Virtual Molecular Tumor Board
Hosted By: Dr. Lee Schwartzberg
West Cancer Center

February 23, 2016

Housekeeping:
Please identify yourself and organization when asking / responding to questions. Please keep phone on mute when not speaking.

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Patient 1
History

- Male, early 50’s
- Presentation:
  - Lower abdominal pain, no bleeding or weight loss
  - Liver lesions noted during evaluation
  - Cecal adenocarcinoma
    - Stage: T3, N1b, M1
    - KRAS WT
  - Treated with right hemicolecotomy
Clinical Course

At DX
- FOLFOX6 + Bevacizumab x 12 cycles with partial response
  - Residual liver lesions ablated, followed by clear CT

At 7 Months
- Liver lesion reappeared on CT and CEA progressed
- Attempted regorafenib, poor tolerance
- FOLFIRI + Cetuximab x 2-3 cycles: liver lesions progressed
- FOLFOX4 + panitumomab trial, rapid progression

At 2.5 years
- SIR-Speres x2
- CPT-11 + zif-aflivercept
- CPT-11 + ramucirumab, x3 cycles, some improvement in CEA to 21
- Patient sought second opinion at New Therapeutics Program
- Diagnosis:
  - Metastatic cecal adenocarcinoma
  - Biopsy: Adrenal metastasis
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PD-1
PD-L1

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<table>
<thead>
<tr>
<th>Gene</th>
<th>Alteration</th>
<th>Frequency (%)</th>
<th>Exon</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Her2/Neu (ERBB2)</td>
<td>V842I</td>
<td>37</td>
<td>21</td>
<td>Mutated, Pathogenic</td>
</tr>
</tbody>
</table>

**Interpretation:** A pathogenic mutation was detected in ERBB2 (Her2). This mutation has been reported in numerous cancers, and it has been found to be activating and sensitive to Lapatinib and Neratinib by in vitro studies (Bose Cancer Discov 2013 3:224).

ERBB2 (HER2) or v-erb-b2 erythroblastic leukemia viral oncogene homolog 2, encodes a member of the epidermal growth factor (EGF) receptor family of receptor tyrosine kinases. This gene binds to other ligand-bound EGF receptor family members to form a heterodimer and enhances kinase-mediated activation of downstream signaling pathways, leading to cell proliferation. Most common mechanism for activation of HER2 are gene amplification and over-expression with somatic mutations being rare. NCCN NSCLC guidelines recommends trastuzumab for activity against HER2 mutations in patients with NSCLC.

<table>
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<th>Exon</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>PIK3CA</td>
<td>R88Q</td>
<td>41</td>
<td>2</td>
<td>Mutated, Pathogenic</td>
</tr>
</tbody>
</table>

**Interpretation:** A known activating mutation, R88Q, was detected in PIK3CA. R88Q has been reported as a somatic mutation in numerous tumors. As a germline mutation, it has been reported to be causal for Megalencephaly-Capillary Malformation syndrome (Riviere 2012 Nat Genet 44:934).

PIK3CA or phosphoinositide-3-kinase catalytic alpha polypeptide encodes a protein in the PI3 kinase pathway. This pathway is an active target for drug development. PIK3CA somatic mutations have been found in breast (26%), endometrial (23%), urinary tract (19%), colon (13%), and ovarian (11%) cancers. Somatic mosaic activating mutations in PIK3CA are said to cause CLOVES syndrome. PIK3CA exon 20 mutations have been associated with benefit from mTOR inhibitors (everolimus, temsirolimus). Evidence suggests that breast cancer patients with PIK3CA mutation have a significantly shorter survival following trastuzumab treatment. PIK3CA mutated colorectal cancer patients are less likely to respond to EGFR targeted monoclonal antibody therapy.

