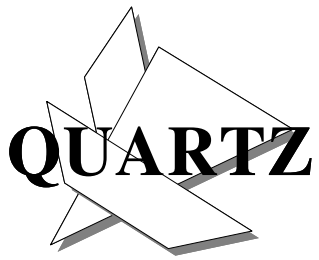


QUARTZ Trial Interim Data Release

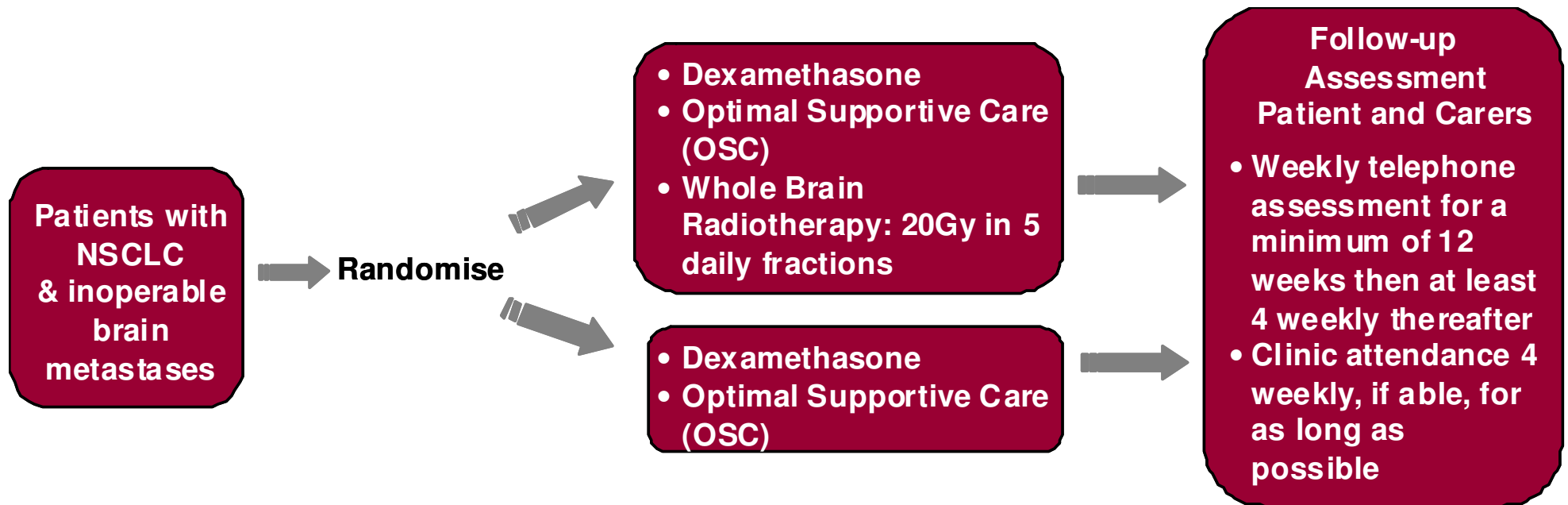
Results and Caveats

Agenda

- QUARTZ trial
- Background and data release caveats
- Baseline data
- Treatment
- Patient assessments and follow-up
- Carer assessments
- Survival
- Quality Adjusted Life Years



QUARTZ Trial



QUARTZ Trial

- All patients with inoperable brain metastases from non-small cell lung cancer (NSCLC) are eligible.
- As long as they have not previously received whole brain radiotherapy (WBRT), have not had surgery or chemotherapy within the last 4 weeks and have not taken EGFR inhibitors within last week.
- 534 patients are required.
- Primary outcome measure is Quality Adjusted Life Years (QALYS), a combination of survival and quality of life.
- Secondary outcome measures include Overall Survival.
- Also collecting data on carer concerns, and carer opinion of patient quality of life.

Why release interim data?

- Main reason is low recruitment rates
 - QUARTZ clinical question remains important
 - QUARTZ remains very well supported, over 70 centres
 - Trial Management Group have been active in promoting the trial
 - Running the trial over 10 years is not feasible
 - Therefore recruitment needs to improve, as funding for the trial may be withdrawn

Why is recruitment lower than expected?

