Exploratory Study on Anti-inflammatory Effect and QOL by Low Molecular Fucoidan (LMF) for Advanced Cancer Patients in Japan.

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BACKGROUND

- Standard chemotherapy (Cx) against advanced cancers still face to their limited efficacies and side-effects as yet and thus the patients are forced to search for various complementary and alternative therapies.
- One in Japan is fucoidan, a high molecular weight sulfated polysaccharide, extracted from seaweeds.
- In particular, enzyme digested fucoidan as low molecular weight (LMF) has been reported to exhibit broad biological activities such as anticancer and anti-inflammatory effects in basic research.

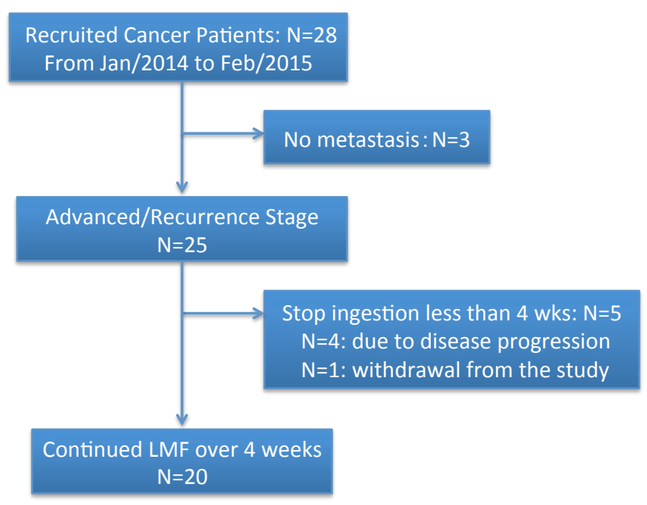
METHODS

Study was carried out from January 2014 to February 2015 under the Institutional Ethics Committee approval.

Patients with advanced cancer were recruited to ingest LMF (Trade name: Power Fucoidan) 400ml/day for at least 4 weeks (wks).

The changes of some inflammatory biomarker values and QOL score were monitored before, after 2 wks, and after 4 wks.

Flow Diagram of the patients



Patient Characteristics

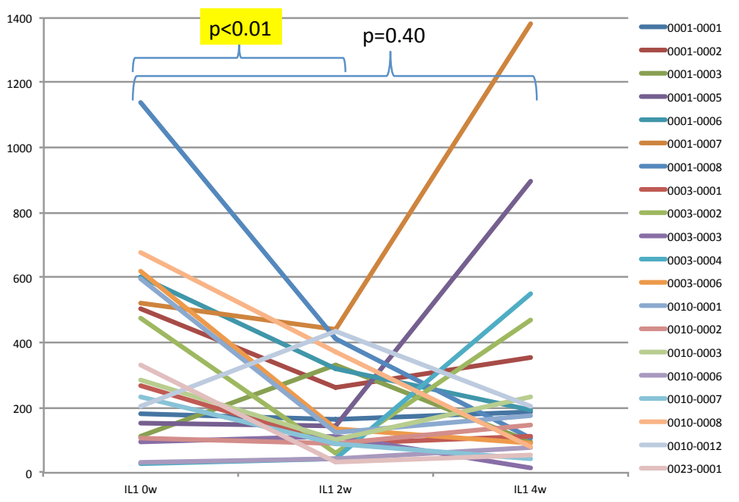
N=20		N (=20)	% (=100%)
Age (range)		58.9 (18–76)	
Sex	Male	12	60.0%
	Female	8	40.0%
Primary Diagnosis	Lung	4	20.0%
	Colon	4	20.0%
	Liver	2	10.0%
	Stomach	2	10.0%
	Pancreas	2	10.0%
	Sarcoma	2	10.0%
	Uterus	1	5.0%
	Breast	1	5.0%
	Prostate	1	5.0%
	Head & Neck	1	5.0%
Histology	Adenocarcinoma	13	65.0%
	Squamous Cell Carcinoma	3	15.0%
	Others	4	20.0%
Anticancer Therapy before the Trial	Surgery	10	50.0%
	Chemotherapy	18	90.0%
	Radiotherapy	4	20.0%

Result 1. Change of biomarkers

N=20		0 w	2 w	4 w	p value (0w–2w)	p value (0w–4w)
Blood Cell Counts	WBC	6135 (±3519)	–	6195 (±3148)	–	0.9365
	Hb	11.2 (±1.9)	–	11.4 (±1.9)	–	0.6442
	Plt	23.1 (±13.3)	–	24.9 (±17.2)	–	0.4996
	Neu%	58.2 (±14.2)	–	56.1 (±14.4)	–	0.6384
	Lym%	29.5 (±14.1)	–	31.0 (±10.9)	–	0.7178
	N/L	2.7 (±1.8)	–	2.3 (±1.6)	–	0.4221
CRP	CRP (ng/ml)	20019 (±33133)	21494 (±38580)	17738 (±37284)	0.8152	0.6738
Cytokines	IL-1β (pg/ml)	358.2 (±280.4)	189.9 (±143.0)	273.4 (±336.4)	0.0057*	0.3987
	IL-6 (pg/ml)	2198.6 (±2523.6)	1522.8 (±1641.4)	1624.1 (±1347.6)	0.0311*	0.2429
	TNF-α (pg/ml)	4819.4 (±3452.6)	3257.2 (±2900.5)	3985.1 (±2453.4)	0.0338*	0.1524
	IFN-γ (pg/ml)	2060.4 (±1274.7)	1762.8 (±1186.4)	2048.3 (±1212.8)	0.1799	0.9651

