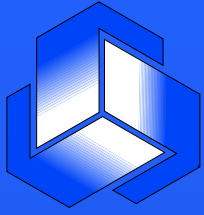


Ovarian Module Field Study Results Protocol 15982

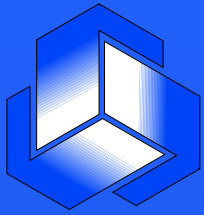
EGAM Meeting, Brussels

April 21-23, 2004



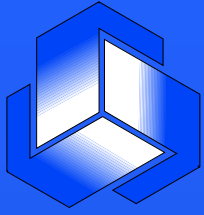
Ovarian Cancer

- Fourth most common cancer in women
- Early detection difficult, 75 % present with advanced-stage disease
- High mortality rate - 50 % die within 5 years of initial diagnosis
- Most women develop recurrent disease within two years



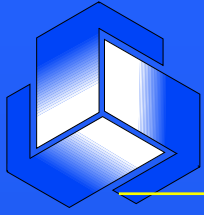
Ovarian Cancer: Treatment

- Radical or debulking surgery followed by platinum-based chemotherapy
- Focus on symptom palliation, due to poor prognosis
- Tolerability of treatment and QOL are important issues
- For clinical trials disease specific QOL measures are required



Development of a Module for Assessing QOL of Ovarian Cancer

- Symptoms related to ovarian cancer
 - Treatment related issues for patients undergoing surgery or chemotherapy
 - Additional QOL issues (sexuality, body image, menopausal symptoms) not covered
 - Supplement to the core questionnaire (QLQ-C30)
-



EORTC Guidelines

PHASE 1: Generation of QOL issues

- Literature search for relevant issues
- HCP and patients interviews

PHASE 2: Construction of items

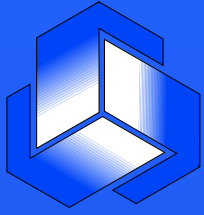
- Formulating items, creating subscales
- Translation

PHASE 3: Pretesting the module

- Pre/pilot-testing (patient interviews)
- Cross cultural adaptation

PHASE 4: International field-testing

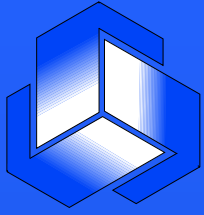
- Psychometric properties
- Scale structure



PHASE IV: Field Study

Study objectives

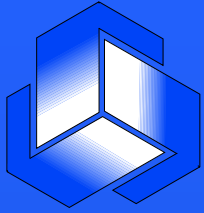
- to test the psychometric properties
- to determine the cross-cultural applicability
- to confirm the hypothesized scale structure



QLQ-OV28 Scale Structure

28 items - 7 subscales

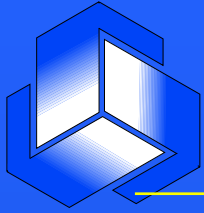
- GI:** Abdominal/intestinal symptoms (7 items)
- PN:** Peripheral neuropathy (3 items)
- CT:** Other chemotherapy side effects (7 items)
- HM:** Hormonal/menopausal symptoms (2 items)
- BI:** Body image (2 items)
- AT:** Attitude to disease and treatment (3 items)
- SF:** Sexual functioning (4 items)



EORTC QLQ-OV28

Item examples

- GI:** Abdominal/intestinal symptoms
,Did you have abdominal pain?'
- PN:** Peripheral neuropathy
,Have you had numbness in your fingers or toes?'
- HM:** Hormonal/menopausal symptoms
,Did you have night sweats?'
- AT:** Attitude to disease and treatment
,How much has your treatment been a burden to you?'
- SF:** Sexual functioning
,To what extent were you sexually active?'
-



Field Study: Protocol 15982

Jan **1999** activated - July **2001** closed

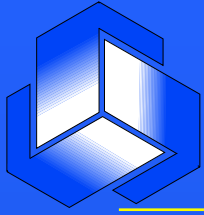
Co-ordinated at the QLU, EORTC Data Center

Inclusion:

- > Ovarian cancer (FIGO I-IV)
- > 3 months expected survival
- > Informed consent

Exclusion:

- > Concurrent malignancies
- > Inability to complete questionnaire
- > Participation in other QOL studies



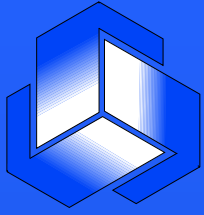
Prospective registration

Group I: Platinum-based chemotherapy after radical or debulking surgery

Group II: 6 courses chemotherapy completed after radical or debulking surgery

Group III: Complete response to 1st line chemotherapy no evidence of disease (NED)

Group VI: Recurrence of disease
2nd line chemotherapy



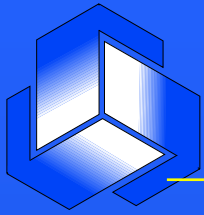
QOL Assessment

Group I: Chemotherapy - QOL 2 x (cycle 1 and 4)

Group II: QOL 8 weeks after completion of chemotherapy (6 cycles)

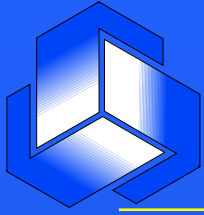
Group III: Complete response - QOL 2 x
(routine follow-up + 3 days later)

Group VI: Recurrence - QOL 2 x (cycle 1 and 4)



