Efficacité des traitements anti-HER2 dans le cancer du sein métastatique avec mutation activatrice d’HER3

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ESOPE study samples ➔ Next Generation Sequencing @MSKCC

Frozen biopsy breast K & liver met

MSKCC

➔ Microdissection & extraction ADN

➔ SNP6

➔ whole exome sequencing - Illumina HiSeq 2000 @ CGL

2 tumor samples (targeted mean depth : 250x)

Germline (100x)

Analysis of sequencing data (KYC Ng)

SNV called by Mutect & MutationSeq

Indels called by GATK HaplotypeCaller

(Correction for cellularity & CNV determined by SNP6)
Couple #34
Depth / AF max
P 179x / 0.32
M 193x / 0.76
G 64x
35 mutations
PT only: 3
PT & Met: 26
Met only: 6

The diagram shows a scatter plot with points labeled TP53, HER3, STAG2, TCF7L2, and KRT1. The plot is titled "IDC-NST HR+ (low) HER2 neg."
Extra-cellular domain

G284R in the domain I/II interface
HER2 co-expression required

immortalized colon epithelial cells

Tumor growth
Sensitivity to anti-HER agents
Sensitivity to anti-HER agents
June 2012
Initial diagnosis
cT3N1M1 breast cancer

Doxorubicin - Cyclophosphamide
+ oral cyclophosphamide maintenance

Primary tumor biopsies
Liver metastasis biopsies

March 2013
Progressive disease (liver)
Docetaxel
+ oral capecitabine maintenance

May 2013
Radiotherapy Mazectomy

Baseline
Day 15
Complete metabolic response

Response confirmed 1 month later

April 2014
Progressive disease (liver)
Trastuzumab - Lapatinib
ongoing (as of Nov, 2014)

Liver metastases resection
1st met.: 90% necrosis
2nd met.: 50% necrosis

Baseline
Day 67
Partial Response

Response confirmed 1 month later
1\textsuperscript{st} in man - Proof of concept with no chemotherapy

Treatment to be continued

pertuzumab more likely active than T-DM1 (?)

\textit{HER3} activating mutations are rare in breast cancer

1 case / 1000 TCGA

2\% of colorectal and gastric cancers