is uncertain
• Complementary diagnostics have less clarity in defining true benefit, and therefore managing access through a PA may prove even more difficult
• Integrating coverage across the medical and pharmacy benefit can improve patient access to the right drug
• Simultaneous negotiation between the diagnostic and drug manufacturers can increase efficiency in access and reimbursement through lower pricing and outcomes based contracting
Q&A

Please send us your questions through the chat box in the upper right corner of your screen

Thank you