Virtual Molecular Tumor Board
Host: MedStar Georgetown University Hospital
Leader: Dr. John Marshall

Thursday, March 17, 2016
5 pm ET
Patient 1
History

- Elderly Male, generally healthy non-smoker
- Progressive 3 month cough and hemoptysis
- CT: RUL mass with mediastinal involvement
- Bronchoscopic biopsy Revealed malignant cells, unclear primary
  - Several nodes negative
- PET revealed RUL uptake, no distant uptake
- VATS performed:
  - Mesenchymal Chondrosarcoma of lung
  - With hilar invasion
- Brain MR negative
Clinical Course

• Surgically unresectable
• Recommended neoadjuvant chemotherapy
  – Few proven options for chemotherapy with overall low published rates of response
  – Anthracycline was decided against due to marginal ejection fraction
  – Gemcitabine / docetaxel
Pathology

H&E 20X  MLH1 20X

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

<table>
<thead>
<tr>
<th>Gene</th>
<th>Alteration</th>
<th>Frequency (%)</th>
<th>Exon</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>ATM</td>
<td>R250X</td>
<td>48</td>
<td>7</td>
<td>Mutated, Pathogenic</td>
</tr>
</tbody>
</table>

**Interpretation:** A pathogenic nonsense mutation was found in the ATM gene.

ATM or ataxia telangiectasia mutated is activated by DNA double-strand breaks and DNA replication stress. It encodes a protein kinase that acts as a tumor suppressor and regulates various biomarkers involved in DNA repair, which include p53, BRCA1, CHK2, RAD17, RAD9, and NBS1. Although ATM is associated with hematologic malignancies, somatic mutations have been found in colon (18%), head and neck (14%), and prostate (12%) cancers. Inactivating ATM mutations make patients potentially more susceptible to PARP inhibitors. Germline mutations in ATM are associated with ataxia-telangiectasia (also known as Louis-Bar syndrome) and a predisposition to malignancy.

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<tbody>
<tr>
<td>BRAF</td>
<td>G466E</td>
<td>48</td>
<td>11</td>
<td>Mutated, Pathogenic</td>
</tr>
</tbody>
</table>

**Interpretation:** An activating mutation has been detected in BRAF. Biochemical studies by Wan et al. have shown that this mutation has reduced BRAF kinase activity compared to wild type BRAF (Wan et al 2004 Cell), but can still activate ERK in vitro in COS cells and in vivo in Xenopus cells. In addition, this mutation has been reported in several publications for several tumor types. The high incidence of this mutation in human cancers coupled with the biochemical data is highly suggestive that this mutation is pathogenic.

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.
### GENES TESTED WITH ALTERATIONS

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</thead>
<tbody>
<tr>
<td>KRAS</td>
<td>F156L</td>
<td>13</td>
<td>5</td>
<td>Mutated, Presumed Pathogenic</td>
</tr>
</tbody>
</table>

**Interpretation:** An activating KRAS mutation was found in the sample. This variant has been found as a germline variant in patients with cardio-facio-cutaneous features (Noonan and Costello Syndromes) (Sovik et al J Med Gen 2007, 44; Zenker et al J Med Genet. 2007 Feb;44(2):131-5). This mutation has been shown to have increased GDP dissociation property which leads to increase in activated form of KRAS (Gremer et al Hum Mut 2011, 32 (1), 33-43). This variant has also been found in melanoma and endometrial cancers as a somatic mutation.

