OncoDNA
THE CANCER THERANOSTIC COMPANY

INFORMATIVE CARD - JULY 2017

Breast HR(+) Cancer

Tests usually made in routine

• **ER / PR / HER2 / KI67** - expression

How to treat metastatic Breast HR(+) Cancer?

• Hormone therapies (tamoxifen, fulvestrant, exemestane and letrozole)
• Chemotherapies (paclitaxel, docetaxel, doxorubicin, cyclophosphamide, epirubicin and fluorouracil)
• Targeted therapies (everolimus, palbociclib and ribociclib)

HOW CAN ONCODNA BE USEFUL?

• For Approved Treatments

OncoSTRAT&GO™

DNA / RNA

ESR1 - *extended mutations*
To predict resistance to anti-estrogen therapies (tamoxifen, fulvestrant, exemestane and letrozole) (22% incidence).

ERBB2 (HER2) - *copy number testing*
To predict (1) poor prognosis/resistance to anti-estrogen therapies (tamoxifen, fulvestrant, exemestane and letrozole) and (2) response to trastuzumab*, pertuzumab*, neratinib* and lapatinib* (12 % incidence).

cMET - *copy number testing*
To predict response to crizotinib* and cabozantinib*.

RB1 - *extended mutations*
To predict resistance to anti-estrogen therapies (tamoxifen, fulvestrant, exemestane and letrozole) (5% incidence).

PROTEINS

TOP2A - *over-expression*
To predict good prognosis for the overall survival but also good prognosis to TOP2A inhibitor (liposomal doxorubicin).

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, atezolizumab* and nivolumab*).

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 good prognosis to mTOR inhibitors (temsirolimus* and everolimus) or dual PIK3CA/mTOR inhibitor (LY3023414)**.

** : Drugs FDA approved for other indications.* *** : Drugs in development*

1 Rue Louis Breguet
B-6041 Gosselies, Belgium
+32 (0)71 18 35 00
infos@oncodna.com
www.oncodna.com

• For Drugs in Development

DNA / RNA

FGFR1/2/3 - *extended mutations, copy number and translocation testing*
To predict good prognosis to anti-FGFRx treatments (AZD4547) and resistance to anti-estrogen therapies (22% incidence).

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) .

* *: 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:

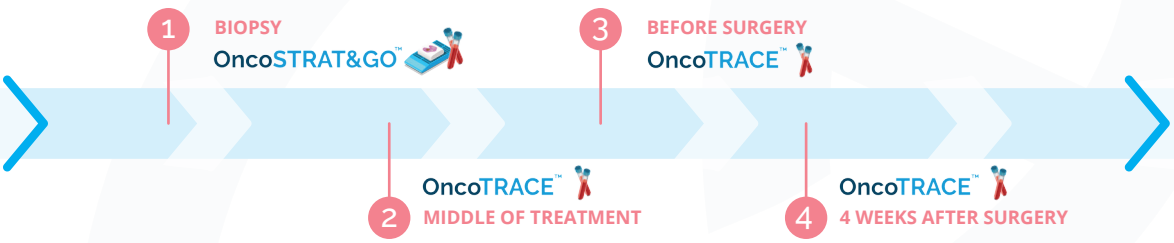
- ✗ Early evaluation after treatment start is difficult because tumor shrinkage can only be detected after several therapeutic cycles.
- ✗ Response is non-evaluable when disease is not measurable (liquid effusion, follow-up post complete tumor resection...)

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.

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