

Current Status Concerning Cancer-Cachexia Syndrome in Japan

~ Challenge to improve functional prognosis ~

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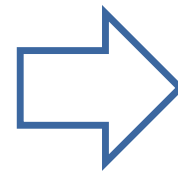


June 29, 2018 (Friday) in JASCC/MASCC joint session at Vienna

And today,
Cachexia was not yet overcome

BMI (kg/m²)

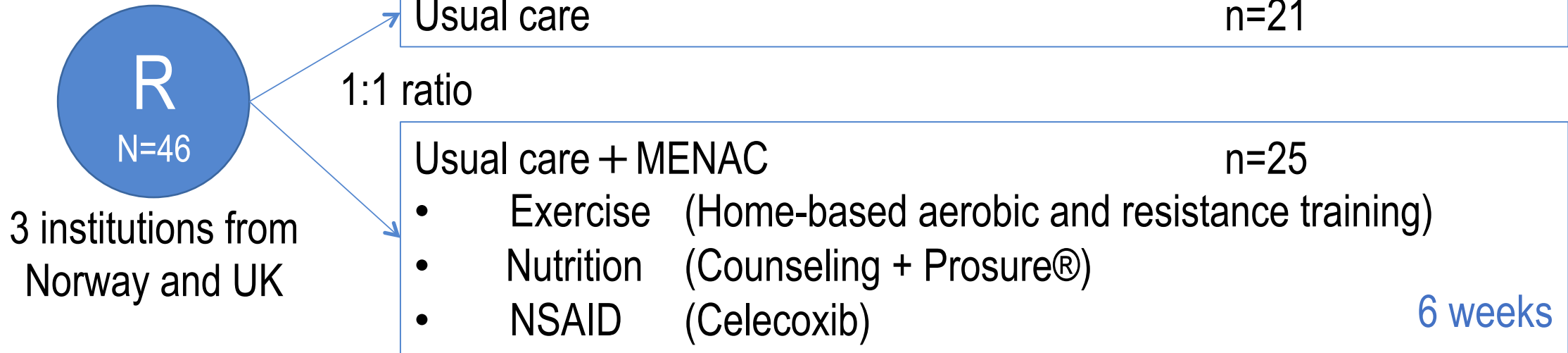
		28	25	22	20	
Weight Loss (%)	2.5	0	0	1	1	3
	6	1	2	2	2	3
	11	2	3	3	3	4
	15	3	3	3	4	4
	15	3	4	4	4	4
	15	3	4	4	4	4



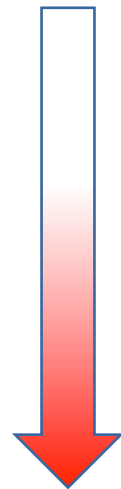
Grade	Estimated Survival time
0	21 months
1	15 months
2	11 months
3	8 months
4	4 months

Pre-MENAC study

Patients: Advanced pancreatic or non-small-cell lung cancer, KPS \geq 70



Number of interventions increases



Combinations	Compliance
Single intervention	76% in NSAIDS
	60% in Exercise
	48% in Supplements
2 combinations	20 – 48%
3 combinations	12%

Solheim TS, Journal of Cachexia, Sarcopenia and Muscle, 2017

Nutritional and EXercise Treatment for Advanced Cancer - The NEXTAC program -

The JASCC cachexia study group

Chief: Koichi Takayama, MD

Kyoto prefectural university of medicine



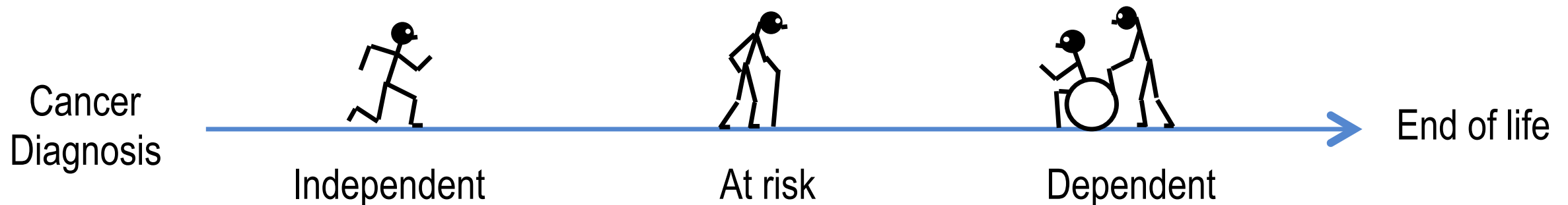
Support from the grant in aid for the Japan Agency
for Medical Research and Development (AMED)

Core concepts of the NEXTAC

We aim to develop a new multimodal intervention specific for **elderly** cancer patients to prevent disability.