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<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>APC</td>
<td>R1450X</td>
<td>41</td>
<td>16</td>
<td>Mutated, Pathogenic</td>
</tr>
</tbody>
</table>

**Interpretation:** A pathogenic mutation was detected in APC

APC or adenomatous polyposis coli is a key tumor suppressor gene that encodes for a large multi-domain protein. This protein exerts its tumor suppressor function in the Wnt/β-catenin cascade mainly by controlling the degradation of β-catenin, the central activator of transcription in the Wnt signaling pathway. The Wnt signaling pathway mediates important cellular functions including intercellular adhesion, stabilization of the cytoskeleton, and cell cycle regulation and apoptosis, and it is important in embryonic development and oncogenesis. Mutation in APC results in a truncated protein product with abnormal function, lacking the domains involved in β-catenin degradation. Somatic mutation in the APC gene can be detected in the majority of colorectal tumors (80%) and it is an early event in colorectal tumorigenesis. APC wild type patients have shown better disease control rate in the metastatic setting when treated with oxaliplatin, while when treated with fluoropyrimidine regimens, APC wild type patients experience more hematological toxicities. APC mutation has also been identified in oral squamous cell carcinoma, gastric cancer as well as hepatoblastoma and may contribute to cancer formation. Germline mutation in APC causes familial adenomatous polyposis, which is an autosomal dominant inherited disease that will inevitably develop to colorectal cancer if left untreated. COX-2 inhibitors including celecoxib may reduce the recurrence of adenomas and incidence of advanced adenomas in individuals with an increased risk of CRC. Turcot syndrome and Gardner’s syndrome have also been associated with germline APC defects. Germline mutations of the APC have also been associated with an increased risk of developing desmoid disease, papillary thyroid carcinoma and hepatoblastoma.

**GENES TESTED WITH AMPLIFICATION DETECTED**

| AKT2 | CCND1 | CDKN2A | FGF3 | FGF4 | FGFR3 |

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Caris Molecular Intelligence®
Tumor Profile Summary

• Pathogenic mutations
  – APC, HER2, PIK3CA, (RAS WT)
• Amplifications
  – AKT1, CCND1, CDKN2A, FGF4, FGFR3
• MSI-high (from previous specimen)
• MSH6 loss by IHC
• PD-L1 negative (0+ in 100% of cells by IHC)
• PD-1 positive
• Other IHC:
  – Beneficial on IHC: irinotecan
  – Non-beneficial: 5-FU, oxaliplatin

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Discussion

• MSI-High and MSH6 loss
  – Germline confirmatory testing?
  – Suggests benefit for checkpoint immunotherapy
  – 24% CR rate in metastatic GI patients who had MMR-deficient tumors and pembro 10mg/kg (Le et al, ASCO GI 2015)
  – Higher mutational load in MSI-High tumors may indicate targets for immunotherapy (Lin et al, Oncotarget 2015)

• PIK3CA exon 9 mutation
  – May confer anti-EGFR resistance
  – Not well-associated with mTOR inhibitor responses

• HER2 V842I mutation
  – Activating ERBB2 mutations such as V842I are associated with MSI-high and may respond to anti-HER2 in preclinical model
  – May confer anti-EGFR resistance
Patient 2
History

- Female, late 60’s
- Presentation:
  - distal pancreatectomy for intraductal papillary mucinous neoplasm
- 4 years later
  - Abd pain-CT A/P showed 5 cm mass in L lobe of liver, segment 2
  - Bx: Adenocarcinoma, c/w pancreatiobiliary origin LU5+, CD31-, CD34-, FVIII-
  - EUS Negative, PET negative except for liver lesion
Pathology

H&E 20x

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Treatment

4.5 years
- Went to L lobe hepatectomy
- Path: Adenocarcinoma c/w pancreatic
- Gemcitabine adjuvant x 6 cycles

5 years
- New lesion in R lobe of liver, 8 mm
- Liver resection sent for Caris Molecular Intelligence® Tumor Profiling
<table>
<thead>
<tr>
<th>Gene</th>
<th>Alteration</th>
<th>Frequency (%)</th>
<th>Exon</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>BRAF</td>
<td>V600E</td>
<td>21</td>
<td>15</td>
<td>Mutated, Pathogenic</td>
</tr>
</tbody>
</table>

**Interpretation:** A pathogenic mutation was detected in BRAF.

BRAF encodes a protein belonging to the raf/mil family of serine/threonine protein kinases. This protein plays a role in regulating the MAP kinase/ERK signaling pathway initiated by EGFR activation, which affects cell division, differentiation, and secretion. BRAF somatic mutations have been found in melanoma (43%), thyroid (39%), biliary tree (14%), colon (12%), and ovarian tumors (12%). BRAF inherited mutations are associated with Noonan/Cardio-Facio-Cutaneous (CFC) syndrome, syndromes associated with short stature, distinct facial features, and potential heart/skeletal abnormalities.