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. Several germline mutations of KRAS (V14I, T58I, and D153V amino acid substitutions) are associated with Noonan syndrome.

| MLH1 | R226X | 25 | 8 | Mutated, Pathogenic |

**Interpretation:** A pathogenic nonsense mutation was found in the MLH1 gene.

MLH1 or mutL homolog 1, colon cancer, nonpolyposis type 2 (E. coli) gene encodes a mismatch repair (MMR) protein which repairs DNA mismatches that occur during replication. Although the frequency is higher in colon cancer (10%), MLH1 somatic mutations have been found in esophageal (6%), ovarian (5%), urinary tract (5%), pancreatic (5%), and prostate (5%) cancers. Its prognostic and predictive utility is under investigation. Germline mutations of MLH1 are associated with Lynch syndrome, also known as hereditary non-polyposis colorectal cancer (HNPCC). Patients with Lynch syndrome are at increased risk for various malignancies, including intestinal, gynecologic, and upper urinary tract cancers and in its variant, Muir-Torre syndrome, with sebaceous tumors.
ATM Activates DNA Checkpoint Signaling After Double Stranded DNA Breaks

Involved in:

1. **Cell Cycle Arrest** and (G1 & G2/M) and **Apoptosis** via p53 activation.

2. **DNA Repair** and **Chromatin Remodeling** via BRCA1/RAD50 activation and H2AX phosphorylation (histone 2).

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van Gent et. al., Nature Reviews Genetics 2, 196-206 (March 2001) | doi:10.1038/35056049

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ATM Serine Threonine Kinase Signaling

Khalil HS, Tummala H, Zhelev N., Biodiscovery 2012; 5: 1.; DOI: 10.7750/BioDiscovery.2012.5.1

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Interpretation: A pathogenic nonsense mutation was found in the ATM gene.

- 66 exon gene
- 3056 amino acids
- Exon 7 mutation (R250X)
- R250X mutation → premature stop (protein truncation)
- Loss of ATM function
MLH1 is essential in the Mismatch Repair Pathway

http://www.ludwigcancerresearch.org/location/san-diego-branch/richard-kolodner-lab

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<tr>
<td>MLH1</td>
<td>R226X</td>
<td>25</td>
<td>8</td>
<td>Mutated, Pathogenic</td>
</tr>
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</table>

**Interpretation:** A pathogenic nonsense mutation was found in the MLH1 gene.

**BRIEF REPORTS**

**Somatic Mutations in MLH1 and MSH2 Are a Frequent Cause of Mismatch-Repair Deficiency in Lynch Syndrome-Like Tumors**

Lynch syndrome is caused by germline mutations in the mismatch repair (MMR) genes. Tumors are characterized by microsatellite instability (MSI). However, a considerable number of MSI-positive tumors have no known molecular mechanism of development. By using Sanger and ion semiconductor sequencing, 25 MSI-positive tumors were screened for somatic mutations and loss of heterozygosity in mutl homolog 1 (MLH1) and muts homolog 2 (MSH2). In 13 of 25 tumors (8 MLH1-deficient and 5 MSH2-deficient tumors), we identified 2 somatic mutations in these genes. We conclude that 2 acquired events explain the MMR-deficiency in more than 50% of the MMR-deficient tumors without causal germline mutations or promoter methylation.


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### MUTATIONAL ANALYSIS BY **Fragment Analysis**

<table>
<thead>
<tr>
<th>Gene</th>
<th>Interpretation</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>MSI</td>
<td>No microsatellite instability detected</td>
<td>Stable</td>
</tr>
<tr>
<td></td>
<td><strong>Procedure:</strong> Fragment Analysis</td>
<td></td>
</tr>
</tbody>
</table>

This tumor sample is microsatellite stable.

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Two major DNA repair pathways are impaired.

NO MSI?

Why?
<table>
<thead>
<tr>
<th>Gene</th>
<th>Alteration</th>
<th>Frequency (%)</th>
<th>Exon</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>NF1</td>
<td>c.3871-1_3871GG&gt;AA</td>
<td>41</td>
<td>29</td>
<td>Mutated, Pathogenic</td>
</tr>
</tbody>
</table>

**Interpretation:** A pathogenic splicing mutation was found in the NF1 gene.

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</thead>
<tbody>
<tr>
<td>NF1</td>
<td>K1714X</td>
<td>38</td>
<td>37</td>
<td>Mutated, Pathogenic</td>
</tr>
</tbody>
</table>

