ASCO Initiatives in Personalized Medicine

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Chief Medical Officer
American Society of Clinical Oncology
Financial Disclosures

• No financial relationships to disclose.
• No discussion of non-approved uses of regulated products.
Outline of Presentation

• ASCO Guidelines
• ASCO University Programs
• ASCO Molecular Tumor Board
• ASCO-NCI-EORTC Workshop on Tumor Marker Development
• Targeted Agent and Profiling Utilization Registry (TAPUR)
• CancerLinQ
ASCO Guidelines

• ASCO guidelines follow CMSS and IOM standards
• Review and approval overseen by Clinical Practice Guideline Committee
• Topic selection is based on criteria such as degree of variation in practice, clinical uncertainty, etc.
• Options for guideline development include:
  – De novo development
    • Systematic review of the health literature to inform recommendations
  – Adaptation
    • Formally assess and adapt recommendations from other high quality guideline developers that use methods similar to ASCO
  – Endorsement
    • Formally assess and endorse guidelines from developers that use methods similar to ASCO
American Society of Clinical Oncology Provisional Clinical Opinion: Testing for KRAS Gene Mutations in Patients With Metastatic Colorectal Carcinoma to Predict Response to Anti–Epidermal Growth Factor Receptor Monoclonal Antibody Therapy


Antonio C. Wolff,* M. Elizabeth H. Hammond,* David G. Hicks,* Mitch Dowsett,* Lisa M. McShane,* Kimberly H. Allison, Donald C. Allred, John M.S. Bartlett, Michael Bilous, Patrick Fitzgibbons, Wedad Hanna, Robert B. Jenkins, Pamela B. Mangu, Soonmyung Paik, Edith A. Perez, Michael F. Press, Patricia A. Spears, Gail H. Vance, Giuseppe Viale, and Daniel F. Hayes*
Coming Soon…

Guidance statements on appropriate molecular work-up of newly diagnosed cancers
Cancer Genetics Program

The Cancer Genetics Program is designed to increase knowledge in the area of hereditary cancer genetics. This slide-based, expert-led course provides a comprehensive collection on an array of topics related to the genetic cancer risk assessment process. The course addresses ways to improve the taking and documenting of family history, as well as interpreting those results. The program is composed of site-specific sections on core concepts that include recognition of hereditary cancer syndromes, quantitative risk assessment, establishing a cancer risk assessment service, and special counseling and ethical, legal, and social issues in cancer genetics.

Just released...

designed to help the busy clinician keep on top of the rapidly developing field of tumor genomics, particularly regarding somatic genomic alterations that drive tumor progression and have implications for clinical research and patient care. The program addresses next-generation sequencing technologies and describes optimal uses with available technology.
Molecular Oncology Tumor Boards

The Molecular Oncology Tumor Boards are a series of monthly user-driven discussions designed to help cancer care providers with the interpretation and understanding of tumor molecular profiling tests and studies. Moderated by an expert pathologist and medical oncologist, each case will be updated with new information over a two week period as user comments are added.

After two weeks, the discussion forum will be locked to further commentary and users will be able to claim CME credit for their participation.

This series is an educational collaboration between the American Society of Clinical Oncology (ASCO), the College of American Pathologists (CAP), and the Association for Molecular Pathology (AMP).

- **April 2015**: TP53 Mutation
- **March 2015**: PIK3CA Mutation
- **February 2015**: ROS1 Rearrangement
- **January 2015**: Extended RAS Mutation

TP53 Mutation: Molecular Oncology Tumor Boards
PIK3CA Mutation: Molecular Oncology Tumor Boards
ROS1 Rearrangement: Molecular Oncology Tumor Boards
Extended RAS Mutation: Molecular Oncology Tumor Boards
TARGETED AGENT AND PROFILING UTILIZATION REGISTRY (TAPUR) STUDY
Problem

• Patient with advanced cancer; no standard Rx options
• Genomic profile test performed
• Potentially actionable variant detected
• How to get the drug?
• How to learn from the treatment?
TAPUR Study Primary Objectives

• To describe the anti-tumor activity and toxicity of commercially available, targeted anti-cancer drugs prescribed for treatment of patients with advanced solid tumors, B cell NHL or MM with a genomic variant known to be a drug target.

