Case Presentation

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Case History: Presentation

- 20 y/o F
- PMHx & PSHx: Unremarkable
- Fam Hx: pGF abdominal cancer – uncertain type, mGF lung cancer, 3 siblings healthy

- 07/2003 – Upper GI bleed (hb 4.3)
  - Endoscopy – gastric tumor
Initial Management

• 07/19/2013 Subtotal gastrectomy w/ Roux-en-Y gastrojejunostomy
  – Multi-focal GIST nodules (largest 7cm), 16/50HPF, mixed spindle, tumor at proximal gastric margin
  – Omentum & LN –ve
  – IHC: Positive – CD117, CD34, vimentin; negative – S100
  – Molecular analysis: KIT & PDGFRα -ve

• Staging CT CAP: 1.2cm liver lesion – cyst

• 08/2003 - 09/2004 Phase II study of adjuvant imatinib 400mg daily
Case History Continued...

- **06/2009 CT**
  - abnormal gastrohepatic LNs measuring 4cm
  - Mesenteric mass 2.9cm
  - R hepatic lobe metastases (max 2.4cm)
- **7/2009 USg FNA LN – GIST**
- **09/2009 – 5/2011 Phase III STAR trial Imatinib vs Nilotinib** – randomized to imatinib 400mg daily
- **06/2011 Sunitinib (cx HTN, HFS, mucositis)**
- **4/2012 Relocated to NYC, transfer to MSKCC**
Pathology Review at MSKCC

- 07/19/2003 Surgical Specimen
  - GIST
  - **Mixed spindle and epithelioid type**
  - Multiple nodules (size range: 0.3 – 7cm)
  - >5/50HPF
  - IHC: +ve CD117; -ve CD34
  - Molecular Analysis:
    - KIT/PDGFRα/BRAF -ve
  - Additional IHC: **loss of SDHB expression**, SDHA preserved
Case History Continued

- Sunitinib continued – slow progression observed
- 11/2012 Hepatectomy (seg 4b & 3), partial transverse colectomy, resection of peritoneal mets
  - Path: Metastatic GIST involving segment 4b (x4) and 3 (x2)(positive margin), retrogastric tumor (4.5cm), transverse colon (6cm), peritoneal nodules (0.5-2cm)
  - MSK-IMPACT NGS (12/2014): SDHA (NM_004168) exon 2p.R31X (c.91C>T)
- 1/2013 Restaging CT – confirmed residual liver metastases
- 2/2013 – 1/2014 Clinical trial IGF-1R inhibitor – eventual slow progression
Case History Continued…

• 1/28/2014 – present Phase I study of imatinib & binimetinib
  – AEs: acneiform rash, peripheral edema
  – 10/2014 Dose reduced MEK 30/45mg from 45mg bid (c/o rash)
• Initial RECIST response
• 07/2015 CT RECIST SD, MRI concerning for slight increase in liver mets
• 11/5/2015 Failed attempted debulking. Intra-operative US revealed more extensive disease then originally seen on pre-op images. Biopsies taken from peritoneal, liver and subcutaneous metastases
Combination Treatment of Imatinib and Binimetinib (MEK162)

Timeline of Rx


Months: 22

Linsitinib imatinib+ binimetinib (MEK162)

(RECIST: -19%)

CT scans of the liver lesions (liver window)

Target lesion #1

Non-target lesion #1

Before treatment

~12 months (RECIST: -20%)

~24 months (RECIST: -14%)

Memorial Sloan Kettering Cancer Center
Exceptional response in a patient with SDH-deficient GIST

Timeline of Rx

**IMPACT:**
- **Linsitinib** (11/20/2012)
- **Debulking Surgery** (11/20/2012)
- **Started trial (1/28/2014)**
- **Biopsy (11/5/2015)**

**Months:**
- -14
- -9
- 0
- 22
- 32

**IMPACT genes**
- SDHA
- SDHA exon 2 p.R31X
- Liver/peritoneal met (<5% necrosis)
- KDR exon 30 p.V1334E
- Peritoneal met (100% necrosis)
- SDHA IHC
- Liver met (70% necrosis)
- SDHB IHC
- Ki67<10% (liver met)
- SDHA IHC

**WES of FFPE**

- Archer negative for fusion

**Cristina R. Antonescu**

Camacho Ordonez/Berger
Case continued

- 12/2015 Resumed therapy on phase I study of imatinib & binimetinib
- Remains on study > 5 years with RECIST SD
Questions???