FDA Companion Diagnostic Testing and Implications for Pharmacy and Medical Directors

Diana Brixner, PhD, RPh, FAMCP
Professor, University of Utah Health Sciences
Executive Director, Pharmacotherapy Outcomes Research Center
Immediate Past-President, Academy of Managed Care Pharmacy

Johnathan Lancaster, MD, PhD
Chief Medical Officer, Myriad Genetics Inc.

The Myriad Pharmacotherapy Outcomes Research Partnership

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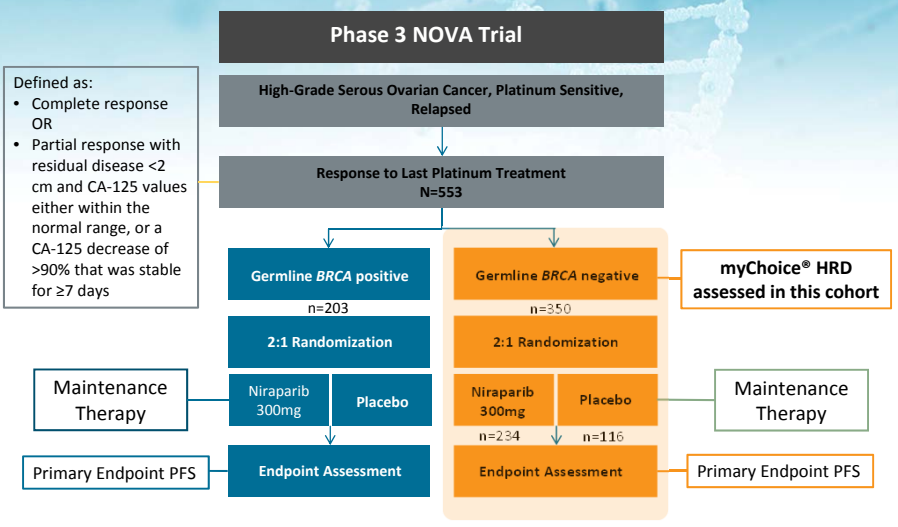
AGENDA

- 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



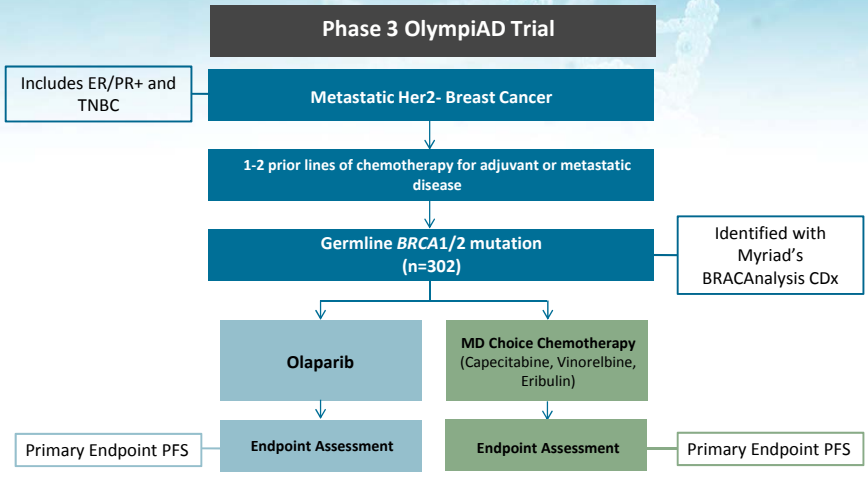
Mirza et al. N Engl J Med. (2016). 375:2154-2164

NOVA Trial Results

NOVA	Companion Diagnostic	Prolonged PFS Benefit (Niraparib vs. Placebo)	Hazard Ratio (95% CI)	P-Value
Germline *BRCA* Positive	BRACAnalysis CDx® positive (n=203)	15.5 months (21.0 vs. 5.5 months)	0.27 (0.17-0.41)	<0.001
Germline *BRCA* Negative	myChoice HRD positive (n=162)	9.1 months (12.9 vs. 3.8 months)	0.38 (0.24-0.59)	<0.001
	myChoice HRD negative (n=134)	3.1 months (6.9 vs. 3.8 months)	0.58 (0.36-0.92)	0.02