<table>
<thead>
<tr>
<th>Gene</th>
<th>Alteration</th>
<th>Frequency (%)</th>
<th>Exon</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>ROS1</td>
<td>S565L</td>
<td>38</td>
<td>12</td>
<td>Mutated, Variant of Unknown Significance</td>
</tr>
</tbody>
</table>

**Interpretation:** A rare missense mutation was found in the ROS1 gene. There is limited or no clinical and functional data available at this time to assess the clinical significance of this variant.

The proto-oncogene ROS1 is a receptor tyrosine kinase of the insulin receptor family. The ligand and function of ROS1 are unknown. Dimerization of ROS1-fused proteins results in constitutive activation of the receptor kinase, leading to cell proliferation and survival.
Whole-genome sequencing of pancreatic cancer defines genetic diversity and therapeutic targets


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**Table 2. Preliminary Best Response According to Cohort.**

<table>
<thead>
<tr>
<th>Variable</th>
<th>NSCLC (N = 20)</th>
<th>Colorectal Cancer</th>
<th>Cholangiocarcinoma (N = 8)</th>
<th>ECD or LCH (N = 18)</th>
<th>Anaplastic Thyroid Cancer (N = 7)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Vemurafenib (N = 10)</td>
<td>Vemurafenib + Cetuximab (N = 27)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients with ≥1 postbaseline assessment — no.</td>
<td>19</td>
<td>10</td>
<td>8</td>
<td>14</td>
<td>7</td>
</tr>
<tr>
<td>Complete response — no. (%)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1 (7)</td>
<td>1 (14)</td>
</tr>
<tr>
<td>Partial response — no. (%)</td>
<td>8 (42)</td>
<td>0</td>
<td>1 (4)</td>
<td>1 (12)</td>
<td>5 (36)</td>
</tr>
<tr>
<td>Stable disease — no. (%)</td>
<td>8 (42)</td>
<td>5 (50)</td>
<td>18 (69)</td>
<td>4 (50)</td>
<td>8 (57)</td>
</tr>
<tr>
<td>Progressive disease — no. (%)</td>
<td>2 (11)</td>
<td>5 (50)</td>
<td>7 (27)</td>
<td>3 (38)</td>
<td>4 (57)</td>
</tr>
<tr>
<td>Missing data — no. (%)</td>
<td>1 (5)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Overall response — no. (%) [95% CI]</td>
<td>8 (42)</td>
<td>0</td>
<td>1 (4)</td>
<td>1 (12)</td>
<td>6 (43)</td>
</tr>
</tbody>
</table>

* The denominator for patients with a complete or partial response, stable disease, or progressive disease is the number of patients with a postbaseline assessment or early withdrawal. Of the 19 patients in the NSCLC cohort, 1 patient withdrew before the assessment of response but was included in the denominator for the efficacy assessment (as having had no response).

† All patients with missing data withdrew early.

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C All-Others Cohort

Target Tumor Diameter Sum (percent change from baseline)

- Glioma
- Pleomorphic xanthoastrocytoma
- Head and neck cancer
- Esophageal cancer
- Sarcoma (unknown subtype)
- Pancreatic cancer
- Unknown primary type
- Ovarian cancer
- Salivary-duct carcinoma
- Thoracic clear-cell sarcoma
- Anaplastic ependymoma

267% 110%


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Time to Events in Individual Patients and According to the Best Overall Response.


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Patient 3
History

• Male, late 70’s

• PMH:
  – 40 pack-year smoking history, quit 20 years ago

• Presentation:
  – shortness of breath, needed 2-3 liters left sided thoracentesis
  – Had thoracoscopy and pleurodesis
  – Pathology second opinion on pleural fluid suggested adenocarcinoma

• Clinical Evaluation:
  – Presumptive left sided lung adenocarcinoma
  – Underwent staging CT, PET
  – Specimen from left pleural scraping sent to Caris
Pathology

H&E 20x

PD-L1 20x

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## Genes Tested with Alterations

<table>
<thead>
<tr>
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<th>Frequency (%)</th>
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</tr>
</thead>
<tbody>
<tr>
<td>BRAF</td>
<td>K601E</td>
<td>18</td>
<td>15</td>
<td>Mutated, Presumed Pathogenic</td>
</tr>
</tbody>
</table>

**Interpretation:** A rare BRAF mutation, K601E, was detected. This mutation has been identified in a number of malignancies. Dahlman et al (2012 Cancer Discov 2:791) reported that K601E activated BRAF, and that cells harboring this mutation responded to both Vemurafenib and MEK inhibitors.