Patient characteristics N=368

		N	%
Age:	Mean 59 yrs (SD 11.60)		
Stage:	FIGO I, II	137	41
	FIGO III, IV	200	59
Education:	Compulsory or less	241	66
	Post-compulsory	103	28
	University level	23	6
Employment:	Full/part time	111	31
	Homemaker	99	27
	Retired	135	31
	Unemployed/other	23	6
Living:	Alone	75	20
	With family	267	73
	With others	26	7



Analysis plan

Discriminant validity:

Correlation between each item and its own scale
→ convergent/discriminant validity

Reliability:

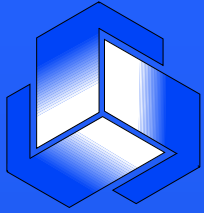
Cronbach's alpha coefficients → internal consistency
Intra class correlation coefficient → test-retest rel.

Responsiveness:

Comparison of pre-treatment vs on-treatment
assessment

Clinical validity:

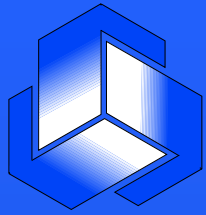
Known-group comparison using clinical information



Results

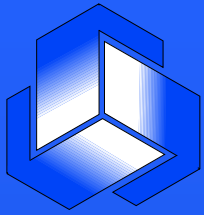
Compliance rate

Baseline	88 %
Follow-up	72 %
Item compliance	< 3 % missing
Sexuality items	4-26 % missing
Completion (C30+OV28) <15 min	76 %
No help required	72 %
Item were found to be clear	87 %
Sexuality items upsetting	8 %



Internal Consistency - Test-retest reliability

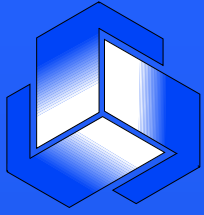
Subscale	Cronbach's alpha		ICC
	On-tx	Off-tx	
Abdominal/ G astro I ntestinal	.86	.84	.91
P eripheral N europathy	.77	.83	.88
C hemotherapy side effects	.79	.77	.84
H ormonal/ M enopausal	.80	.83	.94
B ody I mage	.79	.58	.82
A ttitude to disease/ T reatment	.87	.78	.84
S exual F unctioning	.78	.90	.74



Responsiveness of scales

Subscale	mean	p
Abdominal/ G astro I ntestinal	-7.4	<.05
P eripheral N europathy	8.4	<.05
C hemotherapy side effects	15.3	<.05
H ormonal/ M enopausal	0.6	.53
B ody I mage	-1.1	.67
A ttitude to disease/ T reatment	-7.5	<.05
S exual F unctioning	4.1	<.05

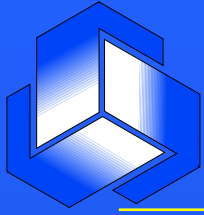
Sign. differences between pre- and on-chemotherapy
in all scales except HM and BI



Clinical validity: Known-group comparison

Clinical parameter

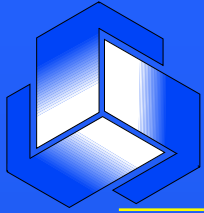
Primary disease vs NED	good discrimination
Recurrent disease vs NED	good discrimination
Performance status (KPS)	no clear discrimination
Absence/presence of ascites	no clear discrimination
FIGO stages	no clear discrimination



Summary

- Multi-trait scaling analysis confirmed the hypothesized scale structure
- Good psychometric properties
- QLQ-OV28 module well accepted by patients with ovarian cancer
- QLQ-OV28 module should be supplemented with the QLQ-C30
- Cross culturally tested – available in 15 languages for use in clinical trials

Chinese, Taiwan Chinese, Croatian, Danish, Dutch, Finnish, French, German, Italian, Norwegian, Polish, Portuguese, Russian, Spanish, Swedish



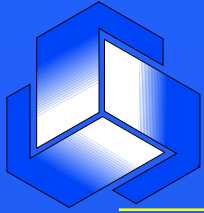
Clinical Trials with QOL Outcome

QLQ-OV28 use in EORTC trials

Protocol 55971: Randomized phase III study comparing upfront debulking surgery versus neo-adjuvant chemotherapy in patients with stage IIIc-IV ovarian cancer

Protocol 55012: A phase III study of Cisplatin plus Topotecan followed by Paclitaxel plus Carboplatin versus Paclitaxel plus Carboplatin as first line chemotherapy in women with newly diagnosed advanced epithelial ovarian cancer

QLQ-OV28 use outside the EORTC trials



Collaborators and Centres

Arraras A, Hospital of Navarre, Pamplona, Spain

Chauvenet L, Hotel Dieu, Paris, France

Cull A, Western General Hospital, Edinburgh

Greimel E, Dept Ob&Gyn University Hospital Graz, Austria

Holzner B, Dept Biological Psychiatry, University Innsbruck, Austria

Kuljanic-Vlasic K, Dept Ob&Gyn University Hospital Rijeka, Croatia

Rios M, Centre Alexis Vautin, Vandoevre, France

Waldenström AC, Sahlgrenska University Hospital, Gotenborg, Sweden

Quality of Life Unit, EORTC Data Centre, Brussels

D'haese S, Lebrec, J, Bottomely A

EORTC Quality of Group