- Many reasons
- Recurring themes surrounding the trial discussion
- Patients often arrive with the expectation that they'll have WBRT. Others have already decided they don't want WBRT
- Clinicians often have their own preference about whether to give WBRT to individual patients
- No preliminary/phase II data suggesting WBRT may be omitted, which can be used in discussions

Why show interim data?

- **Doing nothing is not an option as funding will be withdrawn if recruitment does not improve**
- The hypothesis is that having some preliminary evidence will benefit investigators and patients in a number of ways
 - Will provide high quality data on which to base decisions regarding trial participation
 - May help structure the discussion of the trial with patients
 - May give basis to discuss the trial even when the patient expresses an initial preference for or against WBRT

What are the risks in releasing interim data?

- The trial requires 534 patients and a specific length of follow-up
- We all know the question can't be fully answered at this stage, with this number of patients
- There is a greater risk of chance findings with a smaller sample size
- There is a risk of early data being over-/misinterpreted
- There is a risk that we 'kill' the trial

Points to consider

- Data are from 151 patients: the trial requires 534 in total
- We cannot conclusively answer the trial questions yet
- However, seeing the current data may help doctor and patient make a more 'informed' decision
- Decision to show the data was made independently of the trial results eg the Independent Trial Steering Committee who approved the release of interim data did not see the data prior to giving their consent

Summary

- Unusual step taken due to continued interest but lower than anticipated recruitment
- Insufficient patients to fully answer trial question
- Looking to give some information on which to base your decisions regarding trial entry
- There are dangers in doing this and we need to guard against over-interpretation of the current data
- Dangers of doing this are outweighed by the dangers of not doing this

Interim Data

First 151 patients randomised
into QUARTZ

Baseline Data

(N = 151)

Characteristics	Category	Patients
Sex	Male	91 (60%)
Age	Median (IQR)	67 (62 – 73)
	Range	38 – 85
Karnofsky PS	Poor (<70)	75 (50%)
Extra-cranial metastases	Yes	58 (38%)
RPA	I	12 (8%)
	II	64 (42%)
	III	75 (50%)

Baseline Data

(N = 151)

MRC

Clinical
Trials
Unit

Characteristics	Category	Patients
Newly diagnosed brain metastases	Yes	119 (79%)
NSCLC histology	Adenocarcinoma	53 (36%)
	Squamous	43 (29%)
Solitary brain metastasis	Yes	57 (39%)
Patient health	Good/Very good	56 (37%)

Baseline Symptoms

Moderate/severe symptoms over the previous week, as assessed by the patient

MRC

Clinical
Trials
Unit

Symptom		Symptom	
Any	118 (78%)		
Tiredness	71 (47%)	Confusion	17 (11%)
Weakness	46 (30%)	Speech	17 (11%)
Drowsiness	46 (30%)	Indigestion	14 (9%)
Insomnia	45 (30%)	Thrush	13 (9%)
Sight	29 (19%)	Headache	13 (9%)
Memory	26 (17%)	Weight gain	10 (7%)
Dizziness	24 (16%)	Hair loss	8 (5%)
Mood	24 (16%)	Nausea	6 (4%)
Weight loss	23 (15%)	Seizures	6 (4%)
Appearance	18 (12%)	Dryness/Itchiness	2 (1%)

Baseline Quality of Life

Individual questions from EQ5D

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Question	Response	n (%)
Mobility	No problem	45 (30%)
	Some/major problems	105 (70%)
Self-care	No problem	94 (63%)
	Some/major problems	55 (37%)
Usual activities	No problem	40 (27%)
	Some/major problems	109 (73%)
Pain/discomfort	No problem	75 (50%)
	Some/major problems	74 (50%)
Anxiety/depression	No problem	83 (56%)
	Some/major problems	66 (44%)

