

# Breast HER2(+) Cancer



## Tests usually made in routine

- ER / PR / HER2 / KI67 - expression



## How to treat metastatic Breast HER2(+) Cancer?

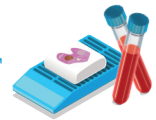
- Chemotherapies (paclitaxel, docetaxel, doxorubicin, cyclophosphamide, epirubicin, fluorouracil, gemcitabine and carboplatin)
- Targeted therapies (trastuzumab, pertuzumab, lapatinib,...)

## HOW CAN ONCODNA BE USEFUL?

### • For Approved Treatments



OncoSTRAT&GO™



DNA / RNA



#### ERBB2 (HER2) - *copy number testing*

To (1) predict poor prognosis/resistance to anti-estrogen therapies (tamoxifen, fulvestrant, exemestane, letrozole) and (2) predict response to trastuzumab, pertuzumab, neratinib and lapatinib (12 % incidence).

#### ERBB2 (HER2) - *extended mutations*

To (1) predict poor prognosis/resistance to lapatinib therapy, (2) predict response to trastuzumab (12 % incidence) and (3) predict resistance to anti-estrogen therapies (tamoxifen, fulvestrant, exemestane and letrozole).

#### ERBB3 (HER3) - *copy number testing*

To predict resistance to trastuzumab and pertuzumab.

#### JAK1/2/3 - *extended mutations and copy number testing*

To predict good prognosis to anti-JAK treatments (ruxolitinib\*).

PROTEINS



#### TOP2A - *over-expression*

To predict good prognosis for the overall survival but also good prognosis to TOP2A inhibitors (liposomal doxorubicin and epirubicin).

#### TLE3 - *over-expression*

To predict good prognosis and response to taxane-based therapies (docetaxel and paclitaxel).

#### TS - *over-expression*

To predict poor prognosis and resistance to 5-FU therapies.

#### PGP - *over-expression*

To predict poor prognosis and resistance to doxorubicin and paclitaxel therapies.

PROTEINS + DNA



#### Tumor Burden - *testing* + PD-L1 & CD8 - *over-expression* + MSI - *testing* + POLE, POLD1 - *mutations & copy number testing*

To predict good prognosis to anti-PDL1 / anti-PD1 treatments (pembrolizumab and atezolizumab\*).

#### CDK4 / CDK6 / RB1 / CDKN2A - *extended mutations & copy number testing* + pRB1 - *expression*

To predict good prognosis to anti-CDK4/6 treatments (palbociclib and ribociclib)\*.

#### MTOR / TSC1 / TSC2 / PTEN / PIK3CA - *extended mutations & copy number testing* + p4EBP1 / PTEN - *expression*

To predict (1) good prognosis to mTOR inhibitors (temsirolimus and everolimus)\* and (2) poor prognosis to ERBB2 inhibitors (trastuzumab, pertuzumab and lapatinib).

\* : Drugs FDA approved for other indications.

\*\* : Drugs in development



## • For Drugs in Development

RNA



### **NTRK1/2/3 - translocation testing**

To predict good prognosis to anti-NTRKx treatments (entrectinib and LOXO-101).

PROTEINS



### **IGF1R - over-expression**

To predict good prognosis to anti-IGF1R treatment (dalotuzumab) and poor response to HER2 inhibitors.

\* : Drugs FDA approved for other indications.

## WHY AND WHEN A PERSONALIZED LIQUID BIOPSY COULD BE MADE ?



OncoTRACE



### • Neoadjuvant Settings

The evaluation of the response to anti-tumor therapies for solid tumors is based on the monitoring of the size of lesions and must be accurately measured in at least one dimension (longest in plane diameter is to be recorded) (RECIST criteria).

#### LIMITATIONS OF THIS APPROACH:

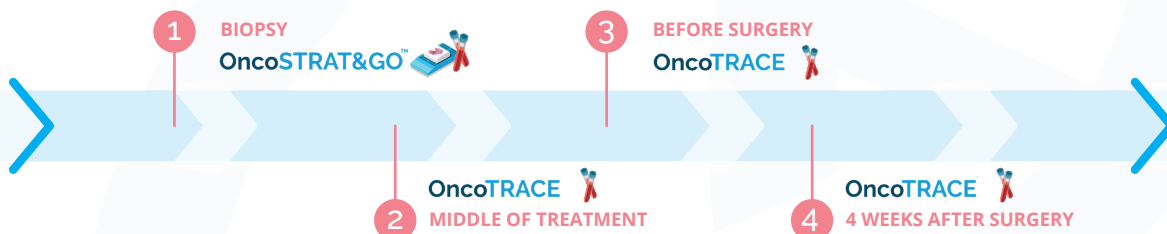
- ✗ Early evaluation after treatment start is difficult because tumor shrinkage can only be detected after several therapeutic cycles.
- ✗ Response is non-evaluable when disease is not measurable (liquid effusion, follow-up post complete tumor resection...)

#### OUR SUGGESTED ALTERNATIVE:

ctDNA can be used as a non-invasive tool to monitor the disease evolution during treatment. But which mutations must be followed and how many ?

Our solutions are able to:

- ✓ Predict a relapse sooner than conventional imaging technologies
- ✓ Detect resistance mutations to anticipate therapy changes
- ✓ Predict sensitivity to new therapies



### • Adjuvant / Systemic settings



2 weeks before the scheduled visit with the patient.