It was designed to ...

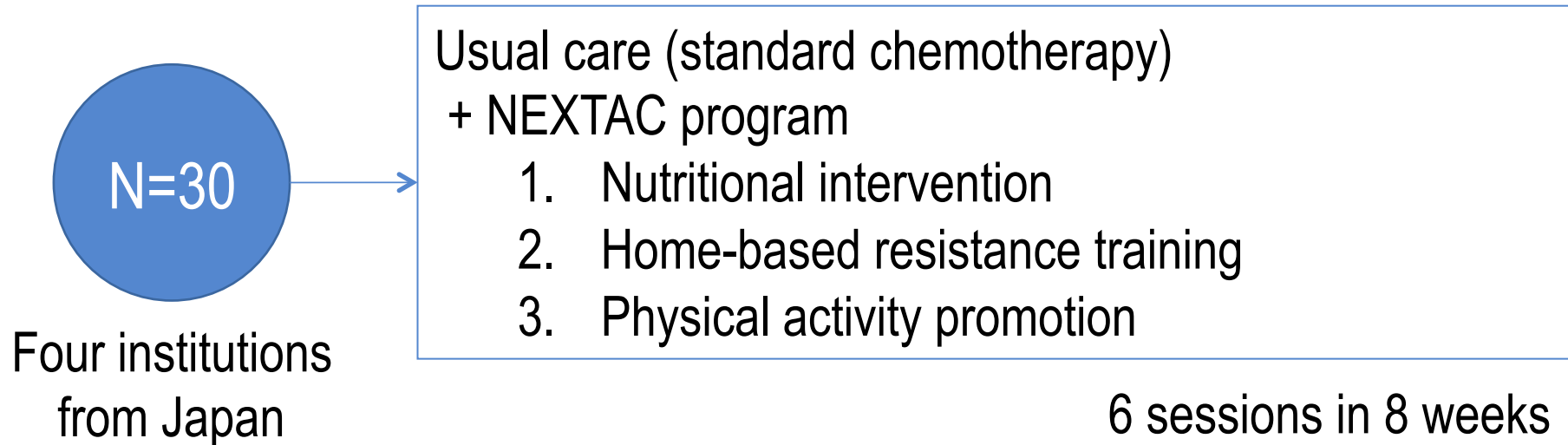
1. Be accepted not only by fit elderly but also **frail** elderly
2. Maximize compliance **without** reducing efficacy
3. Start as **early** as possible
4. Keep motivation and promote behavioral changes by **education**



The NEXTAC-ONE feasibility study

Patients:

Advanced NSCLC or Pancreatic cancer, being to start chemotherapy
ECOG-PS 0-1, ≥ 70 y.o., no disability (Barthel index ≥ 95 points)



Endpoint

Primary: Feasibility (attendance, threshold 0.45, expectation 0.70)

Secondary: Safety, Compliance, Adherence

1. Nutritional Intervention

- 1) Nutritional advice
- 2) BCAA-rich supplements
- 3) Management of NIS (nutritional impact symptoms)
e.g. mucositis, taste disturbance, and anorexia



BCAA: branched-chain amino acid

2. Home-based resistance training

Level	Prescription
1	Sit and stand up + Calf raises + Knee extensor
2	Level 1 + Hip flexion + Hip Abductor
3	Level 2 + Strap 1kg weight on ankle

Sit and stand up



Calf raises



Hip flexion



±


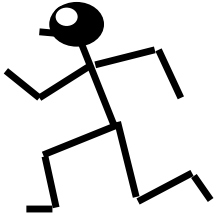
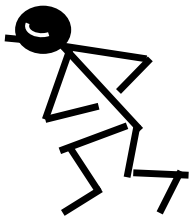

Knee extensor



Hip Abductor



3. Physical activity Promotion

	4 steps	Examples
	Goal setting & Feedback	<ul style="list-style-type: none">• Set step goal: baseline + 2000 steps• Self-monitoring: taking diary
	Action planning	<ul style="list-style-type: none">• Regular walking & House chores• Stay in the job
	Active management of symptoms	<ul style="list-style-type: none">• Cosmetic problems (e.g. Skin rash)• Physical problems (e.g. Diarrhea)
	Fall prevention	<ul style="list-style-type: none">• Do not use sandals or slippery shoes• Maintain a clutter-free floor