Baseline Quality of Life

Number of problems reported

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Unit

Question		
Number of problems reported on EQ5D	0	11 (8%)
	1	23 (16%)
	2	29 (20%)
	3	36 (24%)
	4	26 (18%)
	5	22 (15%)

WBRT Data

Patients with WBRT data		75
Was WBRT given as planned? (20 Gy in 5 fractions)	Yes	57 (76%)
	Delayed	3 (4%)
	Reduced	1 (1%)
	Stopped	3 (4%)
	Not given	11 (15%)
Time to starting WBRT (days)	Median	13
	Range	2 – 29
Total dose delivered (Gy)	0	11 (15%)
	<20	5 (7%)
	20	59 (79%)

Additional Treatment

		OSC + WBRT (N=70)	OSC alone (N=66)
Patient received	Any treatment	8 (12%)	20 (34%)
	Chemotherapy	3 (4%)	5 (8%)
	Radiotherapy	6 (9%)	17 (27%)
	Other therapy (1 blood transfusion, 5 Tarceva)	3 (4%)	3 (5%)
Median steroid dose	Baseline	8mg	8mg
	Post-baseline (average dose)	6mg	6mg
Required overnight hospital stay	No	34 (49%)	33 (50%)
	Yes	36 (51%)	33 (50%)
	Median stay	8 nights	9 nights

Patient Assessment Data

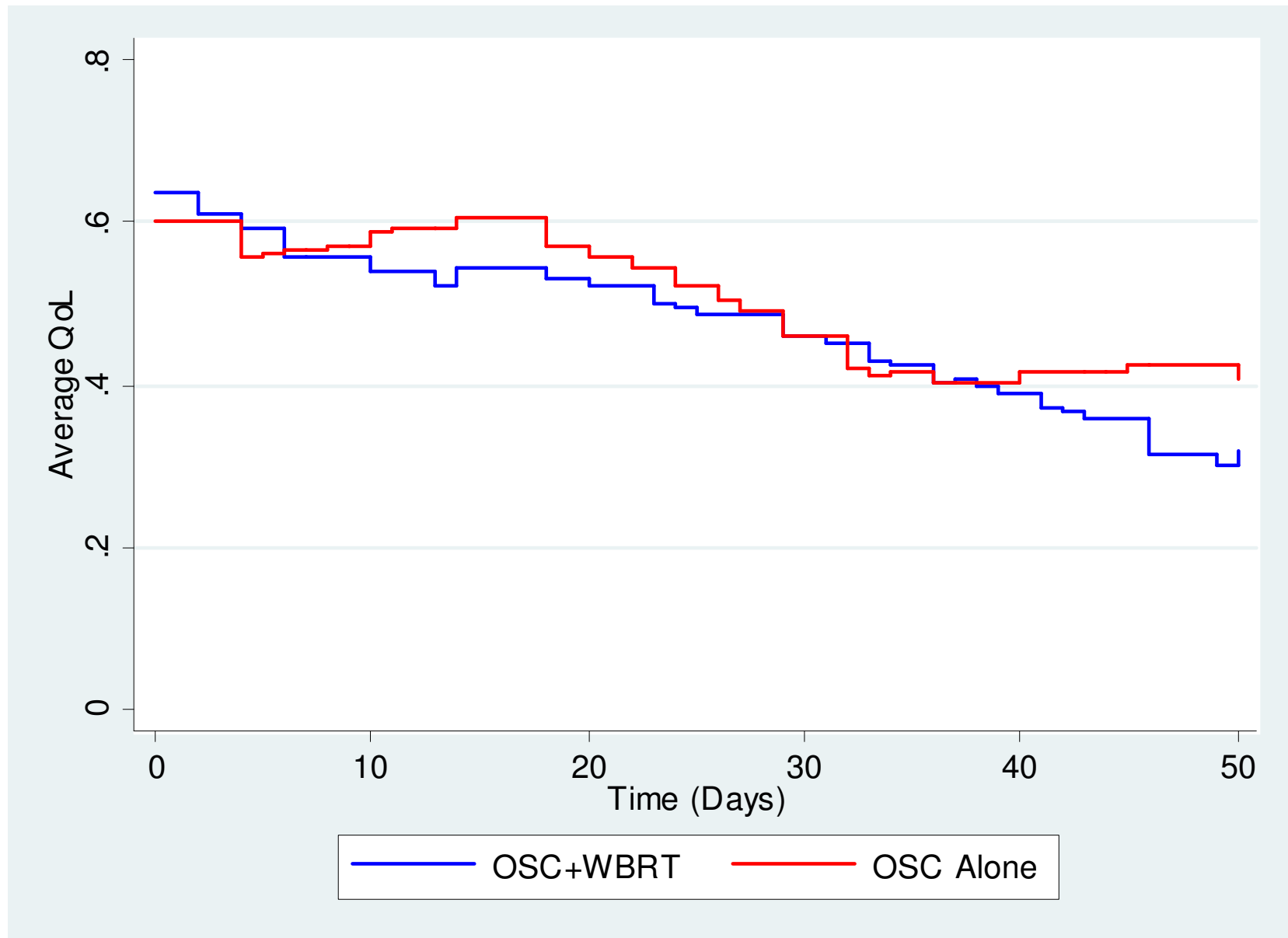
		OSC + WBRT (N=70)	OSC Alone (N=66)
Total number of assessments		564	487
Was assessment completed?	Yes, on planned day	411 (73%)	343 (70%)
	Yes, but not within 2 days	25 (4%)	15 (3%)
	Yes, but no QoL	70 (12%)	77 (16%)
	No	58 (10%)	52 (11%)
	All QoL questions answered	427 (76%)	332 (68%)
Number of assessments per patient	Median	7	7
	Range	1 – 37	1 – 26

