

#3841 Non-AIDS Serious Adverse Events Are As Important As AIDS Events in Patients With Advanced Multi-drug Resistant HIV Disease.

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INTRODUCTION

There is evidence that, since the advent of HAART, non-AIDS illnesses are as important to overall morbidity as AIDS-defining conditions.¹ Treatment experienced patients with advanced HIV disease and multi-drug resistant virus have the highest risk of AIDS progression. AIDS illnesses might therefore be expected to dominate morbidity in such patients. The present study evaluates the contribution of AIDS-defining conditions versus serious non-AIDS morbidity in patients who are at highest risk for progression of AIDS because they lack confident anti-retroviral treatment options. The effect of AIDS and non-AIDS morbidity on quality of life were also compared.

OPTIMA: STUDY DESIGN

OPTIMA is a tri-national collaboration between the Canadian Institutes of Health Research (CIHR), the United Kingdom Medical Research Council (UK-MRC), and the United States Veterans Health Administration (VHA).² OPTIMA evaluates alternate treatment strategies in subjects with advanced multi-drug resistant HIV disease having few treatment options.

Eligibility:

- CD4 = 300 cells/mm³, HIV RNA > 5,000 copies/mL.
- Evidence of multi-drug resistant HIV or intolerance to NRTI, NNRTI, and PI classes.

Intervention:

Randomization in a 2 X 2 factorial design to:

- three month anti-retroviral drug free period (ARDFP) vs no ARDFP followed by:
- four or fewer ARV drugs (Standard ART) vs five or greater ARV drugs (Mega-ART)

Endpoints:

- Primary: New AIDS-defining events or death
- Secondary: Non-AIDS Serious Adverse Events (SAE).

Other measures for analysis gathered at scheduled visits include laboratory tests of immunological and virological status, safety measures, quality of life (QOL) instruments including the Medical Outcomes Survey (MOS-HIV), and extensive Health Economics data.

METHODS

Data Sources

Unblinded data from the OPTIMA study were analyzed. The data set was closed in May 2004.

Data elements used:

- Baseline demographics
- Baseline HIV characteristics
- Serious Adverse Events classified by MedDRA*
- AIDS defining illnesses, new and recurrent (CDC Guidelines)
- Summary scores of Quality of Life using MOS-HIV in 2 domains by the method of Revicki, et al.⁴
- Physical Health Status (PHS)
- Mental Health Status (MHS)

Statistical Analysis

Mean PHS and MHS scores were calculated for each group - SAE, AIDS, and No-Event - at baseline of entry into study, at nearest visit prior to event (Pre-Event), and at first study evaluation following the event (Post-Event). Significance of differences between means was determined using Students t-test.

RESULTS

BASELINE CHARACTERISTICS

Baseline Demographics of Patients Enrolled in OPTIMA (n=289)		Baseline HIV Characteristics of Patients Enrolled in OPTIMA (n=289)	
	n (%)		n (%)
Mean Age (SD)	47.8(8.26)	AIDS at entry	282(98)
Gender (%):		CD4 at entry	
Male	282(98)	CD4 <= 100	127(44)
Female	6(2)	100 < CD4 <= 200	97(34)
Race:		CD4 > 200	63(22)
White	146(51)	Median CD4 (SD)	119(107)
Black	102(35)		
Asian	2(1)	HIV RNA copies/ml	N (%)
Hispanic	28(10)	<5k	34(12)
Other	3(1)	5-50k	103(37)
Pending*	8(3)	50-100k	50(18)
Mode of Infection:		>100k	94(33)
Blood	26(9)	Mean Log (SD)	4.63 (.77)
Heterosexual	62(21)		
IDU	37(13)	OI Prophylaxis	
MSM	142(49)	Anti - PCP	207(70)
Other	15(6)	CMV	2(1)
Pending*	5(2)	Antibacterial	93(32)
		Antifungal	53(18)