Patient characteristics

Variables	N = 30
Median age (range)	75 (70-84)
Women:Men	10:20
ECOG-PS	n (%)
0	11 (37)
1	19 (63)
Lung cancer	24 (80)
Pancreatic cancer	6 (20)
Stage IV	27 (90)
Chemotherapy	
Cytotoxic	20 (67)
Targeted	10 (33)
Lifestyle, n (%)	
Unemployed	18 (60)
No exercise habit	16 (53)
Living alone	4 (13)
Nutritional status	
Cancer cachexia	12 (40)
Skeletal muscle depletion	21 (70)

Feasibility was defined as attendance

Sessions	Proportion
Nutritional sessions	98%
Exercise sessions	97%
Total attendance ratio (95% CI) % of patients who attended $\geq 2/3$ sessions	97% (83-99)

Statistical design
Expected proportion: 70%
Threshold proportion: 45%

This study met the primary endpoint and the NEXTAC is feasible.

Compliance

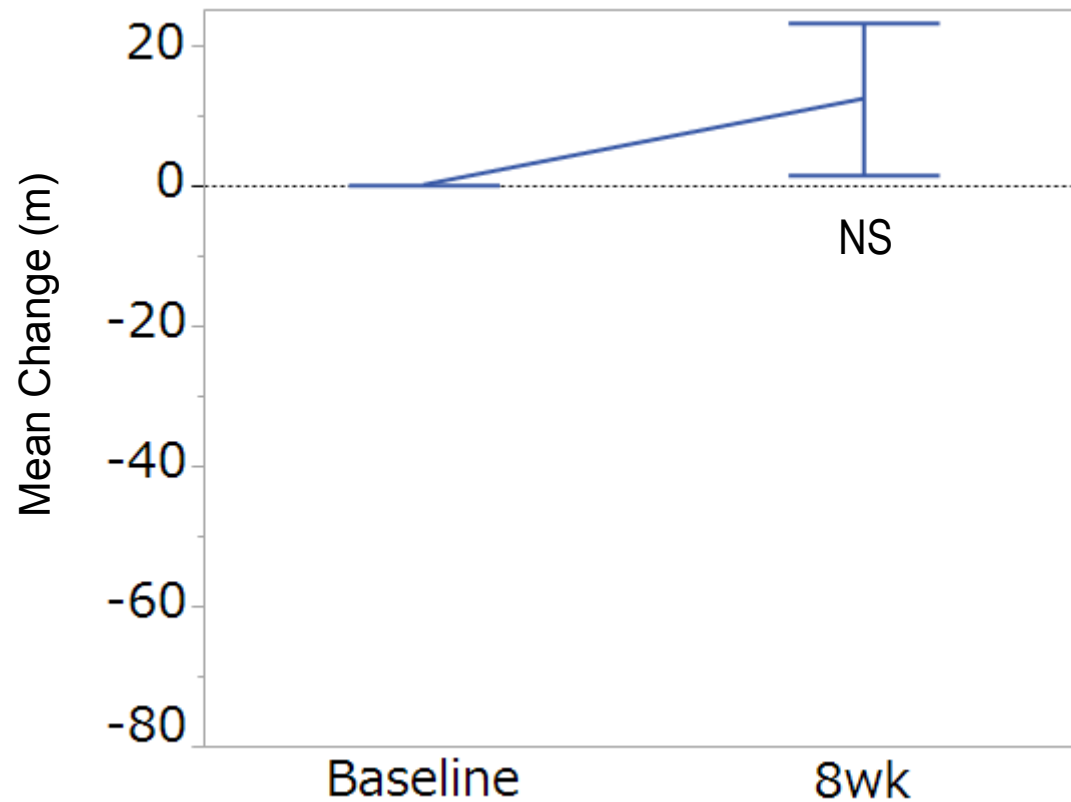
Number of patients	29
Nutrition	Median % (IQR)
Diet diary fill-in day	90 (14-98)
Supplement consumption day	99 (88-100)
Daily resistance training	
Exercise diary fill-in day	94 (51-98)
Performance day	91 (69-95)
Physical activity	
Pedometer wear day (≥ 5 h/day)	98 (85-100)