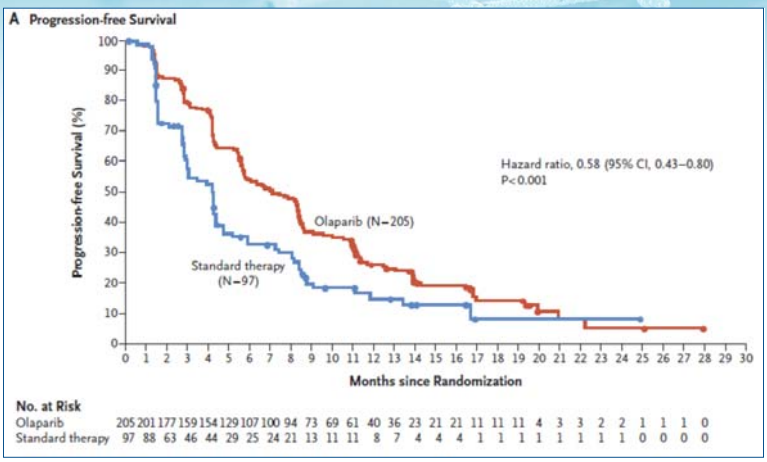
Mirza et al. N Engl J Med. (2016). 375:2154-2164

OlympiAD Trial Design



Robson et al. Olaparib for Metastatic Breast Cancer in Patients with a Germline BRCA Mutation. N Engl J Med (2017). 10.1056/NEJMoa1706450

OlympiAD Trial Results - PFS

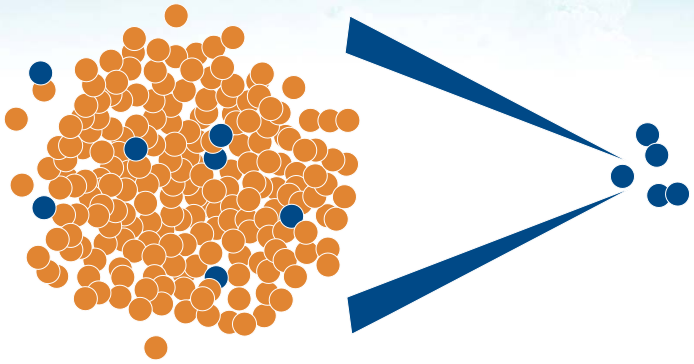


Robson et al. Olaparib for Metastatic Breast Cancer in Patients with a Germline BRCA Mutation. N Engl J Med (2017). 10.1056/NEJMoa1706450

Summary of Trials

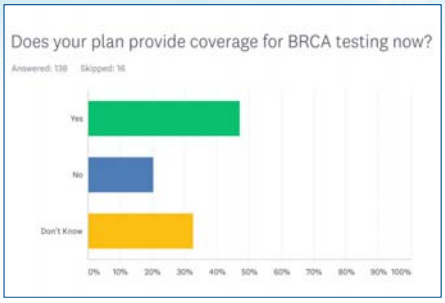
- NOVA data (Ovary): allcomers, no biomarker
- OlympiAD data (Breast): BRACAnalysis CDx (Companion Diagnostic)
- Breast vs Ovary
  - Differences in FDA biomarker labeling
  - Financial implications

Biomarkers: Gateway or Gatekeeper?