BRAF encodes a protein belonging to the raf/mil family of serine/threonine protein kinases. This protein plays a role in regulating the MAP kinase/ERK signaling pathway initiated by EGFR activation, which affects cell division, differentiation, and secretion. BRAF somatic mutations have been found in melanoma (43%), thyroid (39%), biliary tree (14%), colon (12%), and ovarian tumors (12%). Patients with V600E BRAF mutation have a reduced likelihood of response to EGFR targeted monoclonal antibodies in colorectal cancer and sensitivity to BRAF inhibitors, vemurafenib and dabrafenib, and MEK1/2 inhibitor, trametinib in various solid tumors. BRAF inherited mutations are associated with Noonan/Cardio-Facio-Cutaneous (CFC) syndrome, syndromes associated with short stature, distinct facial features, and potential heart/skeletal abnormalities.

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<tr>
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<th>Frequency (%)</th>
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<th>Result</th>
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</thead>
<tbody>
<tr>
<td>KRAS</td>
<td>G12D</td>
<td>41</td>
<td>2</td>
<td>Mutated, Pathogenic</td>
</tr>
</tbody>
</table>

**Interpretation:** A pathogenic mutation was detected in KRAS

KRAS or V-Ki-ras2 Kirsten rat sarcoma viral oncogene homolog encodes a signaling intermediate involved in many signaling cascades including the EGFR pathway. KRAS somatic mutations have been found in pancreatic (57%), colon (35%), lung (16%), biliary tract (28%), and endometrial (15%) cancers. Mutations at activating hotspots are associated with resistance to EGFR tyrosine kinase inhibitors (erlotinib, gefitinib) in NSCLC and monoclonal antibodies (cetuximab, panitumumab) in CRC patients. Retrospective clinical studies raised the possibility that KRAS G13D mutations may not be absolutely predictive of non-response; however, this finding is not supported by published analysis of 3 randomized controlled phase III trials. Several germline mutations of KRAS (V14I, T58I, and D153V amino acid substitutions) are associated with Noonan syndrome.
<table>
<thead>
<tr>
<th>Biomarker</th>
<th>Staining Intensity (0, 1+, 2+, 3+)</th>
<th>Percent of cells</th>
<th>Result</th>
<th>Conditions for a Positive Result:</th>
</tr>
</thead>
<tbody>
<tr>
<td>TOPO1</td>
<td>2 +</td>
<td>100</td>
<td>Positive</td>
<td>Intensity ≥2+ and ≥30% of cells stained</td>
</tr>
<tr>
<td>TUBB3</td>
<td>3 +</td>
<td>100</td>
<td>Positive</td>
<td>Intensity ≥2+ and ≥30% of cells stained</td>
</tr>
<tr>
<td>Her2/Neu</td>
<td>0</td>
<td>100</td>
<td>Negative</td>
<td>Intensity ≥3+ and &gt;10% of cells stained</td>
</tr>
<tr>
<td>ERCC1</td>
<td>2 +</td>
<td>50</td>
<td>Positive</td>
<td>Intensity of ≥3+ with ≥10% or ≥2+ with ≥50% of cells stained</td>
</tr>
<tr>
<td>PD-L1</td>
<td>2 +</td>
<td>100</td>
<td>Positive</td>
<td>Intensity ≥2+ and ≥5% of cells stained</td>
</tr>
<tr>
<td>PTEN</td>
<td>1 +</td>
<td>100</td>
<td>Positive</td>
<td>Intensity ≥1+ and &gt;50% of cells stained</td>
</tr>
<tr>
<td>RRM1</td>
<td>2 +</td>
<td>60</td>
<td>Positive</td>
<td>Intensity ≥2+ and ≥50% of cells stained</td>
</tr>
<tr>
<td>TS</td>
<td>1 +</td>
<td>4</td>
<td>Negative</td>
<td>Intensity ≥1+ and ≥10% of cells stained</td>
</tr>
<tr>
<td>ALK</td>
<td>0</td>
<td>100</td>
<td>Negative</td>
<td>Intensity ≥3+ and ≥1% of cells stained</td>
</tr>
</tbody>
</table>

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Caris Molecular Intelligence®
Tumor Profile Summary