Adherence

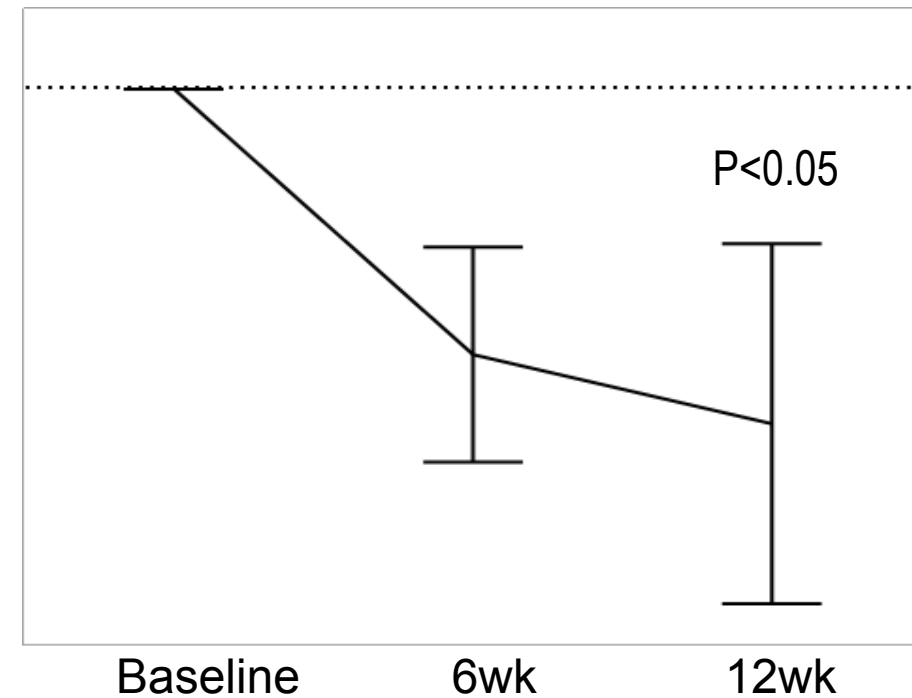
Period	First month N (%)	Second months N (%)
Number of patients	29	29
Nutrition		
Adequate caloric intake	25 (89)	25 (86)
Adequate protein intake	24 (83)	24 (83)
Physical activity		
Indoor activity ↑ or →	25 (86)	23 (79)
Outdoor activity ↑ or →	20 (69)	20 (69)
Daily steps ↑	20 (69)	13 (45)