• To facilitate patient access to commercially available, targeted anti-cancer drugs of potential efficacy for treatment of patients with an advanced solid tumor, B cell NHL or MM with a genomic variant known to be a drug target.
TAPUR Study Secondary Objectives

- To record the treatment-related adverse events.
- To create a prospective registry of patient outcomes following treatment.
- To create a prospective registry of commercially available tumor genome profiling tests used by clinical oncologists in the usual care setting.
- To determine the concordance of the treatment plan proposed by the treating oncologist with that recommended by the molecular tumor board in applicable situations.
TAPUR Eligibility

- Patients with advanced solid tumors, B cell NHL and multiple myeloma for whom no standard treatment options exist
- Adequate organ function; PS 0-2
- Results available from a genomic test (FISH, PCR, NGS, IHC for HER2) performed in a CLIA certified, CAP accredited lab. Labs located or offering services in NY must also have NY State accreditation.
MD reviews results of genomic test performed in CLIA certified/CAP accredited lab

MD determines if drug match exists in protocol

Patient registered on study

No match, Rx at MD discretion

Data monitoring committee regularly reviews RR of tumor-variant-drug groups

Results released when protocol-specified endpoints met

Matched therapy administered; safety and efficacy outcomes recorded
Data Collection

• Patient demographics to confirm eligibility
• Genomic test performed and results
• Treatment and dose each cycle
• MTB recommendation, if applicable
• Patient’s most recent prior treatment and best response
• Efficacy: ORR, PFS, OS, time on treatment
• Safety: SAEs, Gr 3-5 AEs
Study Endpoints and Analysis

• Primary endpoint: ORR per RECIST
• Other endpoints: PFS, OS, time on treatment, grade 3-5 AEs per CTCAE, SAEs
• Each tumor type-variant-drug is a “group”
• Enroll 8 patients/group. If no responses, stop
• If at least 1 response, enroll additional 16
• 4 or fewer responses/24, no interest
• 5 or more responses/24, further study
• 85% power and an alpha error rate of 7.8%
<table>
<thead>
<tr>
<th>Company</th>
<th>Drug</th>
<th>Target</th>
</tr>
</thead>
<tbody>
<tr>
<td>Genentech</td>
<td>Erlotinib</td>
<td>EGFR</td>
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<tr>
<td></td>
<td>Vemurafenib</td>
<td>BRAF</td>
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<td></td>
<td>Vismodegib</td>
<td>SMO, SHH, PTCH</td>
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<td></td>
<td>Trastuzumab emtansine</td>
<td>ERBB2</td>
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<td>Pfizer</td>
<td>Crizotinib</td>
<td>ALK, ROS1, MET</td>
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<td></td>
<td>Palbociclib</td>
<td>CDK 4/6</td>
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<td></td>
<td>Sunitinib</td>
<td>VEGFR, PDGFR, KIT, FLT3, RET</td>
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<td>Temsirolimus</td>
<td>mTOR</td>
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<td></td>
<td>Axitinib</td>
<td>VEGFR</td>
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<td>Bosutinib</td>
<td>Bcr-abl</td>
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<td>Lilly</td>
<td>Cetuximab</td>
<td>EGFR</td>
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<tr>
<td>Bristol Myers Squibb</td>
<td>Dasatinib</td>
<td>Bcr-abl, SRC, KIT, PDGFR</td>
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<tr>
<td>Astra-Zeneca</td>
<td>Olaparib</td>
<td>BRCA</td>
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Who Benefits?

- **Patients** receive targeted agent matched to tumor genomic profile
- **Physicians** receive interpretation of genomic test results, guidance in treatment recommendations, access to drugs, clinical data on off-label use
- **Pharma** receives data on drug use and outcomes to inform R&D plans and life cycle management
- **Payers** receive data on test and drug use and outcomes to inform future coverage decisions
- **Regulators** receive data on extent and outcomes of off label drug and test use and real world safety data
Breakthroughs in cancer care are rapidly expanding the complexity of disease management …

… creating a huge need for complex information management by doctors, patients, product developers and payers
Lung Cancer - from one cancer to many...

1986

One disease

2015

7 molecular drivers—and more
to be discovered

Every common cancer is a collection of rare cancers!
Data required for medical decision-making relative to human cognitive capacity

Abernethy A P et al. JCO 2010;28:4268-4274

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Clinical trials drive our understanding and treatment of cancer, but only 3% of adult cancer patients enroll in clinical trials …
... and patients we see every day tend to be ...

older...

25% of clinical trial patients are
65+ vs
61% of real-world patients are
65+

less healthy...

40% of kidney cancer patients were not healthy enough to qualify for the trials that supported the approval of their treatments

and more diverse...

90% of patients in NCI trials are white vs
23% of the US POPULATION is non-white

...than clinical trial patients.

“We seek the development of a learning health system in which science, informatics, incentives, and culture are aligned for continuous improvement and innovation – with best practices seamlessly embedded in the delivery process and new knowledge captured as an integral by-product of the delivery experience.”
The Virtuous Cycle of Learning Healthcare

In a learning healthcare system, research influences practice and practice influences research.