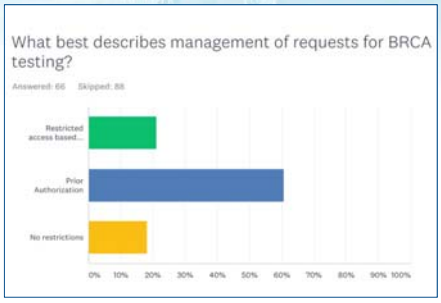


AMCP Survey Description Statistics

AMCP Survey Results

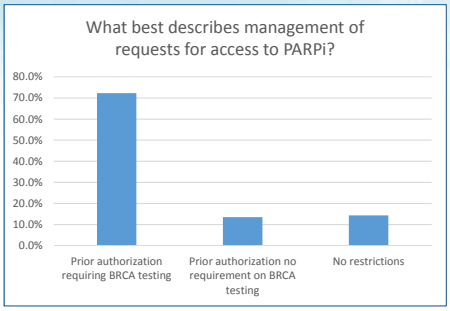


- Majority of respondents **cover *BRCA* testing**

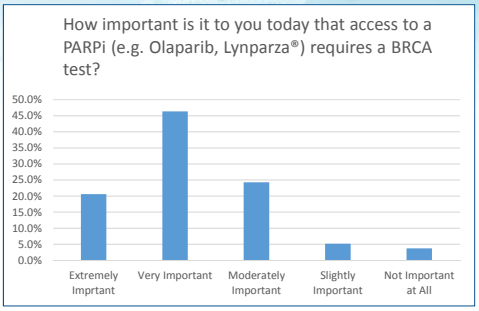


- Access is primarily managed through **prior authorization**

AMCP Survey Results

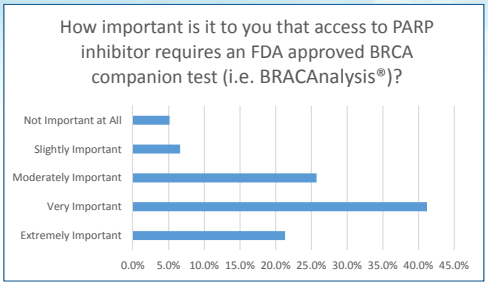


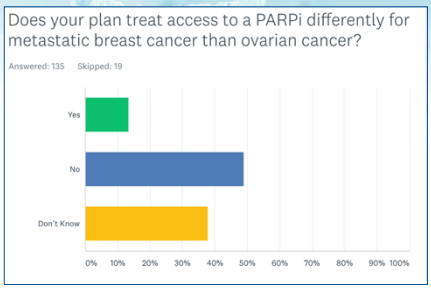
- Majority of respondents **require evidence of *BRCA* testing** for access to PARPi



- Although the majority find *BRCA* testing for PARPi access important, roughly a third of **respondents thought *BRCA* testing was moderately to not important**

AMCP Survey Results





- Whether the test is **FDA approved or not did not influence response very much**, with a slight increase in those who felt is was extremely important
- Majority **do not treat PARPi access differently for ovarian or breast**, however a significant portion do, or do not know

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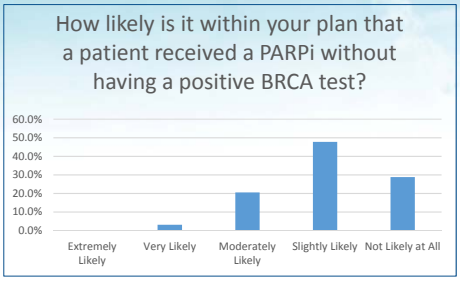
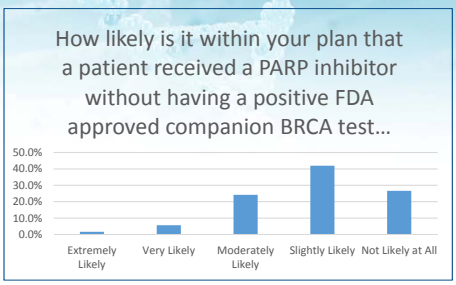
AMCP Survey Results