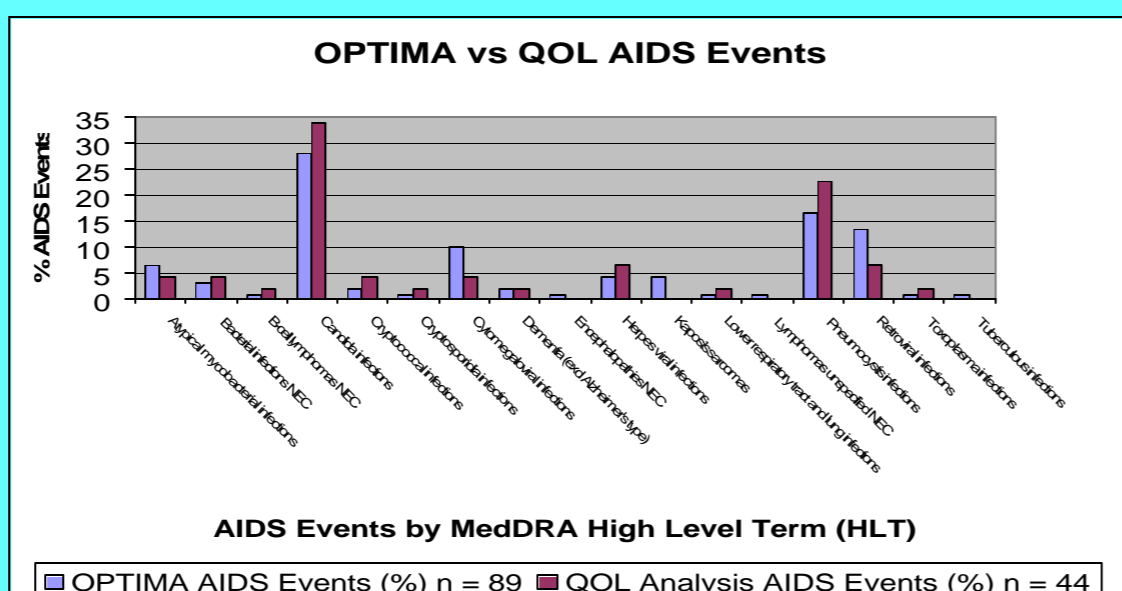
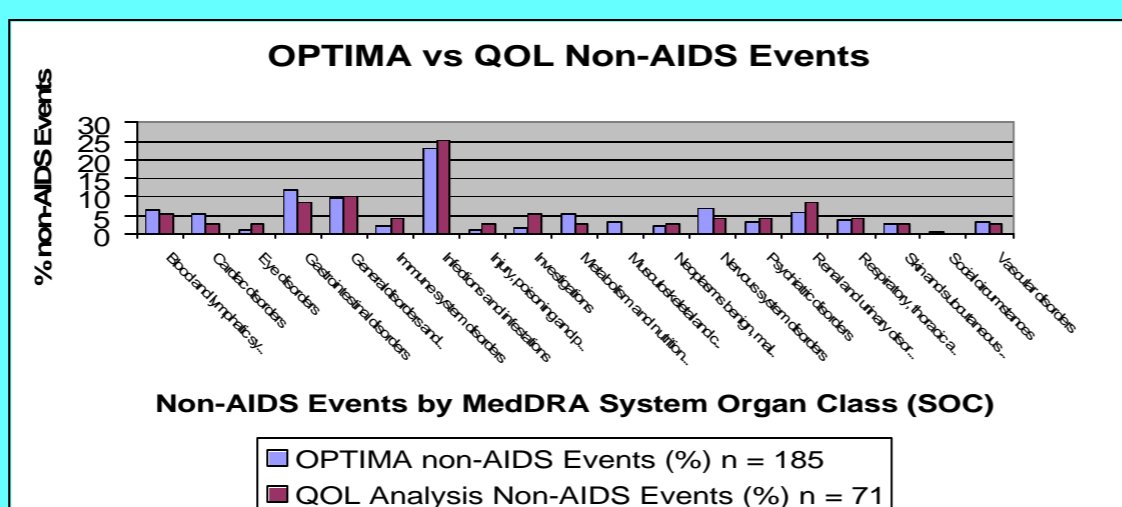
* Data pending as of 12/03
Total < 289 (100%) due to pending data

OPTIMA patients were heavily drug experienced, failing their current ARV regimen, and immunologically at risk for progression of HIV disease.