Change in 6-minute walk distance

NEXTAC-ONE study

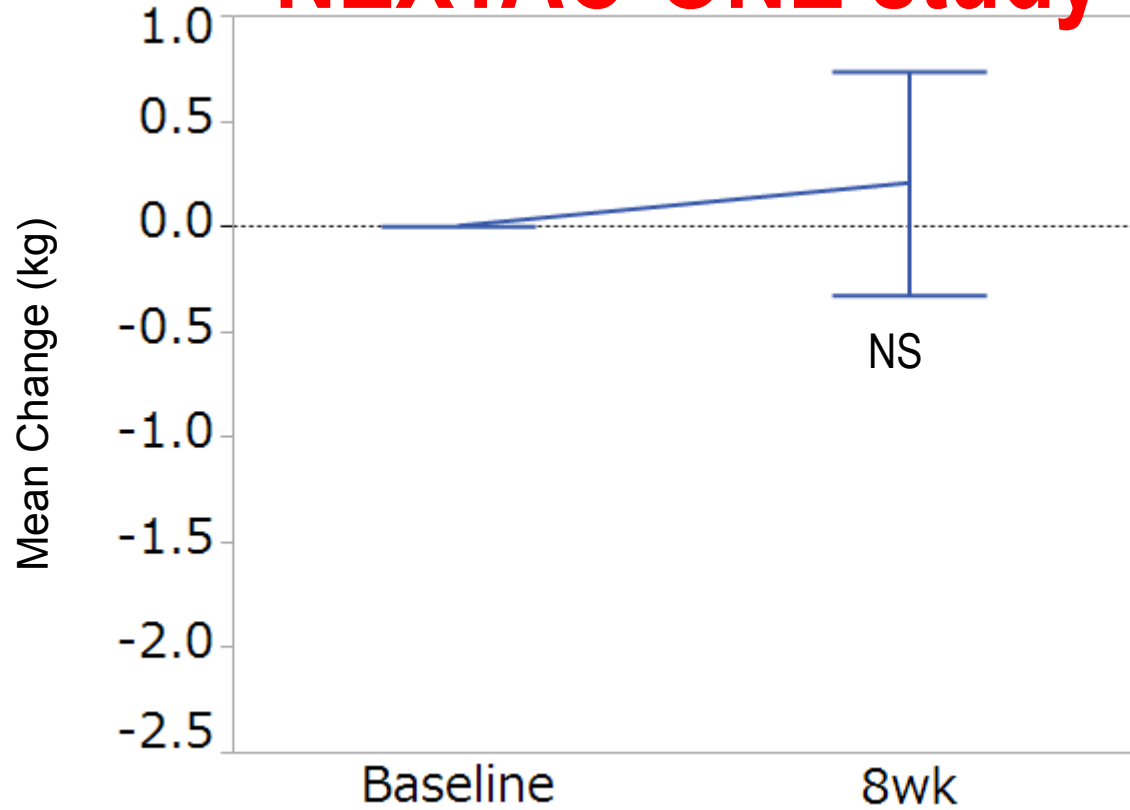


Historical control

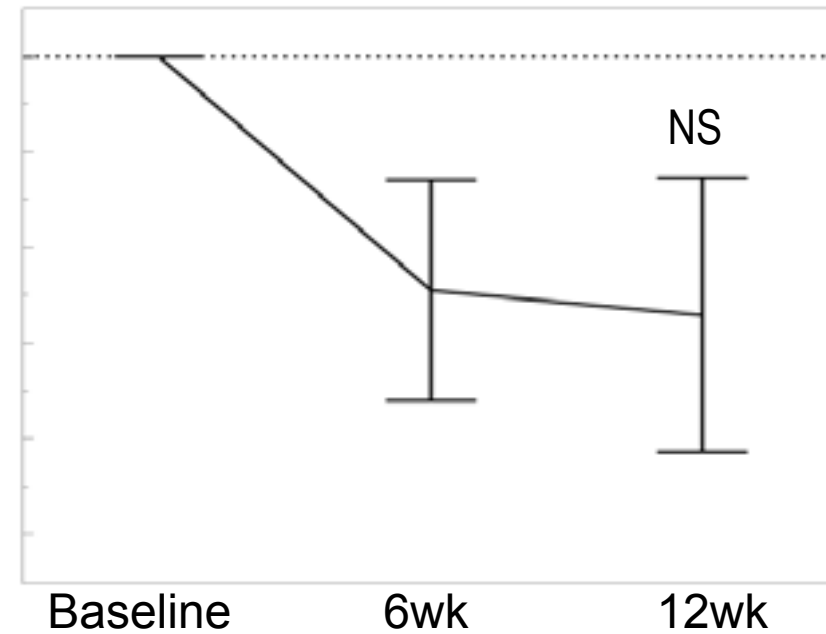


Change in Hand-grip strength

NEXTAC-ONE study

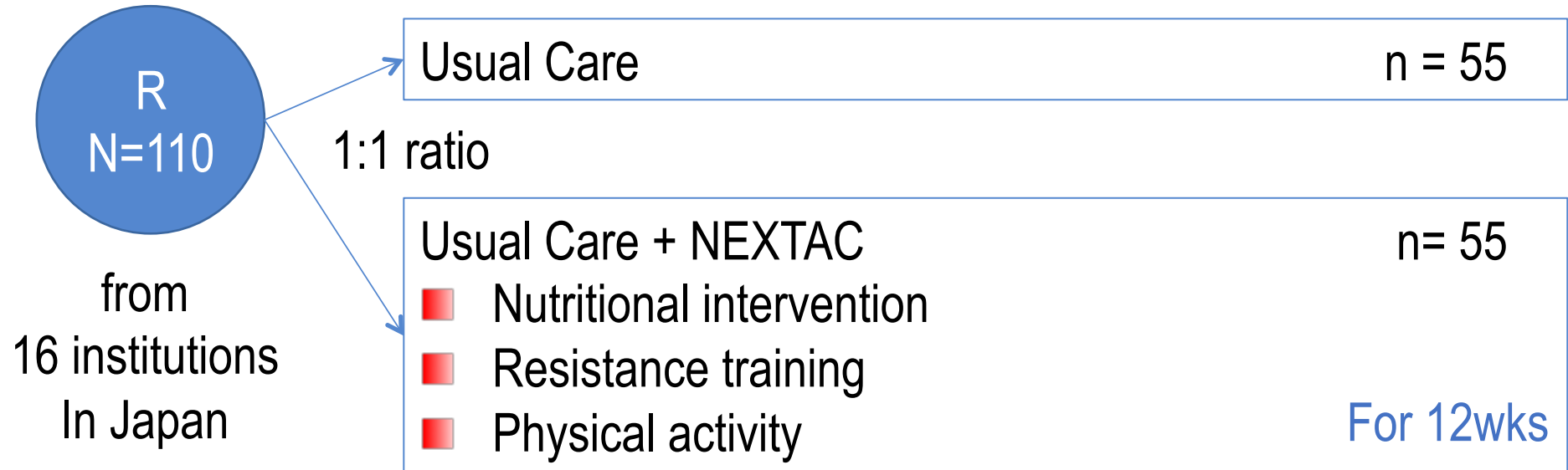


Historical control



The NEXTAC-TWO study, a randomized P2 study

Patients: Advanced NSCLC or Pancreatic cancer, ECOG-PS 0-2



Primary Endpoint

Disability-free survival

Definition: Time until development of disability
(modified KATZ index)

Preliminary prospective observational study for elderly with advanced NSCLC