Quality of Life over Time

Patient assessed, using the EQ5D questionnaire

MRC

Clinical
Trials
Unit



Calculation of QALYs using EQ-5D questionnaire

- Primary outcome measure is Quality Adjusted Life Years (QALYS), a combination of survival and quality of life.
- This is calculated using the EQ-5D questionnaire using the 5 questions on the next 2 slides, which are asked at baseline and at patient assessments.
- Answers from the 5 EQ-5D questions are combined to give an overall QoL score ranging from -0.594 = if a patient answers 3 to each question to 1 (if a patient answers 1 to each question)
- A graphical representation of the QALYs is shown in a few slides

Calculation of QALYs using EQ-5D questionnaire

1. Mobility

1. = No problems in walking about.
2. = Some problems walking about.
3. = Confined to bed.

2. Self-care

1. = No problems with self care.
2. = Some problems with washing/dressing.
3. = Unable to wash or dress.

3. Usual activities (e.g. work, study, housework, family or leisure activities)

1. = No problems with performing usual activities.
2. = Some problems performing usual activities.
3. = Unable to perform usual activities.

EQ-5D questionnaire

4. Pain/discomfort

1. = No pain or discomfort.
2. = Moderate pain or discomfort.
3. = Extreme pain or discomfort.

5. Anxiety/depression

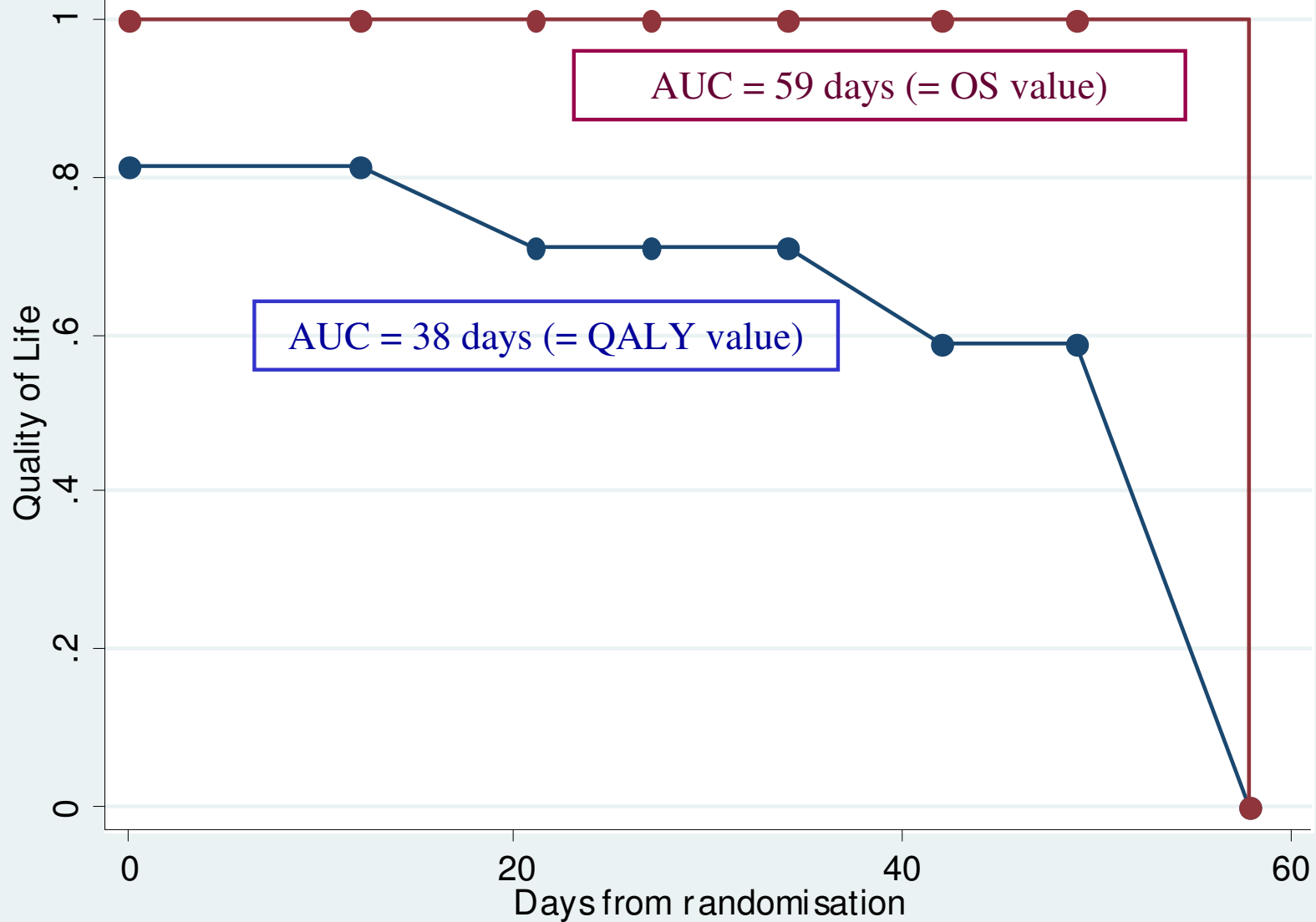
1. = Not anxious or depressed.
2. = Moderately anxious or depressed.
3. = Extremely anxious or depressed.