**Interpretation:** A pathogenic mutation was found in the NF1 gene.

The NF1 gene encodes neurofibromin, a protein that activates RAS GTP-ase, causing inactivation of RAS and serving as a negative regulator of the RAS pathway. Preclinical studies suggest that mutations in NF1 are associated with a decreased sensitivity to EGFR inhibitory drugs in lung cancer, perhaps due to an increased level of RAS activity that allows the tumor to escape the negative regulation of EGFR. Further preclinical studies have shown that NF1 mutations/deletions cause sensitivity to MEK inhibitors in sarcoma cell lines and resistance to RAF inhibition in melanoma cell lines. NF1 mutations have been observed in urothelial, ovarian, lung and triple negative breast cancer.
Molecular Tumor Summary

- MLH1 R226X pathogenic mutation
  - MLH1 intact by IHC (1+ in 90% of cells)
- Microsatellite stable
- Multiple other mutations
  - (high mutation phenotype)
  - NF1 x2
  - KRAS
  - BRAF
- No CNV / amplifications or fusions detected
- PD-L1 negative (0+ in 100% by IHC)
Patient 2
History

• Woman, late-60s
• PMH: type 2 DM, HTN, hypercholesterolemia
• Presented to ER with epigastric pain and vomiting
• EGD revealed obstructing mass in duodenum
• Surgery: Whipple procedure
  – Pathology: small bowel carcinoma
  – Poorly differentiated
  – Stage 3B (T4 N2 M0)
  – 11 of 14 nodes positive
Clinical Course

- Performance status 2
- Clinical progression within six weeks of surgery
- Began FOLFOX chemotherapy
- Early tolerance of chemotherapy appears poor
Pathology

H&E 20X

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<tbody>
<tr>
<td>CDKN2A</td>
<td>RS8X</td>
<td>54</td>
<td>2</td>
<td>Mutated, Pathogenic</td>
</tr>
</tbody>
</table>

**Interpretation:** A pathogenic nonsense mutation was detected. Germline inheritance of this mutation has been detected in hereditary melanoma patients (Hussussian 1994 Nat Genet 8: 15).

CDKN2A, or cyclin-dependent kinase inhibitor 2A, is a tumor suppressor gene that encodes two cell-cycle regulatory proteins, p16INK4A and p14ARF. As upstream regulators of the retinoblastoma (RB) and p53 signaling pathways, CDKN2A controls the induction of cell cycle arrest in damaged cells that allows for repair of DNA. Loss of CDKN2A through whole-gene deletion, point mutation, or promoter methylation leads to disruption of these regulatory proteins and consequently dysregulation of growth control. Somatic CDKN2A mutations are documented to occur in squamous cell lung cancers, head and neck cancer, colorectal cancer, chronic myelogenous leukemia and malignant pleural mesothelioma. Currently, there are agents that target downstream of CDKN2A such as CDK4/6 inhibitors which function by restoring the cell’s ability to induce cell cycle arrest. Germline CDKN2A mutations are associated with melanoma-pancreatic carcinoma syndrome, which increases the risk for familial malignant melanoma and pancreatic cancer.

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<tbody>
<tr>
<td>RAF1</td>
<td>S257L</td>
<td>86</td>
<td>7</td>
<td>Mutated, Pathogenic</td>
</tr>
</tbody>
</table>

**Interpretation:** This mutation has been reported in several cancers including stomach, skin, and large intestine. In vitro studies have shown that this variant increases RAF1 kinase activity and enhances ERK activation (Pandit et al Nat Genet. 2007 Aug;39(8):1007-12). Germline inheritance of this variant has also been associated with LEOPARD and NOONAN syndrome (OMIM 164760).

The RAF1 gene encodes a protein that is a member of the RAF family of serine/threonine kinases, along with BRAF and ARAF. RAF-family kinases are involved in the ras-MAPK signaling cascade. Active RAF1 directly phosphorylates MEK1 and MEK2, which then activate the ERK pathway, leading to cell proliferation and differentiation.