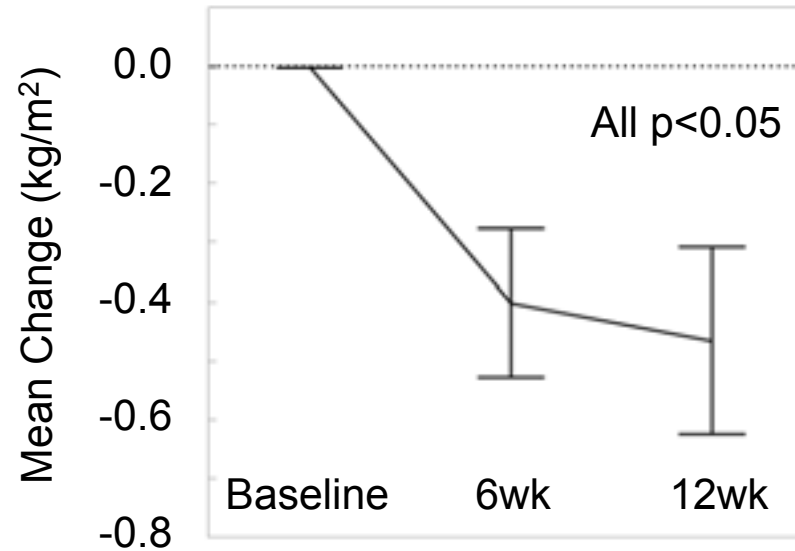
- Patients: Advanced NSCLC (≥ 70 y.o)
ECOG-PS 0-2
Being to start chemotherapy
- Aim: To visualize **functional prognosis**
- Sample size: n=30
- Study period: 2013-2015
- Trial No: UMIN000009768

Characteristics	All (N=30)
Age (range)	74 (70-82)
Gender (F:M)	11:19
Stage IV	29 (97%)
ECOG-PS 0-1	29 (97%)
Cytotoxic regimen	24
Targeted regimen	6
Cachexia	18 (60%)
Pre cachexia	7 (23%)
Muscle depletion	20 (67%)

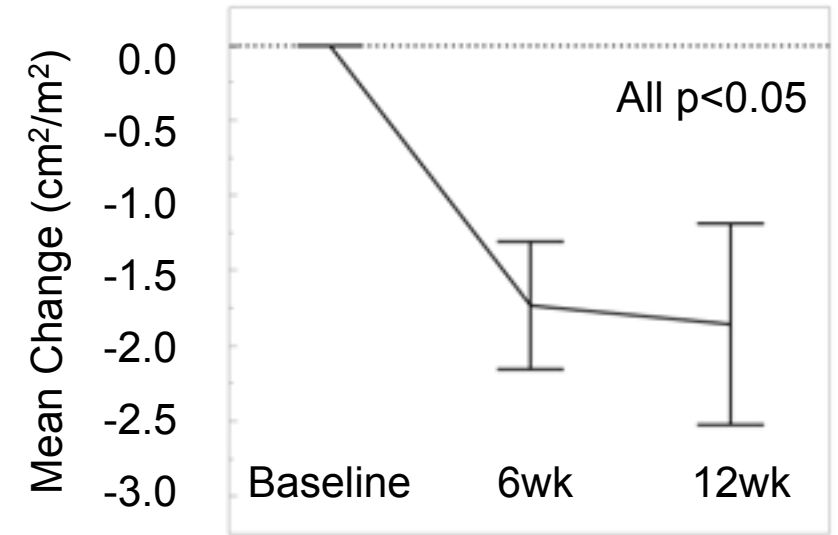
} **83%**

Longitudinal changes in physical parameters within 6-12 weeks from initiation of chemotherapy.