Two possible QALYs

Same survival time, but different quality of life

MRC

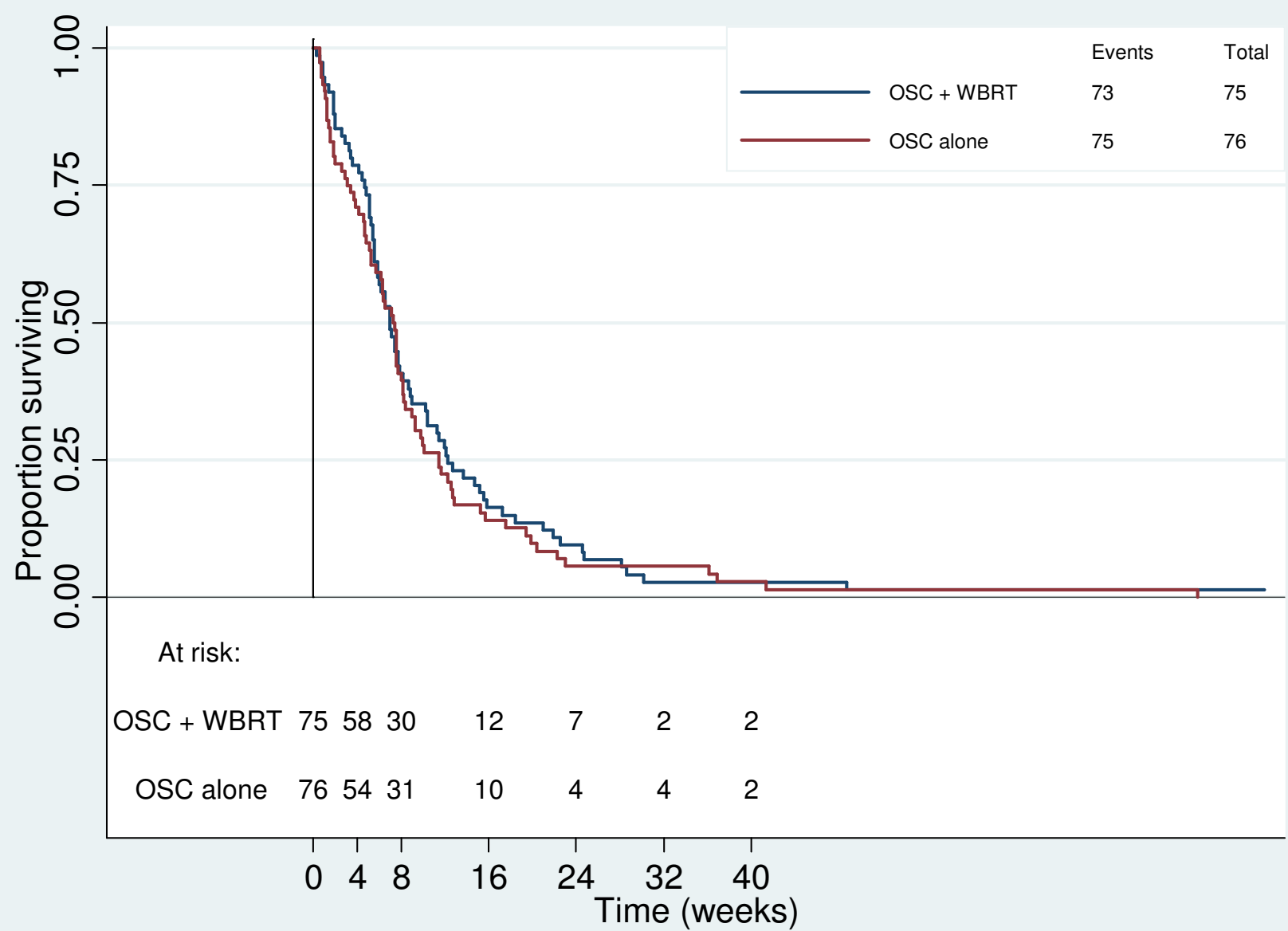
Clinical
Trials
Unit



Patient Survival

		OSC + WBRT (N=75)	OSC alone (N=76)
Number of deaths		73	75
Cause of death	Disease related	73 (100%)	75 (100%)
Survival (weeks)	Median (95% CI)	7 (5.6, 8.7)	7.3 (5.3, 8.1)
	HR	1.11	
	95% CI	(0.80, 1.53)	
	P-value	0.542	

