



Memorial Sloan Kettering
Cancer Center

Case Presentation

May 9th 2019

Dr. Ciara Kelly

Assistant Attending

Sarcoma Medical Oncology Service



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 & PDGFR α -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/PDGFR α /**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



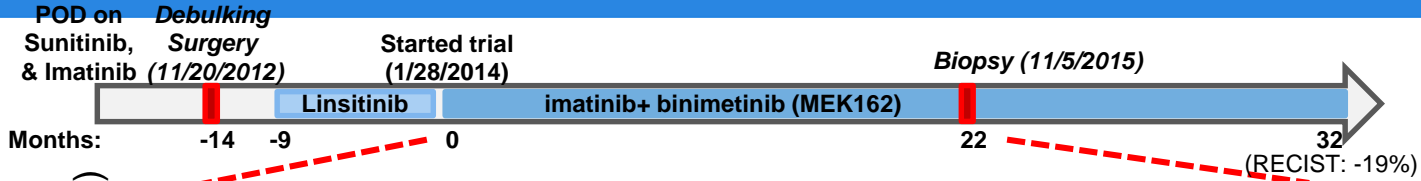
Case History Continued...

- 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 than originally seen on pre-op images. Biopsies taken from peritoneal, liver and subcutaneous metastases

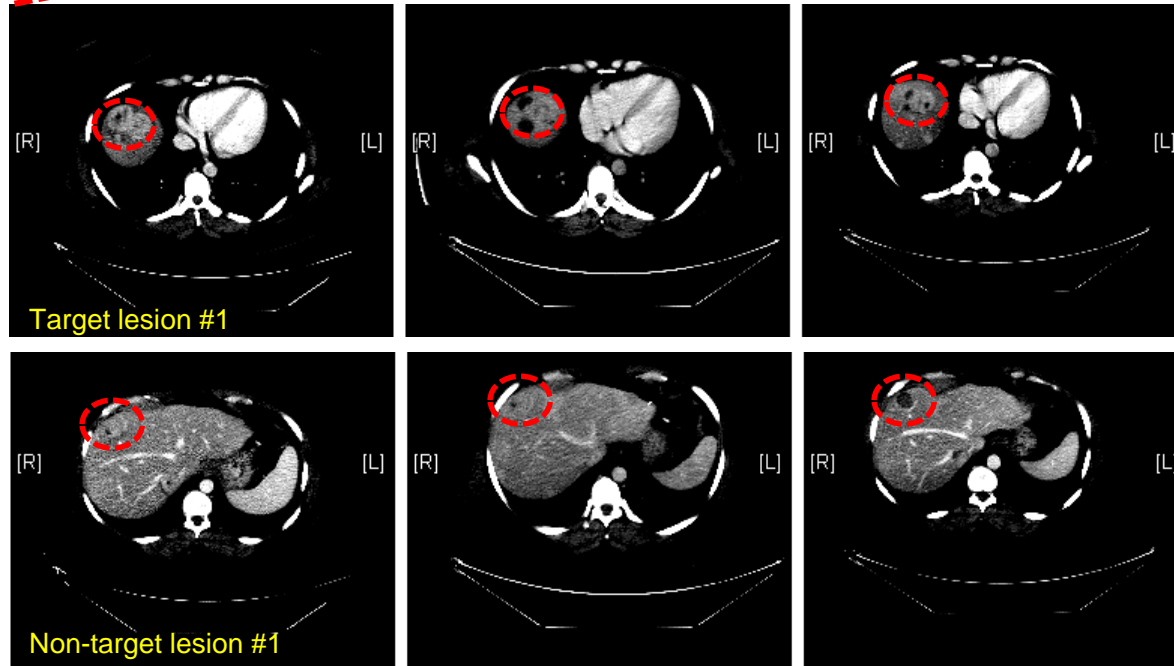


Combination Treatment of Imatinib and Binimetinib (MEK162)

Timeline of Rx



CT scans of the liver lesions (liver window)



Target lesion #1

Non-target lesion #1

Before treatment

~12 months
(RECIST: -20%)

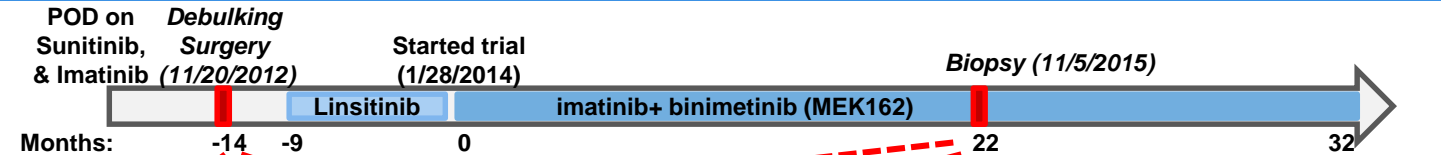
~24 months
(RECIST: -14%)



Memorial Sloan Kettering
Cancer Center

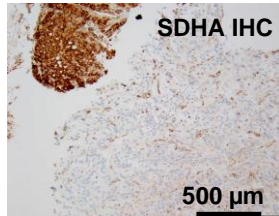
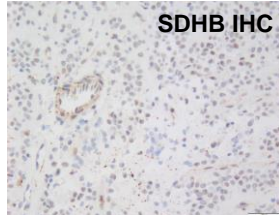
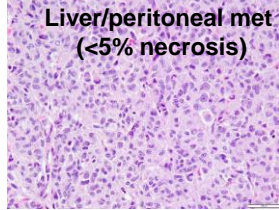
Exceptional response in a patient with SDH-deficient GIST

Timeline of Rx

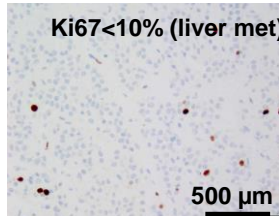
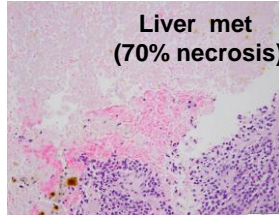
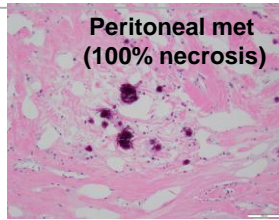


IMPACT:

SDHA exon 2 p.R31X



SDHA exon 2 p.R31X
KDR exon 30 p.V1334E



*SDHA	100%
TTN	100%
STAM	100%
OR13C3	100%
SLCO6A1	100%
ITGB6	100%
FAT2	100%
LRP10	50%
CASKIN1	50%
SCNN1G	50%
GRIK5	50%
SH3RF3	50%
SPON2	50%
*KDR	50%
UPP1	50%
ASNS	50%

P-0002594-To1-IM3 (Pre)
 P-0002594-To2-IM5 (Post)

*IMPACT genes

WES of FFPE

Archer negative for fusion

■ Shallow Deletion ■ Truncating Mutation ■ Inframe Mutation ■ Missense Mutation

Case continued

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





Memorial Sloan Kettering
Cancer Center

Questions???

