

健康評価とQOL — 神経毒性 —

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July 7, 2012@Tokyo Univ.



大津SAから琵琶湖を臨む

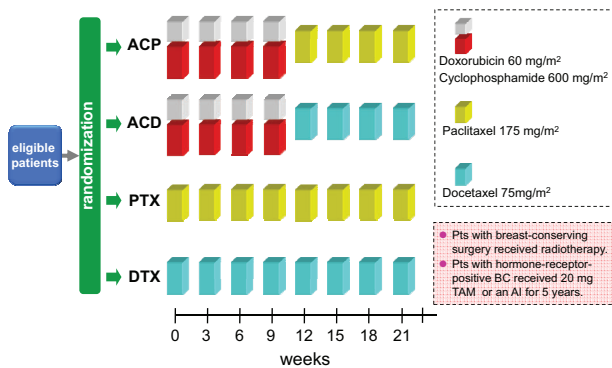
N-SAS BC 02 (2001-)

本研究は、全国の患者さん、および、CSPOR、CSP-HOR、CSPOR データセンター、支援企業をはじめとして、多くの方々のご協力、ご支援のもとに行われました。

皆様に、改めて感謝を申し上げます。

Kuroi K, et al: Jap J Clin Oncol, 2008
Shimozuma K, et al: Support Care Cancer, 2009
Shirowa T, Shimozuma K, et al: Value in Health, 2011
Watanabe T, et al: 2011 SABCS
Onsumi S, et al: Oncology, 2012
Shimozuma K, et al: Support Care Cancer, 2012

Study Design



Watanabe T, et al 2011 SABCS

エンドポイント

- Primary endpoint
 - Disease free survival (DFS)
- Secondary endpoints
 - Recurrent free survival (RFS), Overall survival (OS),
 - CIPN (Chemotherapy-Induced Peripheral Neuropathy), HRQOL (Health-Related Quality Of Life), Incidence and severity of adverse events, cost-effectiveness

CIPN(化療による末梢神経毒性)測定の意味

- 背景
 - 一般に、疼痛、疲労感、しびれ、については医療者などの第三者による評価と患者の評価に乖離があることが知られている。
- 目的
 - タキサン系抗がん剤の神経毒性の詳細の把握と、患者の主観的評価の重要性を確認する。

CIPNとHRQOLの評価尺度

Patient-based	Physician-based
PNQ* (Patient Neurotoxicity Questionnaire)	NCI-CTC (Version 2.0) (Neuro-sensory & Neuro-motor)
FACT/GOG-Ntx** (Functional Assessment of Cancer Therapy-Neurotoxicity)	PNEF*** (Physician Neurotoxicity Examination Form)

* Hausheer, et al., Semin Oncol 2006, Shimozuma, et al., 2004 SABCS
** Calhoun, et al., Int J Gynecol Cancer 2003
*** Developed by Hausheer, et al

Patient Neurotoxicity Questionnaire (PNQ)

Item	A	B	C	D*	E*
Item 1.	I have no numbness, pain, or tingling in my hands or feet.	I have mild tingling, pain or numbness in my hands or feet. This does not interfere with my activities.	I have moderate tingling, pain or numbness in my hands or feet. This does not interfere with my activities of daily living.	I have moderate to severe tingling, pain or numbness in my hands or feet. This interferes with my activities of daily living.	I have severe tingling, pain or numbness in my hands or feet. It completely prevents me from doing most activities.
Item 2.	I have no weakness in my arms or legs	I have mild weakness in my arms or legs. This does not interfere with my activities.	I have moderate weakness in my arms or legs. This does not interfere of my activities of daily living.	I have moderate to severe weakness in my arms or legs. This interferes with my activities of daily living.	I have severe weakness in my arms or legs. It completely prevents me from doing most activities.

*Patients answering D or E provided additional information on specific Activities of Daily Living (ADL's) that were affected.

HRQOL尺度

- General HRQOL
 - FACT-G (Functional Assessment of Cancer Therapy)
- Disease-specific HRQOL
 - FACT-Taxane (FACT/GOG-Ntx)
- Utility index
 - EQ-5D

FACT-Gの構成

Scale	Item	Scale
Physical Well-Being	PWB	1 to 7
Social/Family Well-Being	SWB	8 to 14
Emotional Well-Being	EWB	15 to 20
Functional Well-Being	FWB	21 to 27

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効用値測定の意義

医療経済評価、中でも、「費用効用分析」に用いるため。

1単位の「効用」あたりの「費用」を算出、比較する。

- 「効用」とは、QOL（効用値）で調整した生存年
- 医療でよく使われる効用の指標
 - 質調整生存年 Quality-Adjusted Life Years: QALY

