AminoIndex™ Cancer Screening (AICS) Follow-Up Study, Interim Analysis Report.

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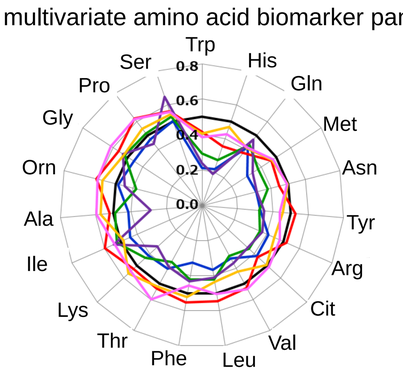
Summary

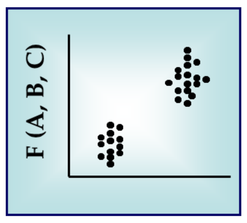
Backgrounds: AminoIndex™ Cancer Screening (AICS) is a test to evaluate the likelihood of having a cancer, such as gastric, lung, colorectal, pancreatic, prostate, breast, and gynecological cancer, from only 5ml blood sample. The large-scale study to evaluate its performance in actual clinical field was yet to be implemented.
Aim of this study: Aimed to evaluate the effectiveness of AICS in actual clinical field, we started AICS Follow-Up Study in 2012, which is a prospective cohort study and one of the projects supported by Life Innovation in Keihin Coastal areas Comprehensive Special Zones for International Competitiveness Development.
Conclusion: We performed interim analysis against 5490 participants' clinical information. Among participants classified in the AICS rank C category, 26.5% had detailed examination and 5 participants were diagnosed with cancer. Within the AICS rank C category, some forms of precancerous states were diagnosed as well. Here we report the results of interim analysis, and we will continue the study to finally evaluate the effectiveness of AICS.

AICS

A blood based multivariate amino acid biomarker panel for aid in early detection of cancer.



Amino Acid Balance



AICS
(AminoIndex™ Cancer Screening)

One blood test enables evaluations of probability of having one or more cancer types from early to late stages, according to AICS values calculated from plasma amino acid concentrations.
Male : Gastric, Lung, Colorectal, Pancreatic, Prostate
Female : Gastric, Lung, Colorectal, Pancreatic, Breast, Gynecological

Cut off value

Specificity 80% Specificity 95%

Rank Classification	rank A	rank B	rank C
AICS value	0.0～4.9	5.0～7.9	8.0～10.0

Low ← Possibility of cancer → High

AICS value and rank classification

As shown in upper Fig., the minimum and maximum AICS values are 0.0 and 10.0, respectively, and the AICS values for specificities of 80% and 95% for each cancer are defined as 5.0 and 8.0, respectively.
We presume that the higher the subject's AICS value, the greater the likelihood that the subject is suffering from cancer.

AICS values are divided into 3 categories: rank A, <5.0; rank B, 5.0-7.9, rank C, ≧8.0.
The rank B and C cutoff are defined as 5.0 and 8.0, respectively.
Thus, if the specificity is 95%, then 5% of the healthy controls are assessed as rank C (a false-positive rate of 5%), whereas if the specificity is 80%, then 20% of the healthy controls are assessed as rank B or C (a false-positive rate of 20%).

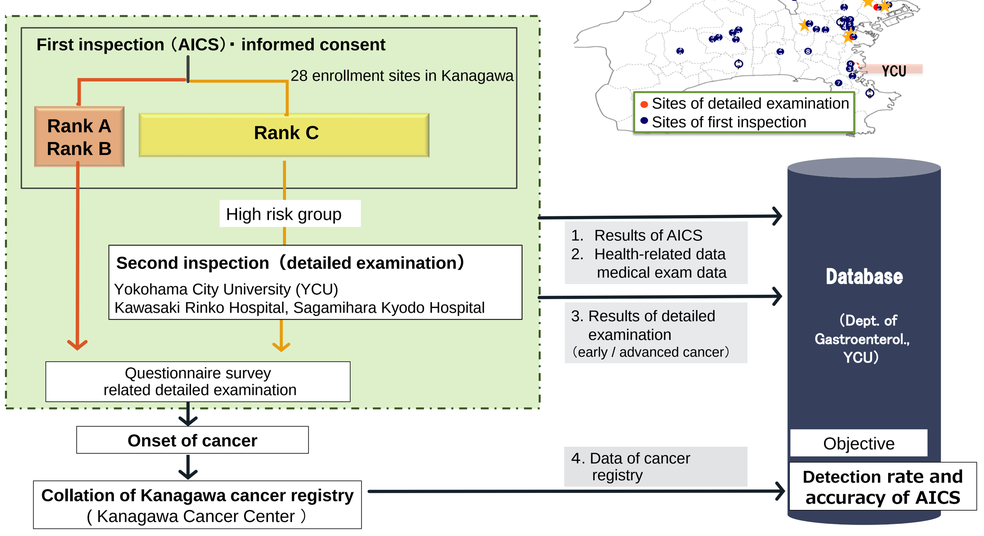
Life Innovation in Keihin Coastal Areas Comprehensive Special Zones For International Competitiveness Development

In 2011, Kanagawa Prefecture, Yokohama City, and Kawasaki City was specified by the country as "Life Innovation in Keihin Coastal Areas Comprehensive Special Zones for International Competitiveness Development".
In this special zone, special measures are allowed in support of creation, development, and manufacturing of health-related industries, such as innovative pharmaceuticals and medical devices, regenerative medicine, diagnosis and preventive medicine. The local governments promote these industries together with global companies, local small and medium-sized enterprises, universities, and research institutions.