Clinical Events in OPTIMA and QOL

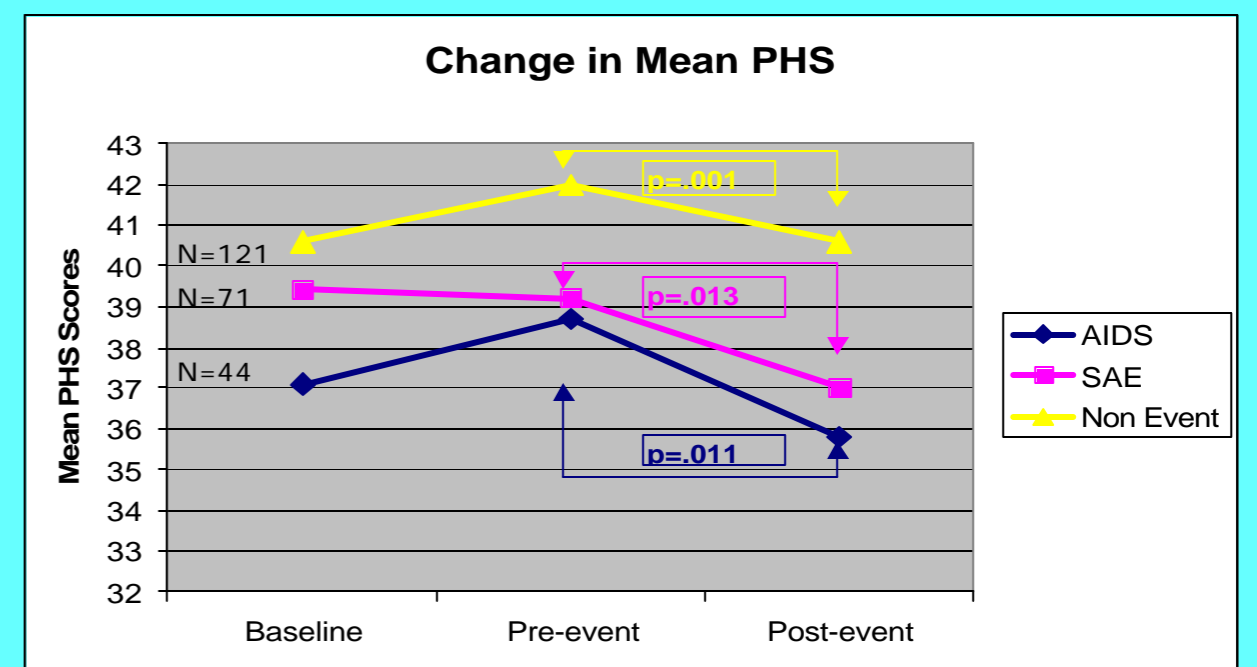
Clinical Events in OPTIMA	Exclusions from QOL Analysis
Number randomised	289
Total number of AIDS events/ # pts.	89/53
Total number SAE events/ # pts.	185/81
SURVIVAL	
Total number of deaths	37
Likely HIV/ARV-related	14
Uncertain HIV/ARV-related	7
Unlikely HIV/ARV-related	3
Pending adjudication	13
AIDS events or death/ 100 person years.	22
	106 of 185 non-AIDS SAE's
	Concurrent SAE
	48
	Concurrent AIDS
	21
	Concurrent death
	12
	No QOL assessment
	25
	Other
	8
	41 of 89 AIDS Events
	Concurrent AIDS event
	13
	Concurrent SAE
	6
	Concurrent death
	10
	No QOL assessment
	12
	Other
	7

The overall frequency of events in the OPTIMA study were similar to those selected for Quality of Life (QOL) Analyses. (See following figures)