- ALK, EGFR, ROS1 WT
- BRAF K601E pathogenic mutation
- KRAS G12D pathogenic mutation
- PD-L1+ by IHC (2+ in 100% of cells)
Discussion

• First line therapy options
  – Standard options
    • TS low: suggests pemetrexed beneficial
    • ERCC1/BRCA1,2 suggest platinum non-beneficial
  – Immunotherapy as a first-line option or later?
    • PD-L1 positive
  – BRAF inhibitor candidate?
    • 18% allele frequency
Patient 4
History

- Female, early 60’s
- Presentation
  - headaches
  - previous squamous cell ca lung dx’ed
- Diagnosis
  - Large L cerebellar lesion and a small temporal lobe metastasis
  - Resection of cerebellar lesion showed met sq cell ca lung
  - W/u: L lower lobe mass, mediastinal and hilar adenopathy
- Treatment
  - Received weekly carbo/taxol
  - radiation to lung and mediastinum
  - Whole brain radiotherapy
Clinical Course

- CR in brain; excellent PR in lung and LNs with calcified LNs felt to be residual granulomatous disease
- Approx 1 year post DX- Progression in LLL mass
  - Rx’ed with RFA
- Approx 2 years post DX- new RUL nodule
  - Bx-sq cell ca.
  - PET and MRI otherwise negative
  - Rx’ed with RFA
  - Caris Molecular Intelligence® tumor profiling on R lung nodule bx
Clinical Course

• 3 year post Dx
  – Progression of disease
  – Right pleural nodularity, pleural effusion
  – extension into a rib laterally and multiple small lung nodules
  – MRI negative

• Started carbo/taxol
**AMPLIFICATION BY CHROMOGENIC IN SITU HYBRIDIZATION (CISH)**

<table>
<thead>
<tr>
<th>Gene / ISCN</th>
<th>Cells Counted</th>
<th>Result</th>
<th>Total/Avg Gene Copy Number</th>
<th>Total/Avg Control Copy Number</th>
<th>Cells with ≥4 Copies</th>
<th>Cells with ≥15 Copies</th>
<th>Ratio Calculation</th>
<th>Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>EGFR</td>
<td>100</td>
<td>Negative</td>
<td>1.94</td>
<td>1.90</td>
<td>3.00%</td>
<td>0.00%</td>
<td>EGFR/Chromosome 7</td>
<td>1.02</td>
</tr>
</tbody>
</table>

*Reference Range:* Positivity for increased gene copy number with CISH was defined as ≥4 copies in 40% or more tumor cells. Gene amplification was defined by the presence of a gene/chromosome per cell ratio of ≥2 or ≥15 copies of the genes per cell in ≥10% of analyzed cells.

<table>
<thead>
<tr>
<th>Gene / ISCN</th>
<th>Cells Counted</th>
<th>Result</th>
<th>Total/Avg Gene Copy Number</th>
<th>Total/Avg Control Copy Number</th>
<th>Cells with ≥4 Copies</th>
<th>Cells with ≥15 Copies</th>
<th>Ratio Calculation</th>
<th>Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Her2/Neu nuc ish (D17Z1x1-2,HER2x1-2)/[30]</td>
<td>20</td>
<td>Amplified</td>
<td>11.10</td>
<td>2.70</td>
<td>N/A</td>
<td>N/A</td>
<td>Her2/neu/Chromosome 17</td>
<td>4.11</td>
</tr>
</tbody>
</table>

*Reference Range:* Her2/Neu:CEP 17 signal ratio of ≥ 2.0; and non-amplification as <2.0 per Ventana INFORM HER2 CISH Package insert.

<table>
<thead>
<tr>
<th>Gene / ISCN</th>
<th>Cells Counted</th>
<th>Result</th>
<th>Total/Avg Gene Copy Number</th>
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<th>Cells with ≥4 Copies</th>
<th>Cells with ≥15 Copies</th>
<th>Ratio Calculation</th>
<th>Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>cMET nuc ish (D7Z1x1-2,cMETx1-2)[100/100]</td>
<td>20</td>
<td>Not Amplified</td>
<td>2.30</td>
<td>2.00</td>
<td>N/A</td>
<td>N/A</td>
<td>1.15</td>
<td></td>
</tr>
</tbody>
</table>

*Reference Range:* Positivity for increased gene copy number for cMET CISH has been defined as ≥ 5 copies of mean MET gene copy number per cell in NSCLC based on cMET FISH evidence (Cappuzzo et al 2009). The gene copy number threshold for other tumor types has not been determined.