From 2012, we conduct follow-up study as collaborative investigation with Ajinomoto Co., Inc., under the support of Keihin Coastal Areas Comprehensive Special Zone.
We are building a regional medical cooperation network in Kanagawa Prefecture, with Yokohama City University as its center.

AICS follow-up study

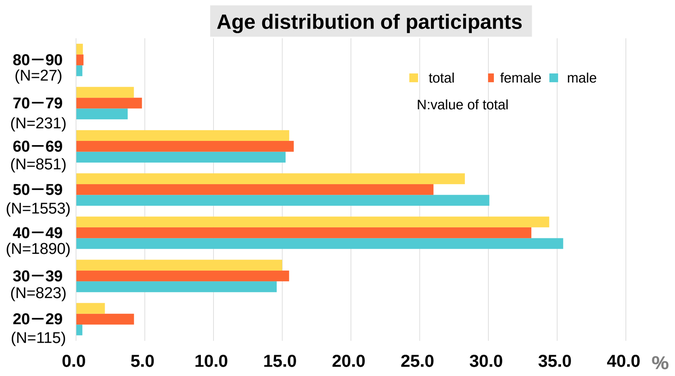
Study design : prospective cohort study



Enrollment & Study Population (interim analysis)

- Participants:**5490（50±11）** Male:**3090（50±10）** Female:**2400（50±12）** ● Age:**24～87**
- Date of informed consent:**2013/6/24～2017/1/24**
- Number of detailed examination:**654** ● Number of cancer registry:**650**

Age distribution of participants



Participants (N=5490)
- **Detailed examination (N=654)**
- **Cancer registry (N=650)**

Results of detailed examination (AICS rank C)

gastric

No. of exam		118
method	endoscopy	114 (96.6%)

No. of finding	
atrophic gastritis	44 (37.3%)

lung

No. of exam		130
method	CT	128 (98.5%)

No. of finding	
cancer	1 (0.77%)
old inflammatory change	17 (13.1%)
bronchiectasis	1 (0.77%)

colorectal

No. of exam		106
method	colonoscopy	104 (98.1%)

No. of finding	
cancer	1 (0.94%)
polyp (≧5mm)	23 (21.7%)

pancreatic

No. of exam		44
method	CT (using contrast)	36 (81.8%)
	CT (detail unknown)	7 (15.9%)
	echo	1 (2.27%)

No. of finding	
IPMN (including suspicion)	3 (6.82%)

prostate

No. of exam		86
method	digital	39 (45.4%)
	PSA	29 (33.7%)
	echo	16 (18.6%)
	urinalysis	10 (11.6%)
	MRI	3 (3.49%)
	biopsy	1 (1.16%)

No. of finding	
cancer	2 (2.33%)
benign prostatic hyperplasia	7 (8.14 %)
dysuria	2 (2.33%)

breast

No. of exam		76
method	mammography	66 (86.8%)
	echo	65 (85.5%)
	MRI	3 (3.95%)
	cytodiagnosis	1 (1.32%)
	needle biopsy	1 (1.32%)

No. of finding	
cancer	1 (1.32%)
calcification	5 (6.58%)
mastopathy	2 (2.63 %)
fibroadenoma	1 (1.32%)

gynecological

No. of exam		62
method	cervical cytology	54 (87.1%)
	cytodiagnosis of corps uteri	41 (66.1%)
	tumor marker	28 (45.2%)

No. of finding	
uterine fibroids	3 (4.84%)
benign ovarian tumor	2 (3.23%)

- No. of AICS rank C (all cancer types) : **2346**
- No. of participants who had detailed examination : **622**
- Rate of having detailed examination : **26.5%**
- Mean age : **51±11**

Follow-up about detailed examination with the use of written questionnaires took place between November 2016 and May 2017. (The rate of response was 50%.)

Theoretical and actual number of cancer found from detailed examinations (AICS rank C)

	AICS rank C (N)	Detailed exam (N)	Rate of having detailed exam (%)	AICS Positive Predictive value (theoretical value) (%)	Expected No of cancer to be found from exam (N)	Actual No of cancer found from exam (N)
gastric	530	118	22.3	1.04	1.2	0
lung	418	130	31.1	0.78	1.0	1
colorectal	403	106	26.3	1.00	1.1	1
pancreatic	152	44	28.9	0.30	0.1	0
prostate	400	86	21.5	0.80	0.7	2
breast	258	76	29.5	0.49	0.4	1
gynecological	185	62	33.5	1.00	0.6	0
total	2346	622	26.5	–	5.1	5

Each incident of cancer found from cancer registry

	Rank of AICS (gastric lung colorectal prostate breast gynecological)	Date of informed consent	Sex	Age	Date of diagnosis	location	Neoplasm progress	Main cure	Alive
lung	A **C** C B – –	2014/6	Male	65	2014/8	upper lobe	localized	symptomatic treatment	alive
colorectal	B A **C** – A A	2013/8	Female	68	2013/11	colon	–	symptomatic treatment	alive
uterine	A A A – A A	2013/9	Female	33	2014/7	cervix	In situ	completely removing	alive
esophagus	B A C C – –	2014/9	Male	75	2014/9	region of chest	spread to lymphnodes	chemo-therapy	alive

Incident rate of cancer in AICS rank C 2/650 =0 .31%

For about 650 participants enrolled between 2013 and 2014 with written informed consent, we obtained information of morbidity and death by cancer from Kanagawa cancer registry.

COI Disclosure Information

Lead Presenter/Responsible Researcher:

Shin Maeda

I have the following financial relationships to disclose.
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