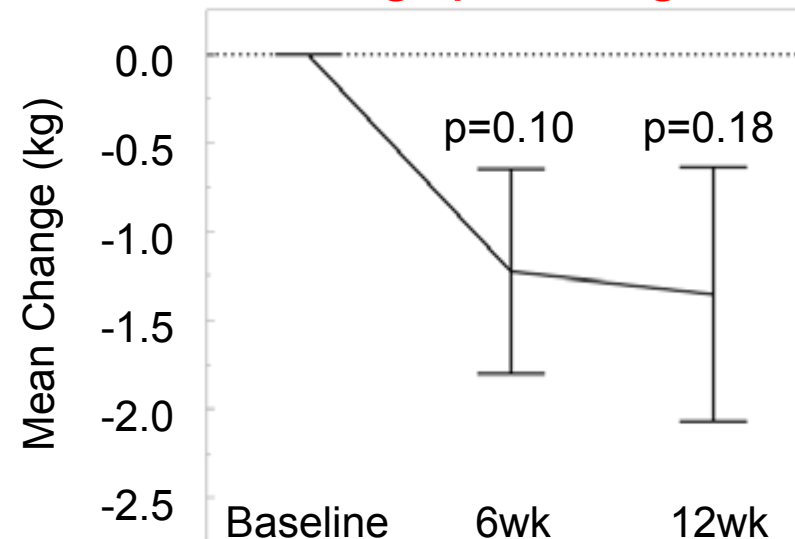
BMI



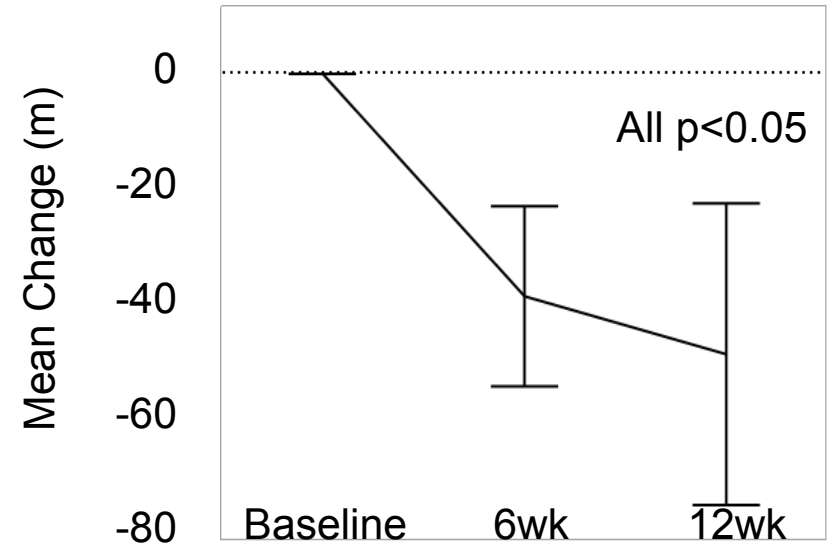
Muscularity index



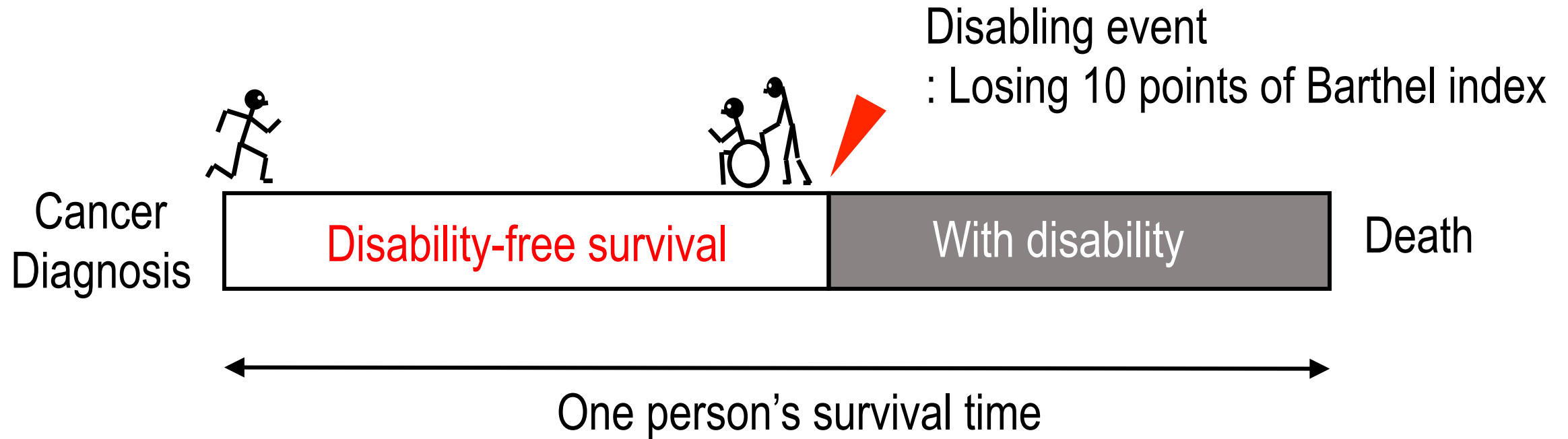
Hand-grip strength



Shuttle walk distance



