THE VALUE OF PROLIFERATION BIOMARKERS

MATTIAS BERGQVIST, Vice President, Clinical Development, **Biovica International**

Mattias Bergqvist is Vice President Clinical Development at Biovica and has over 20 years of experience from the pharmaceutical and biotechnology industry. He has global responsibility for clinical development programs focused on providing proliferation markers in the evaluation of novel oncology drugs. Mattias has authored a number of publications in peer-review journals and studies presented at global scientific conferences.

What key things can a biomarker contribute with during preclinical and clinical drug development?

A biomarker should ideally be able to:

- provide key information across the development continuum
- give dose-response information and early signals of efficacy in vitro
- provide mode of action evidence of target efficacy
- bridge between cell cultures and studies in human
- complement other methods and markers adding valuable data to tollgate decisions
- predict outcome and give early indication of response/ progression in target population
- increase approval probability and speed to market, reduce attrition and cost.

How can proliferation biomarkers add value when evaluating oncology drugs?

Tumors are characterized by uncontrolled cell growth. Biomarkers that measure cell proliferation can be used to measure cell growth rate and provide early information of dose-response, in vitro efficacy, assist in tumor type selection, predict outcome and monitor efficacy. Analyzing the present growth rate can predict future response and time to progression instead of looking at volume change that reflects what has already happened. Ki-67 has been used for a long time to measure cell proliferation but requires a biopsy. Ideally, a proliferation biomarker can be used in cells and blood, providing a bridge between preclinical and clinical studies. Thymidine kinase (TK) activity is such a biomarker.

Are there specific oncology drugs that can be targeted with proliferation biomarkers?

There are many novel drugs within oncology aiming to slow down or shut down cell growth. Many different signaling pathways are targeted that inhibit the cell cycle and shut down uncontrolled cell proliferation. Serum TK activity have demonstrated to be a strong pharmacodynamic marker for new, targeted drugs like CDK4/6 inhibitors and an early efficacy marker for evaluating endocrine therapy. In the era of immuno-oncology and targeted therapy new markers are needed to provide information on surrogate endpoints, cell growth inhibiting potential and apoptosis.

New results with a serum proliferation biomarker, the DiviTum TK activity assay, has recently been presented in breast cancer. What did the new data reveal?

In a study of 142 women with metastatic breast cancer (presented at the 2017 San Antonio Breast Cancer Symposium, P3-08-13) it was demonstrated that DiviTum is an easy, fast and flexible method that predicts progression free- and overall survival. At all measured time points; diagnosis and after 1, 3 and 6 months of therapy, DiviTum accurately predicted outcome. This dramatic shortening of the evaluation window, already after one month of therapy, can be key when making decisions to continue or change treatment and can contribute significantly to improve patient outcome.

In another breast cancer study serum TK reflected the activity of two weeks of treatment with the CDK4/6 inhibitor palbociclib in combination with endocrine therapy. The results also demonstrate that serum TK correlate significantly with Ki-67 (Bagegni N *et al*, Breast Cancer Res. 2017 Nov 21;19(1):123)