Quantitative HER2 protein expression analysis in multiple cancer indications: Identification of candidates for HER2 targeted therapies

Abstract # P5.2

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Background

- Successful, personalized cancer treatment requires the integration of both genomics and proteomics profiling to identify which therapies will likely be most beneficial for an individual patient, based on the biomarker fingerprint for each patient's unique tumor.
- Patients with HER2-positive breast and gastric cancers have responded remarkably well to anti-HER2 therapy, prompting ongoing trials of such therapies in other indications.
- NantOmics multiplexed mass spectrometry (MS)-based proteomic analysis objectively quantifies HER2 and other actionable biomarkers from two FFPE tissue sections. High HER2 protein levels (≥ 740 and ≥ 750 amol/ug in breast and gastric cancers, respectively), as measured by targeted MS, correlate with standard measures of HER2 positivity [1,2]. HER2 levels ≥ 2200 amol/ug were associated with longer OS [2].
- We hypothesized that targeted proteomics would identify high expression of HER2 (≥ 2200 amol/ug) in a range of tumor types, providing the potential to enroll in anti-HER2 clinical trials and may correlate with clinical benefit.

Methods

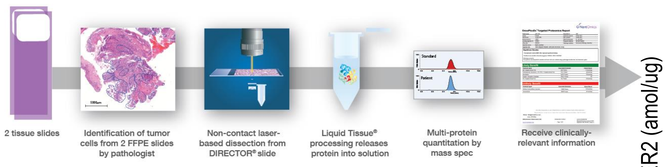


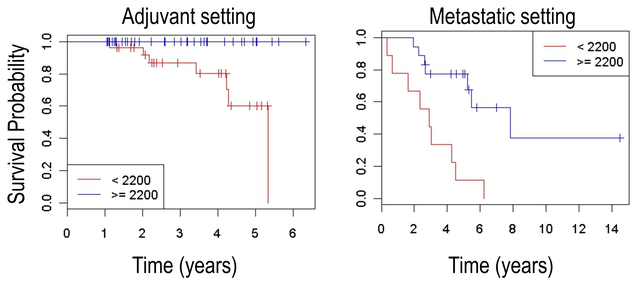
Figure 1: Microdissected tumor areas from FFPE tissue blocks (n=3,444) representing multiple indications were subjected to Liquid Tissue® and MS to quantify multiple protein targets in each patient sample.

Multiplexed Clinical Proteomics Menu

AR, ALK, AXL, CK-5, CK-7, EGFR, ERCC1, FGFR2, FR-alpha, hENT1, HER2, HER3, IGF1R, MET, MGMT, MSLN, PD-L1, p16, RON, ROS1, RRM1, SPARC, TOPO1, TOPO2A, TP63, TUBB3, TTF1

Results

HER2 expression above 2200 amol/ug in breast cancer correlates with increased survival



OVERALL SURVIVAL (OS)		
HR	CI 95% (HR)	p value
na*	na	0.001

OVERALL SURVIVAL (OS)		
HR	CI 95% (HR)	p value
0.20	0.07-0.57	<0.001

*Hazard ratio for OS cannot be determined because all patients with >2200 amol/µg of HER2 were alive after 6 years of anti-HER2 therapy

Figure 2. HER2 levels ≥ 2200 amol/ug were associated with longer OS (2).

HER2 super-expression in multiple tumor indications

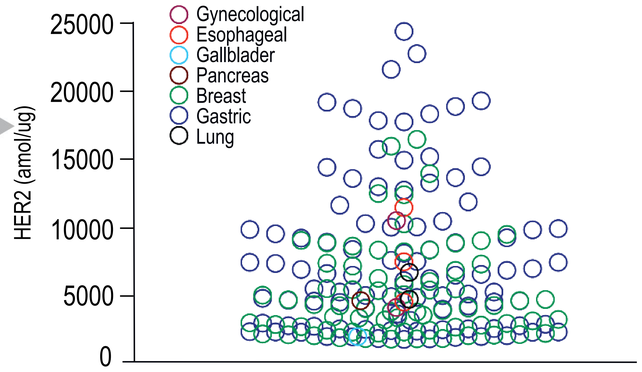


Figure3. HER2 ≥2200 amol/ug in multiple indications may be predictive of enhanced response to trastuzumab.

Response to trastuzumab in gallbladder cancer patient

Patient

Male, age 74; Invasive gallbladder adenocarcinoma

NantOmics Multiplex analysis

Protein marker	Patient Result (amol/ug)
HER2	3105
EGFR	152
HER3	199

1st line therapy

gemcitabine + cisplatin

6 months

Treatment response

- Disease progression
- Increase in CA19-9

Treatment plan

FOLFIRI + trastuzumab

5 months

Treatment response

Positive (RECIST)

Figure 4. A patient with gallbladder cancer had very high HER2 expression (3105 amol/ug) that responded to trastuzumab therapy.

Multiplex proteomic analysis identifies multiple therapeutic options in uterine cancer patient

A

Patient

Female, age 73; Uterine cancer

Initial diagnostic assessment

IHC of mismatch repair proteins was found to be normal. Equivocal HER2 status by genomic analysis.

NantOmics Multiplex analysis

Assay	Protein marker	Patient Result (amol/ug)	Implication
pembrolizumab	PDL1	ND	Unlikely to respond
trastuzumab	HER2	4995	Potential benefit
docetaxel	TUBB3	ND	Potential benefit
doxorubicin	TOPO2A	472	Unlikely to respond
pemetrexed	FRalpha	10500	Potential Benefit

B

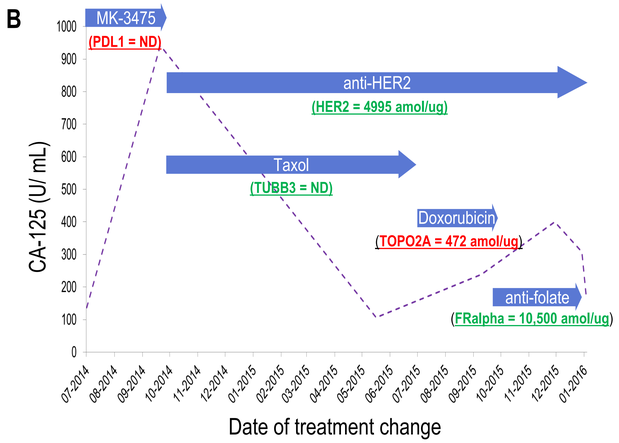


Figure 5. A, B. Multiplex-MS analysis in uterine carcinoma patient identified multiple potential therapies.

Conclusions

- Personalized medicine should include the use of proteomic as well as genomic profiling to characterize all potential biomarkers which may direct therapies.
- Targeted Mass Spec-based proteomics offers a multiplexed, extremely sensitive, uniquely precise and highly reproducible method for tumor biomarker profiling and quantification to identify potential therapies.
- Patients with high HER2 protein expression (≥2200 amol/ug) in multiple cancer types benefit from anti-HER2 targeted therapies.
- Based on these and additional case studies, broader proteomic testing of tumor HER2 expression could extend the benefit of HER2 targeted therapy.

Reference

1. Catenacci, D.V., et al.; Gastric Cancer, 2015.
2. Nuciforo, P., et al.; Mol Oncol, 2016. **10**(1): p. 138-47.