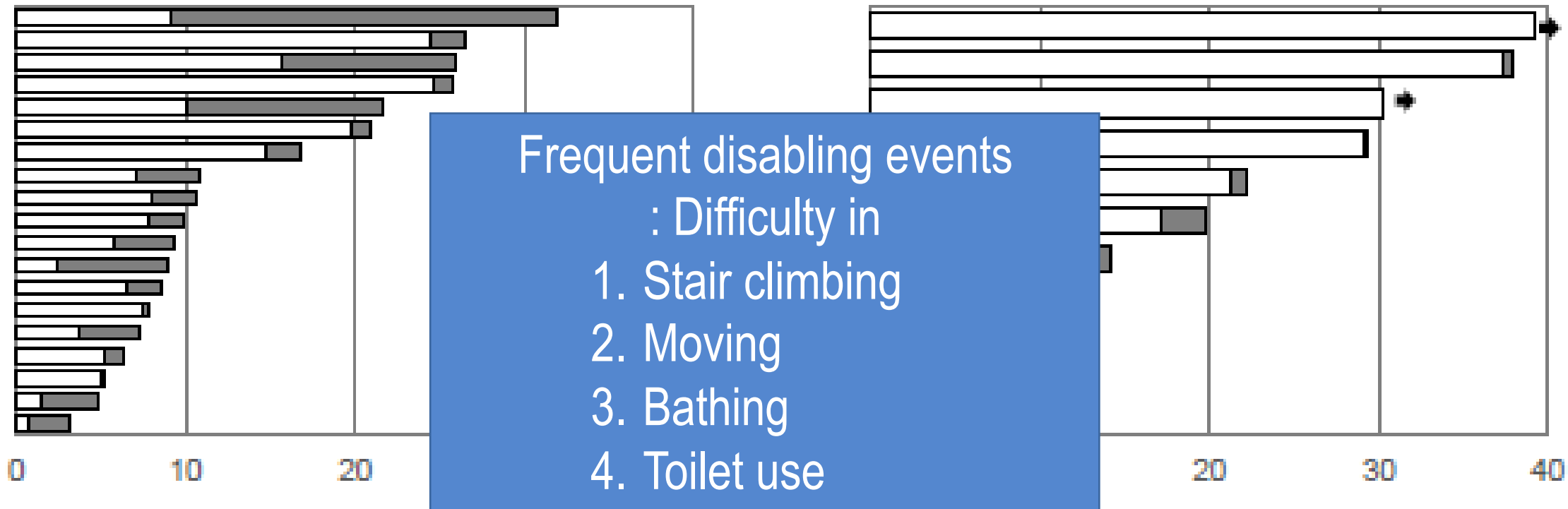
Measuring functional prognosis



Cachectic patients easily develop disability

Cachexia (N=19)

Non-cachexia (N=11)



Disability-free survival: 8 vs 17 months (Log-rank $p < 0.05$)