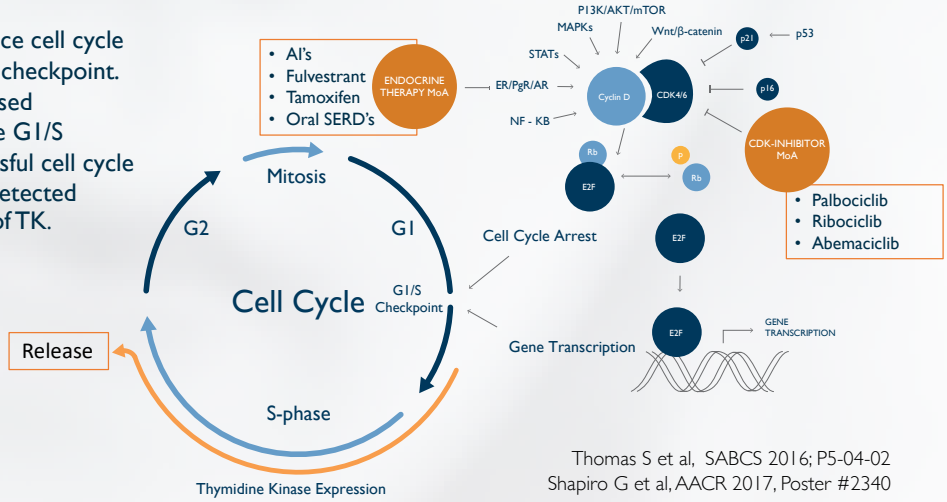
DiviTum® TK assay from Biovica

Thymidine kinase activity biomarker for cancer therapy drug development

TK ACTIVITY – SCIENTIFIC RATIONALE FOR EFFICACY EVALUATION OF CELL CYCLE REGULATING DRUGS

Specific drugs induce cell cycle arrest at the G1/S checkpoint. Since TK is expressed downstream of the G1/S checkpoint, successful cell cycle inhibition can be detected as changed levels of TK.



TK=Thymidine Kinase

Thomas S et al, SABCS 2016; P5-04-02
Shapiro G et al, AACR 2017, Poster #2340

DRUG DEVELOPMENT AND CLINICAL RESEARCH

Thymidine kinase (TK) activity is a biomarker closely related to cell proliferation. The DiviTum® assay allows even small changes in TK activity to be measured accurately and quickly both in cell cultures and animal studies during pre-clinical evaluation.

In clinical trials, DiviTum® is a non-invasive test for TK activity in a serum sample for evaluation of in vivo effects of candidate drugs inhibiting the E2F pathway producing cell cycle arrest.

BIOMARKERS AS TOOLS FROM IN VITRO STUDIES TO CLINICAL TRIALS

CELL CULTURES

- Early Evidence of effect
- Validate targets
- Dose-Response studies

ANIMAL MODELS

- Improved animal model evaluation
- Serum-bridge human trials
- Better support for clinical development

CLINICAL TRIALS

- Early signals of PFS and OS
- Improved evidence in clinical evalution & development
- More informed decision making in trial strategy

WIDE APPLICATION RANGE

DiviTum® is a useful research tool for the pharmaceutical industry for evaluating cell-cycle regulating compounds, CDK inhibitors and endocrine drugs. DiviTum® has a broad application area – DiviTum® can be used all the way from cell culture studies to clinical trials for drug approval. Several clinical trials have demonstrated that DiviTum® accurately reflects the effect of CDK-inhibitors on cell proliferation rate.

CLINICAL STUDIES

DiviTum® has demonstrated its value as a monitoring tool for the treatment of breast cancer by two major therapeutic strategies (endocrine treatment and CDK4/6 inhibitors) as well as a significant correlation to the commonly used tissue proliferation marker Ki67. The market potential of DiviTum® is even greater since there are many other forms of solid tumors and novel cell cycle regulating therapies under development.