**EVALUATE**
Collect data and analyze results to show what works and what doesn’t.

**ADJUST**
Use evidence to influence continual improvement.

**IMPLEMENT**
Apply plan in pilot and control settings.

**DESIGN**
Design care and evaluation based on evidence generated here and elsewhere.

**DISSEMINATE**
Share results to improve care for everyone.

**INTERNAL AND EXTERNAL SCAN**
Identify problems and potentially innovative solutions.
## Improving Quality for Patients, Providers, Researchers

**CancerLinQ** – improving QUALITY of care and enhancing outcomes; additional benefits:

<table>
<thead>
<tr>
<th>Patients</th>
<th>Providers</th>
<th>Research/Public Health</th>
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<tbody>
<tr>
<td>Improved outcomes</td>
<td>Real-time “second opinions”</td>
<td>Mining “big data” for correlations</td>
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<tr>
<td>Clinical trial matching</td>
<td>Observational and guideline-driven clinical decision support</td>
<td>Comparative effectiveness research</td>
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<tr>
<td>Safety monitoring</td>
<td>Real-time access to resources at the point of care</td>
<td>Hypothesis-generating exploration of data</td>
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<tr>
<td>Real-time side effect management</td>
<td>Quality reporting and benchmarking</td>
<td>Identifying early signals for adverse events and effectiveness in “off label” use</td>
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<td>Patient-reported outcomes</td>
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When deployed CancerLinQ will…

1. Analyze medical records to uncover patterns that can improve patient care

2. Provide guidance by identifying the best evidence-based plan of care

3. Provide insights for data exploration and hypothesis generation
CancerLinQ future development

- Assess clinical trial eligibility
- Create longitudinal treatment plan and summary documents
- Develop risk stratification models
- Assess outcomes following off-label prescribing
- Phase IV post-marketing surveillance
- Patient portal/assessment of patient-reported outcomes (PROs)
- Secondary use of reports +/- de-identified data sets for research
CancerLinQ Clinical User Portal
CancerLinQ Quality Performance Indicators

<table>
<thead>
<tr>
<th>Categories</th>
<th>Measures - ALL MEASURES</th>
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<tbody>
<tr>
<td>ALL MEASURES (25)</td>
<td></td>
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<tr>
<td>MY FAVORITES (1)</td>
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<tr>
<td>Breast (2)</td>
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<td>Colorectal (3)</td>
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<td>Core (9)</td>
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<td>End of Life Care (2)</td>
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<td>Gynecology (1)</td>
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<td>Lung (2)</td>
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<td>Non-Hodgkin Lymphoma (2)</td>
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<td>Oral Chemotherapy (1)</td>
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<td>Palliative Care (1)</td>
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<td>Prostate (1)</td>
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<tr>
<td>Symptom and Toxicity Manage</td>
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</table>

- **83%** IV Bisphosphonates or Denosumab Administered
  - 365 days 6 of my patients

- **70%** Tamoxifen or AI Received
  - 365 days 10 of my patients

- **66%** CEA Measured
  - 365 days 9 of my patients

- **80%** Adjuvant Chemotherapy Received
  - 365 days 9 of my patients

- **75%** Colonoscopy
  - 365 days 8 of my patients

- **85%** Pain Assessed, 2 Most Recent Visits
  - 365 days 41 of my patients

- **76%** Pain Quantified, 2 Most Recent Visits
  - 365 days 3 of my patients

- **80%** Staging documented
  - 365 days 30 of my patients

- **67%** Constipation Assessed
  - 365 days 21 of my patients

- **83%** Chemotherapy Intent Documented
  - 365 days 9 of my patients

- **78%** Chemotherapy Consent Signed
  - 365 days 6 of my patients

- **57%** Smoking/Tobacco Use Cessation Counseling
  - 365 days 5 of my patients
CancerLinQ insights (CLQI)
How Will CancerLinQ Transform Clinical Research?

• Hypothesis generation from observational data, e.g., off label use, risk stratification
• Patterns of care and trend analysis
• Cohort identification, frequency of target pop.
• Cohort assembly, location of target pop.
• Eligibility assessment, trial matching
• Registry-driven RCTs
• Comparative effectiveness assessments
• Collection of PROs
Conclusions

• Precision medicine is a key feature of modern cancer care
• ASCO is committed to providing education, training and resources to clinical oncologists in this complex work
• ASCO is developing novel approaches to learn from the real world practice of medicine that will inform and improve delivery of personalized cancer care