- HER2 Amplification also detected by NGS CNV
- PD-L1 negative (2+ in 2% of cells)
- NGS: TP53 pathogenic mutation, 2 ALK VUS mutations

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<table>
<thead>
<tr>
<th>Study</th>
<th>Method (Definition of Amplification)</th>
<th>Frequency (%)</th>
<th>Coexisting Mutation in Cases of HER2 Amplification (%)</th>
<th>Method</th>
<th>Frequency (%)</th>
<th>Coexisting Amplification in Cases of HER2 Mutation (%)</th>
<th>Overall Overlap</th>
</tr>
</thead>
<tbody>
<tr>
<td>Li et al. (this study)</td>
<td>FISH (HER2-to-CEP17 ratio ≥2)</td>
<td>5 of 175 (3%)</td>
<td>0 of 5 (0%)</td>
<td>Fragment analysis, mass spectrometry and Sanger sequencing</td>
<td>4 of 148 (3%)</td>
<td>0 of 4 (0%)</td>
<td>0 of 148 (0%)</td>
</tr>
<tr>
<td>TCGA</td>
<td>NGS, whole exome (significant copy number gain, computational algorithm)</td>
<td>2 of 230 (1%)</td>
<td>0 of 2 (0%)</td>
<td>NGS, whole exome</td>
<td>5 of 230 (2%)</td>
<td>0 of 5 (0%)</td>
<td>0 of 230 (0%)</td>
</tr>
<tr>
<td>Arcila et al.</td>
<td>FISH (HER2-to-CEP17 ≥2)</td>
<td>1 of 50 (2%)</td>
<td>0 of 1 (0%)</td>
<td>Fragment analysis, mass spectrometry and Sanger sequencing</td>
<td>25 of 1478 (2%)</td>
<td>0 of 11 (0%)</td>
<td>0 of 50 (0%)</td>
</tr>
<tr>
<td>Li et al.</td>
<td>FISH (HER2-to-CEP17 ≥2 or homogeneous staining regions with ≥15 copies in ≥10% of cells)</td>
<td>Unknown</td>
<td>Unknown</td>
<td>Direct sequencing</td>
<td>8 of 224 (4%)</td>
<td>4 of 8 (50%)</td>
<td>4 of 8 (50%)</td>
</tr>
<tr>
<td>Mazieres et al.</td>
<td>FISH (HER2-to-CEP17 ≥2 or homogeneous staining regions with ≥15 copies in ≥10% of cells)</td>
<td>Unknown</td>
<td>Unknown</td>
<td>Direct sequencing</td>
<td>65 of 3800 (2%)</td>
<td>3 of 34 (9%)</td>
<td>3 of 34 (9%)</td>
</tr>
<tr>
<td>Yoshizawa et al.</td>
<td>FISH and DISH (HER2-to-CEP17 &gt;2)</td>
<td>By FISH: 5 of 243 (2%)</td>
<td>By FISH: 2 of 5 (40%) DISH: 9 of 243 (4%)</td>
<td>Direct sequencing</td>
<td>6 of 220 (3%)</td>
<td>2 of 6 (33%)</td>
<td>2 of 220 (1%)</td>
</tr>
<tr>
<td>Szulc et al.</td>
<td>Brightfield ISH (HER2-to-CEP17 ≥2)</td>
<td>222 of 1170 (19%)</td>
<td>25 of 222 (11%)</td>
<td>Direct sequencing</td>
<td>46 of 1275 (4%)</td>
<td>25 of 44 (57%)</td>
<td>25 of 1170 (2%)</td>
</tr>
</tbody>
</table>

Discussion

• What to do at progression?
• MyPathway: Trastuzumab and pertuzumab
• PD-1 inhibitor?
Next Virtual Molecular Tumor Board

Hosted by Dr. John Marshall
Chief, Division of Hematology and Oncology
Director of Development Therapeutics and GI Oncology,
Professor of Medicine and Oncology

Date: Thursday March 17, 2016
Time: 5pm EST

Look for an invitation coming soon!

Please direct questions regarding the VMTB to
cariscentersofexcellence@carisls.com

The information contained in these slides is provided for educational purposes only and has been permanently de-identified.