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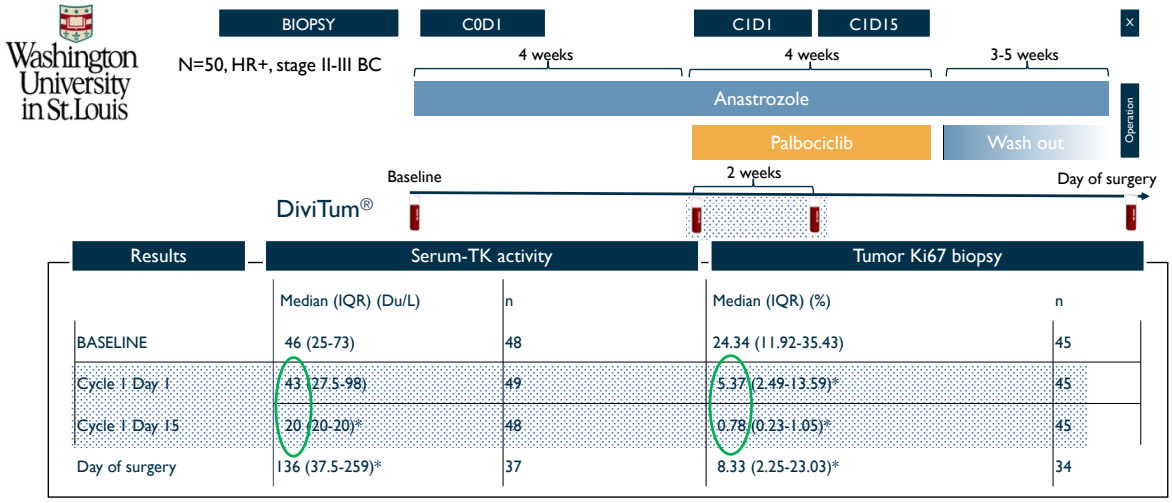
EXPLORATIVE RESEARCH – CDK4/6 INHIBITOR EFFICACY IS REFLECTED BY CHANGES IN STK WITH HIGH CORRELATION TO KI67



Results	Serum-TK activity		Tumor Ki67 biopsy	
	Median (IQR) (Du/L)	n	Median (IQR) (%)	n
BASELINE	46 (25-73)	48	24.34 (11.92-35.43)	45
Cycle 1 Day 1	43 (27.5-98)	49	5.37 (2.49-13.59)*	45
Cycle 1 Day 15	20 (20-20)*	48	0.78 (0.23-1.05)*	45
Day of surgery	136 (37.5-259)*	37	8.33 (2.25-23.03)*	34

*p<0.001 compared to the preceding time point

Bagegni N et al, Breast Cancer Research and Treat 2017:19;123

BENEFITS WITH DIVITUM®

- Provides key information across the drug development continuum.
- Gives dose-response and early signals of effect in preclinical studies.
- A bridge between in vitro effects and clinical study outcome.
- Increases approval probability, reduce attrition and cost.
- A "liquid Ki67" to complement other molecular and imaging biomarkers.

FLEXIBLE AND EASY TO USE

The ELISA technology is a well-established, standardized platform and can be used with a wide range of open systems and with individual research protocols. DiviTum® results are easy to interpret and available within 6–8 hours.

Product code	Item number 950 DiviTum® V2 RUO
Format	96 well plate ELISA
Detection target	Thymidine kinase activity
Tests	40 samples in duplicate, 2 controls and 4 standards in duplicate, 4 background wells
Sample type	Serum (100 µL) / cell culture
Calculation	Semi quantitative
Detection range	90-4000 Du/L
Incubation time	180 + 60 + 30 minutes
Detection system	405 nm and 630 nm for reference
Storage	–18° C
Availability	RUO version

RECOMMENDED READING / REFERENCES

1. Bagegni N et al, Breast Cancer Research and Treat 2017;19:123
2. Shapiro G et al, AACR 2017; Poster #2340
3. Bonechi M et al, Oncotarget 2018;9:16389-16399
4. Malorni L et al, ASCO Annual Meeting 2018; abstract #12031
5. Bonechi M et al, SABCS 2018; Poster P6-09-02

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