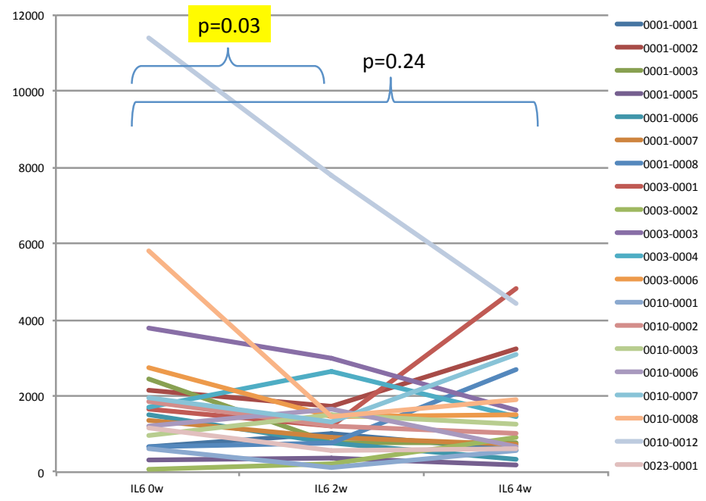
*p<0.05

< IL-1β >



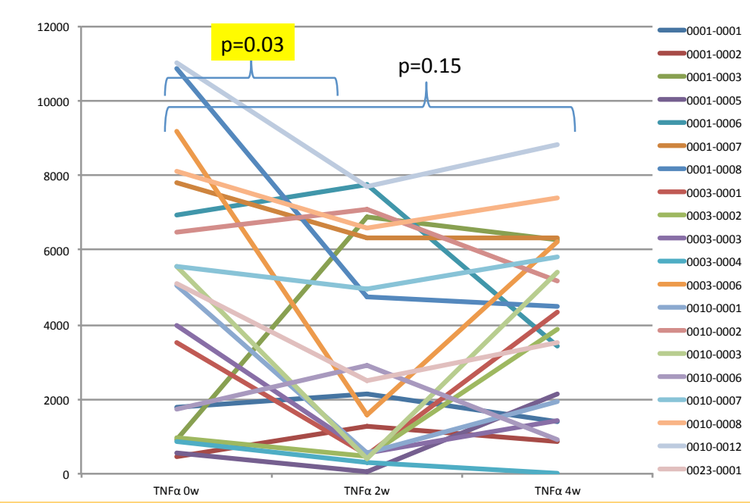
Response Rate (2w IL-1β < 0w IL-1β) during the first 2 wks : 75%（15/20; p<0.01)

< IL-6 >



Response Rate (2w IL-6 < 0w IL-6) during the first 2 wks : 65%（13/20; p=0.03）

< TNF-α >



Response Rate (2w TNF-α < 0w TNF-α) during the first 2 wks : 70%（14/20; p=0.03）

RESULTS 2 : Change of EORTC QLQ-C30 scores

N=20		0w	2w	4w	p値（0w–2w）	p値（0w–4w）
QOL (higher is better)	Global health status / QoL	58.3 (23.9)	53.5 (29.4)	58.3 (21.6)	0.1805	0.7682
Functional Scales (higher is better)	Physical functioning	79.7 (19.4)	76.8 (23.7)	77.7 (22.5)	0.339	0.4298
	Role functioning	76.7 (28.3)	76.5 (26.4)	72.5 (29.3)	0.775	0.6094
	Emotional functioning	82.9 (13.5)	78.5 (19.7)	80.8 (22.1)	0.4527	0.7459
	Cognitive functioning	83.3 (20.2)	75.4 (25.7)	80 (23.3)	0.9052	0.645
	Social functioning	86.7 (19.2)	76.3 (30.1)	81.7 (24.7)	0.1649	0.3308
Symptom Scales (higher is worse)	Fatigue	35.0 (21.1)	38.6 (27.3)	38.6 (24.1)	0.5357	0.3598
	Nausea and vomiting	6.7 (11.3)	4.4 (12.2)	8.3 (23.9)	0.3796	0.7495
	Pain	24.2 (27.3)	20.4 (25.9)	21.7 (27.6)	0.2053	0.5209
	Dyspnoea	20.0 (27.4)	19.3 (27.9)	18.3 (27.5)	0.5414	1
	Insomnia	22.8 (33.4)	19.3 (25.6)	21.7 (29.1)	0.9992	0.9992
	Appetite loss	25.0 (28.4)	29.8 (29.2)	23.3 (26.7)	0.4818	0.7155
	Constipation	13.3 (25.1)	12.3 (25.4)	10.0 (24.4)	0.5778	0.3306
	Diarrhoea	23.3 (32.6)	26.3 (32.5)	21.7 (22.4)	0.6305	0.7894
	Financial difficulties	35.0 (31.5)	31.6 (36.0)	20.0 (25.1)	0.5461	0.0015*

*p<0.05

Conclusion & Discussion

- This exploratory study suggests that LMF could reduced the inflammatory cytokines (IL-1β, IL-6, TNF-α) of advanced cancer patients during the first 2 wks.
- The inflammatory cytokines are considered to be associated with side-effects due to anti-tumor chemotherapy. Recently, a clinical study revealed that fucoidan reduced the toxicities of chemotherapy for advanced cancer patients (Oncology Letter 2011), but the mechanism remains uncertain.
- The anti-inflammatory effect of LMF might contribute to reduce chemotherapy-related side-effects.
- Controlled studies are required to confirm the anti-inflammatory effect and its efficacy of LMF, especially for advanced cancer patients with chemotherapy.

Disclosure of Conflict of Interest

Name of first author: Hidenori Takahashi

I have no COI
with regard to our presentation.