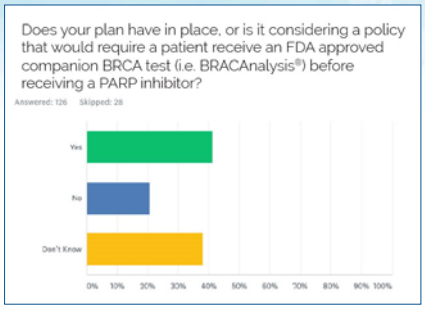


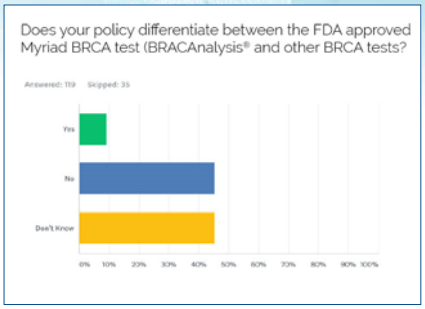


- Over 70% of respondents recognize some likelihood that **a patient may receive a PARPi in the absence of a *BRCA* test**
- Although similar, a few more respondents thought even more likely that **patients may not receive the FDA approved test**

University of Utah Health, 2018

AMCP Survey Results





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

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Companion vs. Complementary Dx Test Use in Metastatic NSCLC

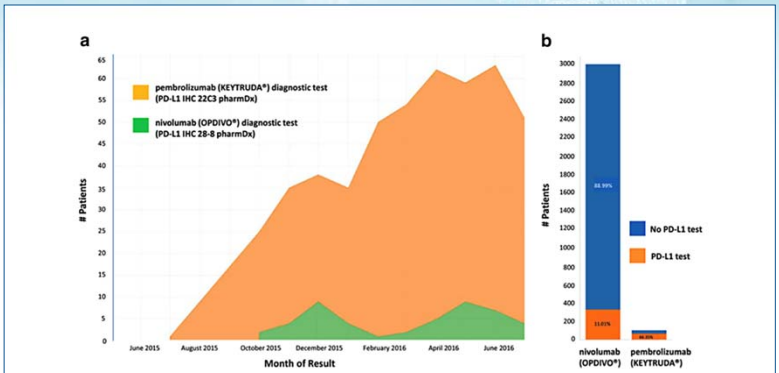
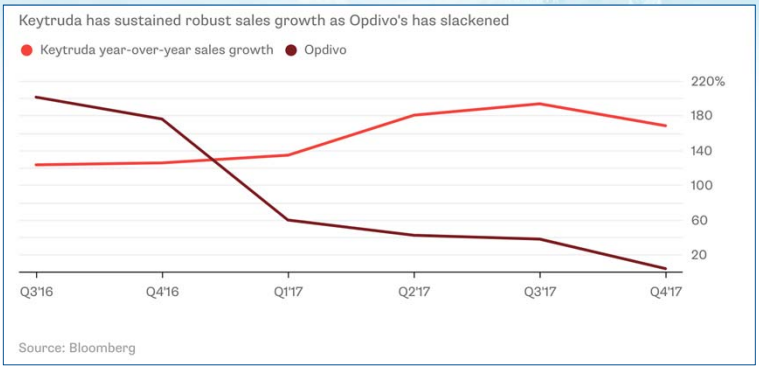


Figure 2 Impact of companion and complementary diagnostic status on (**a**) use of diagnostic test and (**b**) use of drug in advanced NSCLC. Data from Flatiron Health database 31 July 2016.

https://ascpt.onlinelibrary.wiley.com/doi/pdf/10.1111/cts.12455

Fast Forward to 2017 Drug Utilization in Front-line NSCLC



https://www.bloomberg.com/gadfly/articles/2018-04-16/lung-cancer-drug-trial-data-keytruda-tops-opdivo-again

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

DDA_CompanionDiagnostics_WhitePaper_6-16-15.pdf

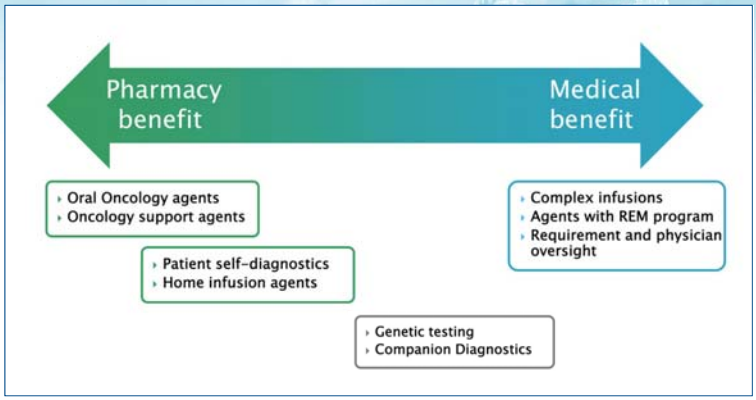
What are Payers Looking for?