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QALYの算出

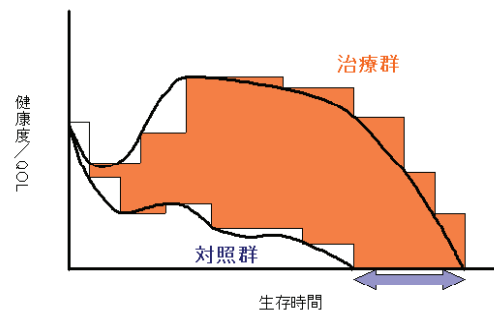
$$QALYs = \sum_H Q_H \times L_H$$

- H : 健康状態
- Q_H : 健康状態HでのQuality Weight (Full health=1, Dead=0)
- L_H : 健康状態Hでの生存年数
- 1QALY : 完全な健康状態で生存する1年

東大 福田敬先生より借用

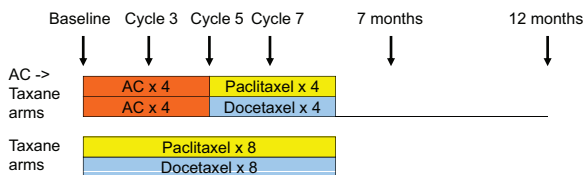
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QALYの概念モデル



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CIPNとHRQOLの調査ポイント



- CIPN and HRQOL assessments were obtained at baseline, 3rd, 5th & 7th cycle, and 7 and 12 months after starting adjuvant treatment.

Shimozuma K, et al Support Care Cancer, 2009 13

医師と患者の評価の不一致

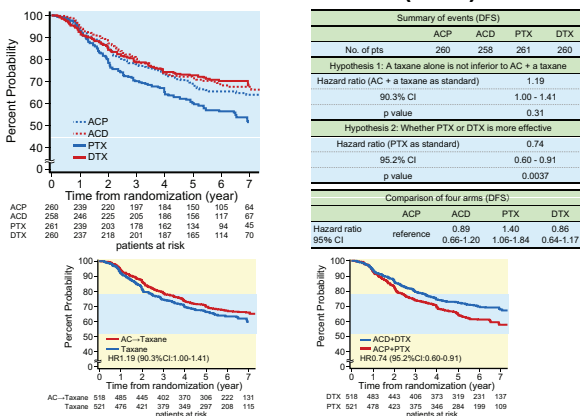
		医師 (NCI-CTC-sensory)					医師 (NCI-CTC-motor)				
		0	1	2	3	4	0	1	2	3	4
患者 (PNQ-sensory)	A(0)	489	38	0	0	0	492	5	1	0	0
	B(1)	432	252	4	0	0	701	37	2	0	0
	C(2)	113	171	5	0	0	231	17	3	0	0
	D(3)	44	66	11	3	1	62	10	5	1	0
	E(4)	9	1	0	0	0	9	0	0	0	0

Kappa=0.16 (Sensory), Kappa=0.02 (Motor)

- PNQ scores distributed between A and E (full range), while NCI-CTC scores mainly distributed between 0 and 1.

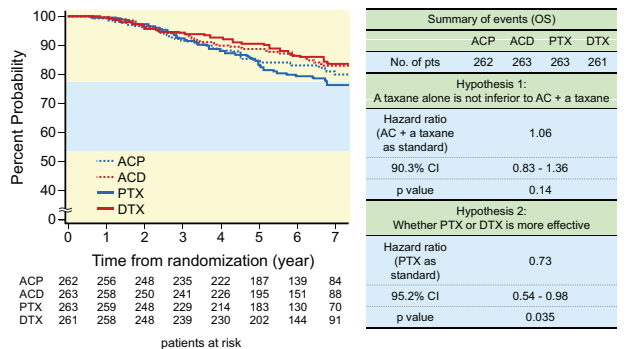
Shimozuma K, et al, Support Care Cancer 2009¹⁴

Disease-free Survival (DFS)



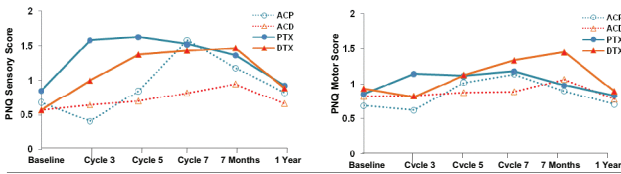
Watanabe T, et al 2011 SABCS

Overall Survival (OS)