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<tr>
<td>TP53</td>
<td>Y234C</td>
<td>53</td>
<td>7</td>
<td>Mutated, Presumed Pathogenic</td>
</tr>
</tbody>
</table>

**Interpretation:** A mutation, Y234C, was detected in TP53. This mutation has been reported previously in numerous publications. In biochemical studies, it has been shown to cause the TP53 protein to become unstable at physiological temperatures, disrupting normal signaling (Dearth 2007 Carcinogenesis 28:289). Y234C has also been reported as a germline mutation, causal for Li-Fraumeni syndrome (Monti 2011 Mol Cancer Res 9:271).

TP53, or p53, plays a central role in modulating response to cellular stress through transcriptional regulation of genes involved in cell-cycle arrest, DNA repair, apoptosis, and senescence. Inactivation of the p53 pathway is essential for the formation of the majority of human tumors. Mutation in p53 (TP53) remains one of the most commonly described genetic events in human neoplasia, estimated to occur in 30-50% of all cancers. Generally, presence of a disruptive p53 mutation is associated with a poor prognosis in all types of cancers, and diminished sensitivity to radiation and chemotherapy. Germline p53 mutations are associated with the Li-Fraumeni syndrome (LFS) which may lead to early-onset of several forms of cancer currently known to occur in the syndrome, including sarcomas of the bone and soft tissues, carcinomas of the breast and adrenal cortex (hereditary adrenocortical carcinoma), brain tumors and acute leukemias.
Do you call a genetic counselor, cardiologist?

Prevalence of CDKN2A mutations in pancreatic cancer patients: implications for genetic counseling

Robert R McWilliams¹, Eric D Wieben², Kari G Rabe³, Katrina S Pedersen⁴, Yanhong Wu², Hugues Sicotte³ and Gloria M Petersen³

Gain-of-function RAF1 mutations cause Noonan and LEOPARD syndromes with hypertrophic cardiomyopathy.


Author information

¹Center for Molecular Cardiology, Department of Pediatrics and Department of Genetics and Genomic Sciences, Mount Sinai School of Medicine, One Gustave L. Levy Place, New York, New York 10029, USA.
Is a gain-of-function mutation in TP53 prognostic/diagnostic?

Clinical Relevance of Gain-Of-Function Mutations of p53 in High-Grade Serous Ovarian Carcinoma

Hyo Jeong Kang¹, Sung-Min Chun¹,², Kyu-Rae Kim¹, Insuk Sohn³, Chang Ohk Sung¹*¹

1 Department of Pathology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea, 2 ASAN Center for Cancer Genome Discovery, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea, 3 Samsung Cancer Research Institute, Seoul, Korea

Characteristics of mutp53 with gain-of-function activity

Patients with GOF mutations showed higher mRNA (p=0.0321) and protein (p=0.0129) expression than patients with NE-GOF mutations. However, MDM2 mRNA expression level was not different between GOF and NE-GOF (p=0.4365) (Table 1). GOF mutations were more likely to result from hotspots mutations (p=0.002) and mutations within CpG sites (p<0.001), and had higher FS scores than NE-GOF mutations (p<0.001). Clinically, patients with GOF mutations showed a higher frequency of platinum resistance (22/58, 37.9%) than patients with NE-GOF mutations (12/56, 21.4%), and a lower frequency of platinum sensitivity (36/58, 62.1%) than patients.
Is a gain-of-function mutation in TP53 prognostic/diagnostic?

Clinical Relevance of Gain-Of-Function Mutations of p53 in High-Grade Serous Ovarian Carcinoma

Hyo Jeong Kang¹©, Sung-Min Chun¹,²©, Kyu-Rae Kim¹, Insuk Sohn³, Chang Ohk Sung¹*

1 Department of Pathology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea, 2 ASAN Center for Cancer Genome Discovery, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea, 3 Samsung Cancer Research Institute, Seoul, Korea

Characteristics of mutp53 with gain-of-function activity.