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

https://www.bcbsnd.com/documents/10476/35335/Technology+Assessment+Evaluation+Criteria/eb7a3305-9a36-47df-8fba-dd366a97672c

The Pharmacy vs. Medical Benefit Challenge



https://aishealth.com/sites/all/files/file_downloads/c2p38f_111312.pdf

The Pharmacy vs. Medical Benefit for Companion Diagnostics

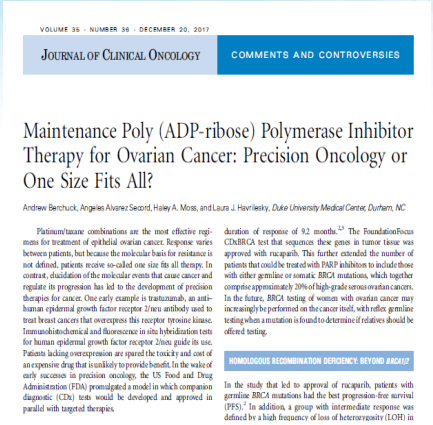
- **Scenarios for CDx associated drug products**
  - Ideally drug is covered by pharmacy, therefore the **companion diagnostic is covered to assure drug used ONLY in those who will benefit**
  - CDx has been reviewed and approved by medical but drug has not yet been reviewed by pharmacy; **leads to no 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



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JOURNAL OF CLINICAL ONCOLOGY | COMMENTS AND CONTROVERSIES

Maintenance Poly (ADP-ribose) Polymerase Inhibitor Therapy for Ovarian Cancer: Precision Oncology or One Size Fits All?

Andrew Berchuck, Angeles Alvarez Secord, Haley A. Moss, and Laura J. Havrilesky, *Duke University Medical Center, Durham, NC*

Platinum/taxane combinations are the most effective regimens for treatment of epithelial ovarian cancer. Response varies between patients, but because the molecular basis for resistance is not defined, patients receive so-called one size fits all therapy. In contrast, elucidation of the molecular events that cause cancer and regulate its progression has led to the development of precision therapies for cancer. One early example is trastuzumab, an anti-human epidermal growth factor receptor 2/neu antibody used to treat breast cancers that overexpress this receptor tyrosine kinase. Immunohistochemical and fluorescence in situ hybridization tests for human epidermal growth factor receptor 2/neu guide its use. Patients lacking overexpression are spared the toxicity and cost of an expensive drug that is unlikely to provide benefit. In the wake of early successes in precision oncology, the US Food and Drug Administration (FDA) promulgated a model in which companion diagnostic (CDx) tests would be developed and approved in parallel with targeted therapies.

duration of response of 9.2 months.[32] The FoundationFocus CDxBRCA test that sequences these genes in tumor tissue was approved with rucaparib. This further extended the number of patients that could be treated with PARP inhibitors to include those with either germline or somatic *BRCA* mutations, which together comprise approximately 20% of high-grade serous ovarian cancers. In the future, *BRCA* testing of women with ovarian cancer may increasingly be performed on the cancer itself, with reflex germline testing when a mutation is found to determine if relatives should be offered testing.

HOMOLOGOUS RECOMBINATION DEFICIENCY: BEYOND *BRCA1/2*

In the study that led to approval of rucaparib, patients with germline *BRCA* mutations had the best progression-free survival (PFS).[7] In addition, a group with intermediate response was defined by a high frequency of loss of heterozygosity (LOH) in

- 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