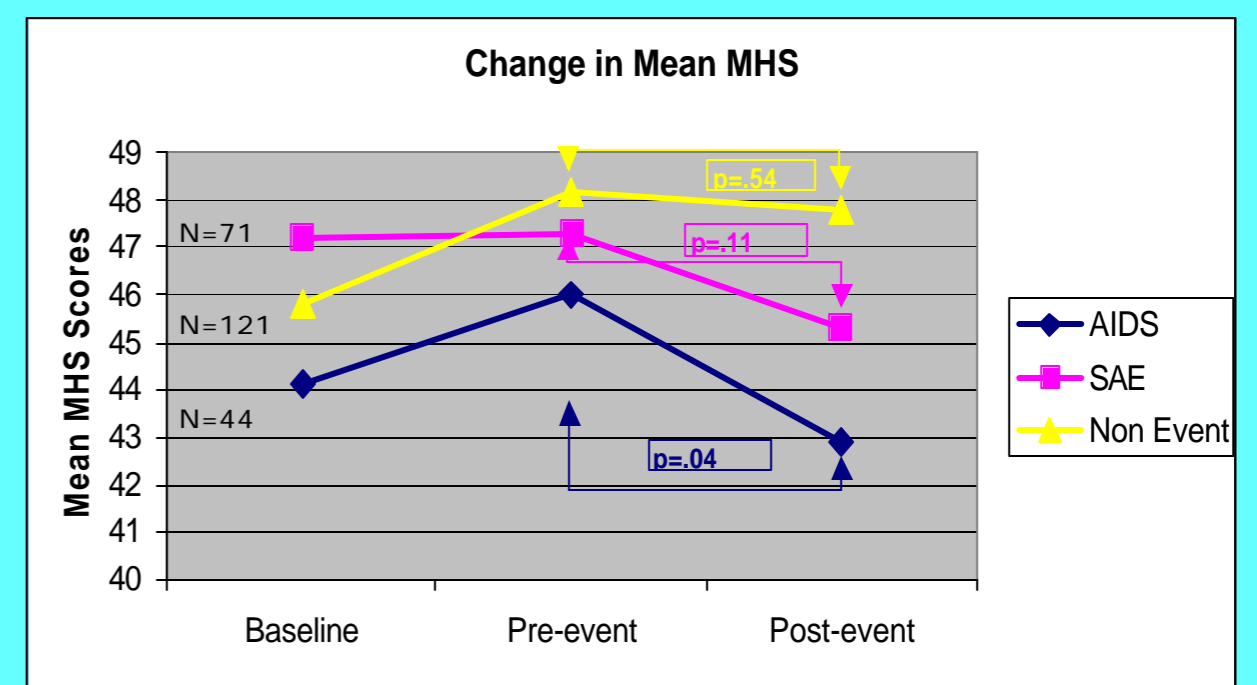


QUALITY OF LIFE (QOL) OUTCOMES

Mean baseline QOL scores for Physical Health Status (PHS) and Mental Health Status (MHS) using the MOS-HIV were low. There were no significant differences at baseline between groups who subsequently developed an AIDS event, a non-AIDS SAE, or who had no event. Changes between baseline, pre-event and post-event scores are shown below.



Physical Health Scores (PHS) declined significantly following AIDS events and for non-AIDS SAE's but not after No-Event. There was no difference between AIDS events and non-AIDS SAE's when the change in pre-event and post-event scores were compared between groups. There were significant declines in PHS (p<.001) when either AIDS or SAE's was compared to No-Event.



Mental Health Scores (MHS) declined significantly following AIDS events but not for non-AIDS SAE's or for No-Event. There was no difference between AIDS events and non-AIDS SAE's when the change in pre-event and post-event MHS scores were compared between groups. There were significant declines in MHS (p<.001) when either AIDS or SAE's was compared to No-Event.

CONCLUSIONS

In patients with advanced HIV having limited treatment options:

- The frequency of non-AIDS serious adverse events is greater than the frequency of AIDS defining illnesses.
- The adverse effects of AIDS events and non-AIDS SAE's on physical and mental health status are similar.
- Significant and similar declines in physical health status are associated with both non-AIDS SAE's and with AIDS events
- Significant declines in mental health status are associated with AIDS events.
- Non-AIDS serious adverse events are more frequent and associated with similar declines in quality of life as AIDS events.
- Non-AIDS SAE's should be considered as a primary outcome measure in future management trials of HIV treatment.

REFERENCES

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