Patients with GOF (p=0.0321) and protein with NE-GOF mutations. level was not different be (Table 1). GOF mutatic hotspots mutations (p=0. (p<0.001), and had high higher frequency of platinum patients with NE-GOF m frequency of platinum sensitivity (36/55, 65.5%) than patients.

marginaly significant (p=0.054) (Figure 3A). Furthermore, there was a different recurrence pattern between patients with GOF mutp53 and patients with NE-GOF mutp53. GOF mutations were associated with the development of distant metastasis (36/55, 65.5%) rather than local recurrence (19/55, 34.5%), whereas patients with NE-GOF mutations showed a higher frequency of locoregional recurrence (26/47, 55.3%) than distant metastasis (21/47, 44.7%) (p=0.035, Figure 3B).
Caris Molecular Intelligence
Summary

- CDKN2A R58X pathogenic mutation
- RAF1 S257L pathogenic mutation
- TP53 Y234C pathogenic mutation
- No copy number variations or fusions detected
- PD-L1 positive (2+ in 5% of cells by IHC)
Patient 3
History

- Male, early 60’s
- Presented with chest pain, cough, weight loss
- Right pleural effusion suspicious for effusion
- Family history: unremarkable
- PET/CT: pleural mass 2.5 cm and right hilar and mediastinal adenopathy, unclear primary
Workup

VATS pleural biopsy:

- Metastatic adenocarcinoma
- Positive CK7, CK19, CA-19-9
- Negative for Napsin, TTF-1, PSA, CK20, CDX2, PAP, CAIX
- Suggestive of pancreatobiliary origin
Staging

- Brain MR: negative
- Bone scan: negative
- Serum CA19-9 elevated, CEA 22, PSA negative
- CT angiogram: bilateral pulmonary emboli
Clinical Course

• Treated as pancreatobiliary adenocarcinoma
• Gemcitabine / nab-paclitaxel x 6 weeks
  – Rising serum CA-19-9
• FOLFOX x10 weeks
  – Rising serum CA-19-9
• Referred for clinical trial consideration
• 5 months post Dx: no malignant cells in right pleural fluid
• Restaging CT: right pleural effusion, no evidence of primary tumor. No mediastinal adenopathy.
Pathology

H&E 20X
MUTATIONAL ANALYSIS BY NEXT-GENERATION SEQUENCING (NGS)

GENES TESTED WITH ALTERATIONS

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<th>Exon</th>
<th>Result</th>
</tr>
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<tbody>
<tr>
<td>APC</td>
<td>E1317Q</td>
<td>64</td>
<td>16</td>
<td>Mutated, Variant of Unknown Significance</td>
</tr>
</tbody>
</table>

Interpretation: A missense variant was detected in the APC gene. There are conflicting reports in the literature concerning the significance of this mutation. Some reports associate it with a slightly increased risk for colon cancer and some find no statistically significant evidence to support pathogenicity. As such, E1317Q is classified as a Variant of Unknown Significance.

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.

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<td>G12C</td>
<td>20</td>
<td>2</td>
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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. Several germline mutations of KRAS (V14I, T58I, and D153V amino acid substitutions) are associated with Noonan syndrome.
Caris Molecular Intelligence
Summary

- KRAS G12C pathogenic mutation
- APC VUS
- No copy number variations or fusions detected
- PD-L1 negative (0+ in 100% of cells by IHC)
Patient 4
History

- Male, Mid 30’s
- Presented with lump on right side of his neck. US and CT showed a large right thyroid mass and right sided adenopathy levels II-IV that were PET avid.
- FNA was paucicellular and atypia of undetermined significance
- Thyroidectomy with medial and right lateral neck dissection.
  - Path: poorly differentiated thyroid cancer, insular carcinoma, 7 cm.
  - ETE. Focal positive margins. Large number of positive nodes.
- Postoperative radioiodine (RAI) ablation.
  - 310mCi at WHC – dosimetry
  - post treatment scan: Post I-131 therapy scan with findings in the thyroid bed. No scan evidence of locoregional or distant metastases.
History