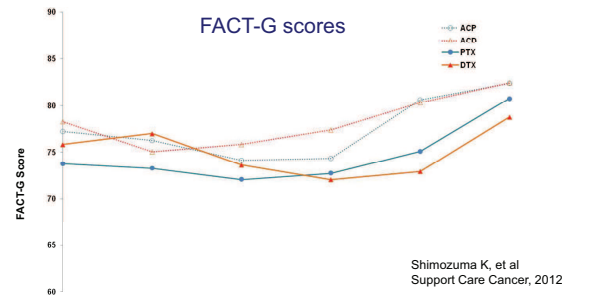
Watanabe T, et al 2011 SABCS

PNQ scores



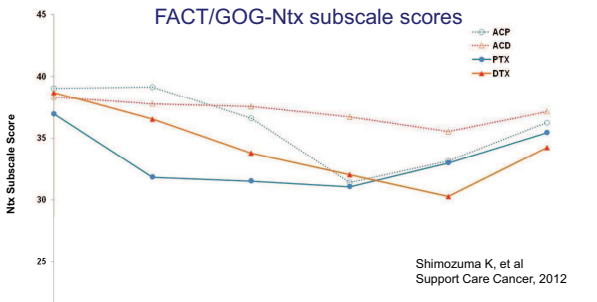
Scale	ACP+ACD vs PTX+DTX				ACP+PTX vs ACD+DTX		
	AUC (from baseline)	ACP+ACD (n = 149)	PTX+DTX (n = 151)	P value	ACP+PTX (n = 150)	ACD+DTX (n = 150)	P value
PNQ sensory							
To cycle 7		3.2 (2.1)	4.9 (2.4)	.003	4.5 (2.4)	3.6 (2.3)	.669
To year 1		5.1 (2.8)	7.2 (3.2)	.041	6.6 (3.1)	5.6 (3.2)	.493
PNQ motor							
To cycle 7		3.5 (2.1)	4.2 (2.4)	.160	3.9 (2.4)	3.8 (2.2)	.358
To year 1		5.2 (2.9)	6.2 (3.1)	.343	5.6 (3.1)	5.9 (2.9)	.17

FACT-G scores



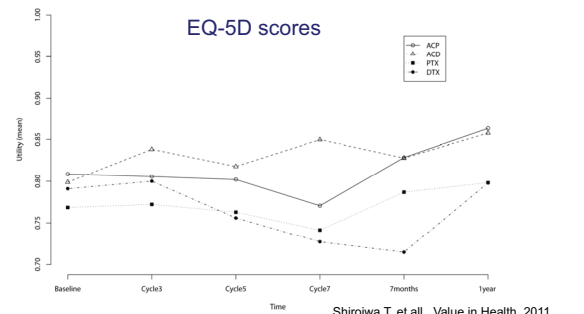
Scale	ACP+ACD vs PTX+DTX				ACP+PTX vs ACD+DTX		
	AUC (from baseline)	ACP+ACD (n = 149)	PTX+DTX (n = 151)	P value	ACP+PTX (n = 150)	ACD+DTX (n = 150)	P value
FACT-G							
To cycle 7		303.9 (49.9)	295.5 (48.7)	.144	297.1 (50.6)	302.2 (48.1)	.372
To year 1		465.9 (68.0)	450.0 (68.1)	.044	456.3 (70.3)	459.5 (66.6)	.18

FACT/GOG-Ntx subscale scores



Scale	ACP+ACD vs PTX+DTX				ACP+PTX vs ACD+DTX		
	AUC (from baseline)	ACP+ACD (n = 149)	PTX+DTX (n = 151)	P value	ACP+PTX (n = 150)	ACD+DTX (n = 150)	P value
Ntx subscale							
To cycle 7		147.8 (11.7)	136.7 (16.1)	<.001	139.2 (15.3)	145.4 (14.3)	<.001
To year 1		218.4 (17.4)	203.5 (22.5)	<.001	208.0 (20.7)	213.9 (21.8)	.19

EQ-5D scores



Comparison	Difference	SE	t_value	p_value	Lower_CI	Upper_CI
ACP vs DTX	0.052	0.0185	2.820	0.0048 **	0.016	0.089
ACD vs DTX	0.077	0.0185	4.137	<.0001 **	0.04	0.113
PTX vs DTX	0.021	0.0186	1.106	0.269	-0.016	0.057
ANTHRACYCLINE vs TAXANE	0.054	0.0132	4.117	<.0001 **	0.028	0.080
PACLITAXEL vs DOCETAXEL	-0.002	0.0131	-0.140	0.889	-0.028	0.204

まとめ(1)

- 末梢神経障害のような医療者が把握しにくい性質の症状については、患者の主観的な健康度 (Patient-reported outcome: PRO) の評価も、医療専門家の評価とともに重要かつ有用であることが明らかになった。
- 乳癌術後補助療法に標準治療として使用されるタキサン8サイクルの治療法は、従来のAC4サイクル⇒タキサン4サイクルと比較して、末梢神経毒性障害は強いものの、1年後にはほぼ回復し、かつ、治療中はQOLを有意に低下させない、忍容性の高い治療法であることが明らかになった。

まとめ(2)

- CIPNやHRQOLのようなPROの測定・評価によって、患者や社会に役立つエビデンスを創出し、EBMIに活かすことは重要である。