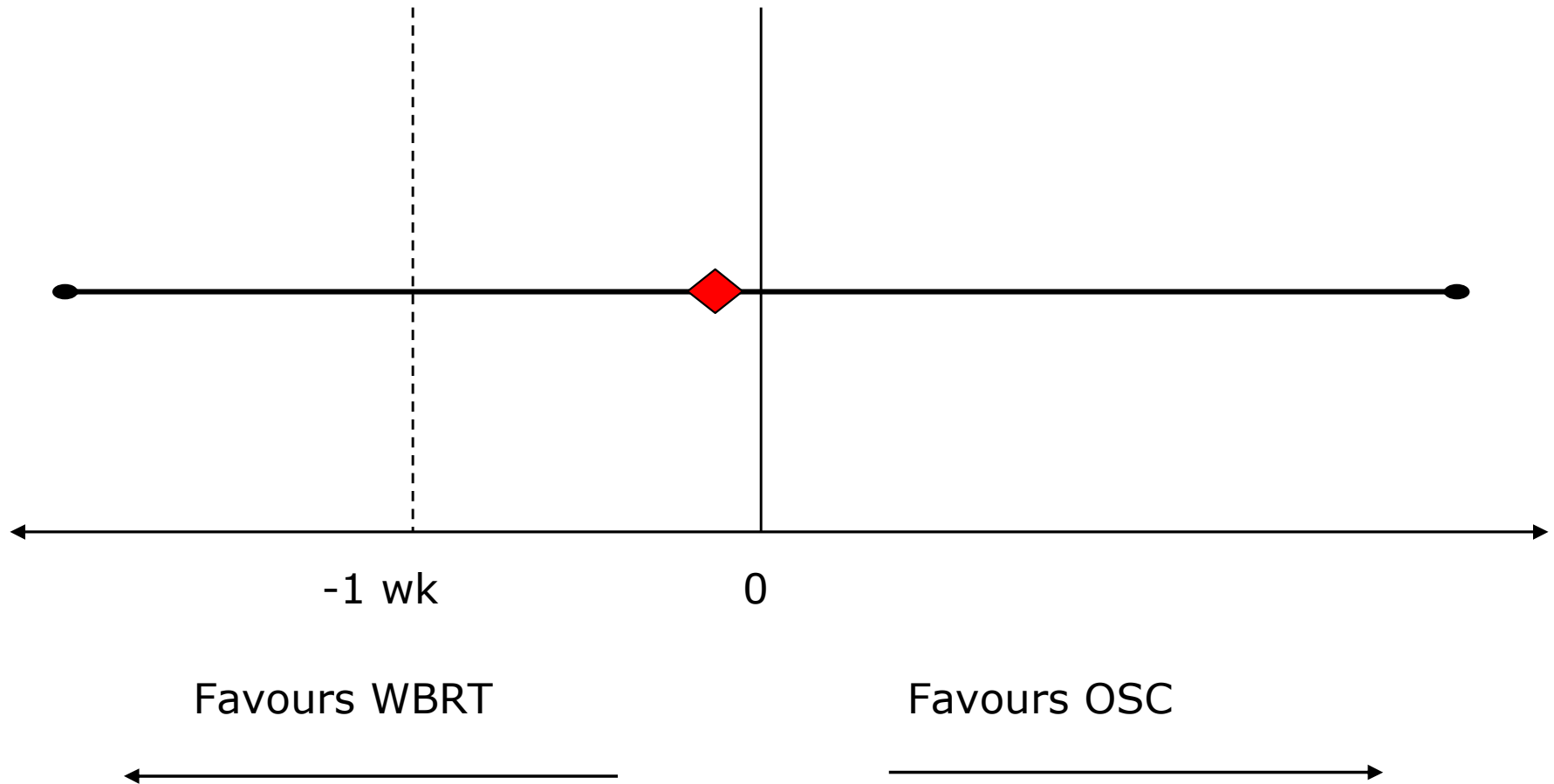
Overall survival



Primary Endpoint: QALYS

	OSC + WBRT	OSC alone
Estimated QALY (days)	31	30
Difference	-1	
95% CI	(-12.0, 13.2)	

Primary Endpoint: QALYS



Summary

- Only 151 patients, so no conclusive data.
- Wide confidence intervals around all estimates.
- No clear difference between the treatment arms in terms of Quality of Life over time.
- Current overall survival estimate is 7 weeks with OSC + WBRT compared to 7.3 weeks with OSC alone.
- Current QALY estimate is 31 days with OSC + WBRT compared to 30 with OSC alone.
- **No evidence that OSC alone is clearly detrimental compared to OSC + WBRT.**



QUARTZ

Quality of Life After Treatment for Brain Metastases