• About 3 months after iodine: PET/CT positive for newly noted neck mass: Interval development of new pathologic lymphadenopathy from levels II -V. The largest lymph node measures 2.3 x 2.4 cm.
• About one year later: Abdominal CT: expansile soft tissue mass in the pancreatic head and uncinate process measuring 4 x 3 cm with ductal dilatation
• EGD with EUS and FNA. 3.5 x 3.7 hypoechoic pancreatic head mass;
  – Pathology: poorly differentiated thyroid cancer
• Medical oncology consultation, Caris Molecular Intelligence testing
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Fusion Testing

EWSR1-FLI1 fusion detected on NGS at Caris Life Sciences

**Molecular Diagnostics**

**Interpretation**
Thyroid (GUH GS-15-07200-D3, 06/09/15):
An EWSR1/FLI1 fusion transcript was detected by RT-DNA amplification. The size of the amplification product is consistent with a type II fusion transcript.

**Interpretation Comment**
Pertinent pathology reports, laboratory data and clinical history in the medical record were reviewed by a molecular pathologist to assist in the interpretation of this assay.
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LSI EWSR1 (22q12) Breakapart Probe

5' EWSR1: Proximal
3' EWSR1: Distal

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## PROTEIN EXPRESSION BY IMMUNOHISTOCHEMISTRY (IHC)

<table>
<thead>
<tr>
<th>Biomarker</th>
<th>Staining Intensity (0, 1+, 2+, 3+)</th>
<th>Percent of cells</th>
<th>Result</th>
<th>Thresholds*</th>
</tr>
</thead>
<tbody>
<tr>
<td>TOP2A</td>
<td>2 +</td>
<td>15</td>
<td>Positive</td>
<td>Intensity ≥1+ and ≥10% 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>15</td>
<td>Negative</td>
<td>Intensity of ≥3+ with ≥10% or ≥2+ with ≥50% of cells stained</td>
</tr>
<tr>
<td>PD-L1</td>
<td>0</td>
<td>100</td>
<td>Negative</td>
<td>Intensity ≥2+ and ≥5% of cells stained</td>
</tr>
<tr>
<td>PTEN</td>
<td>1 +</td>
<td>80</td>
<td>Positive</td>
<td>Intensity ≥1+ and &gt;50% of cells stained</td>
</tr>
</tbody>
</table>

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Caris Molecular Intelligence Summary

- EWSR1-FL1 fusion detected
  - by NGS at Caris Life Sciences
  - by PCR at Outside University
- ABL1 P997L exon 11 VUS detected
- No other mutations detected
- No CNV abnormalities or fusions
- PD-L1 negative (0+ in 100% of cells)
Adamantinoma-like Ewing Family Tumors of the Head and Neck

A Pitfall in the Differential Diagnosis of Basaloid and Myoepithelial Carcinomas

Justin A. Bishop, MD,* Rita Alaggio, MD,† Lei Zhang, MS, MD,‡
Raja R. Seethala, MD,§ and Cristina R. Antonescu, MD‡

Case series of 7 cases.
All were CD99+, pancytokeratin+, p40+
All cases had EWSR1-FLT1 translocation detected
Discussion

• Unusual histology thyroid tumor
  — Adamanthinoma-like Ewing sarcoma
  — Metastatic to pancreas

• Characteristic Ewing’s fusion EWSR1-FL1
  — Detected on NGS and confirmed by PCR and FISH
  — Consistent with previous reports of this histology

• Treatment recommendations
  — Clinical trials?
  — Standard Ewing’s therapy?
Next Virtual Molecular Tumor Board

Host: Levine Cancer Institute
Leader: Dr. Ed Kim

Thursday April 14, 2016
5 pm ET

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