



Companion diagnostics

SNP panel to predict lack of response to bisphosphonate treatment

Value proposition and Field of application

Potential DNA microarray/chip to detect an inheritable risk in a blood sample of non-response to Zoledronic acid treatment and for early death for women with breast cancer and bone metastases.

Technological description

Breast cancer-induced bone disease often continues to progress although patients are given anti-resorptive treatment (bisphosphonates, BPs). Up to 50% of breast cancer (BC) patients receiving monthly zoledronic acid treatment have new skeletal related events (SRE) within 1 year of starting treatment and up to 65% within 2 years. This clearly suggests that the suppression of bone resorption is far less potent than what could theoretically be expected.

We have found that patients possessing specific genetic variations in four genes make them more susceptible to aggressive bone resorption than others once the metastasis nests in the bone marrow.

Table: Multiple logistic regression results for prediction of mortality using 4 SNP profile, from 50 females.

Variable	Estimate (SE) [95% CI]	Odds Ratio (OR) [95% CI]	Z-score	p-value
Intercept	-3.781 (1.483) [-7.705 – 1.571]	0.02280 [0.0004507 – 0.2079]	2.549	0.0108
RANKL (TT genotype)	2.478 (1.319) [0.1170 – 5.757]	11.92 [1.124 – 316.5]	1.878	0.0604
FDPS (AG genotype)	1.159 (2.002) [-3.004 – 5.426]	3.186 [0.04953 – 227.2]	0.5788	0.5627
FDPS (TG genotype)	1.455 (1.790) [-1.685 – 5.655]	4.283 [0.1854 – 285.8]	0.9127	0.4164
ESR1 (AA genotype)	1.189 (1.019) [-0.7916 – 3.321]	3.283 [0.4531 – 27.68]	1.166	0.2434
Area under the ROC curve (AUC):				
Area	0.8516			
SE	0.09695			
95% CI	0.6615 – 1.000			
p-value	0.0033			

Epidemiology & Numbers

- **WHO:** in 2020, 2.3 million women was, globally, diagnosed with breast cancer and 7.8 million were alive 5 years after diagnosis
- App. 80% with the newly diagnosed BCs are postmenopausal and are receiving adjuvant treatment with Zoledronic acid
- Approximately 12% of all BCs metastasise to the bone (numbers from Denmark) and 1/4 of these women do not respond to Zoledronic acid.

Current state of development

The SNPs is identified in 49 samples from women with BC metastasized to the bones. We will investigate the presence of the 4 SNPs in other patient groups suffering from bone resorption and that are treated with BPs, such as women suffering from osteoporosis and bone metastases in males derived from prostate cancer. This, to investigate if the 4 SNPs are likewise predictive of lack of sensitivity to BPs and the disastrous outcome.

The TEAM



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Intellectual property rights

Patent application was filed for priority February 2023.

Business opportunity and Call to action

We are seeking out-licensing or collaboration to develop the DNA microarray/chip for marketing and sales.

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