

## **Prospective Evaluation Of Quality Of Life And Patient Reported Outcomes As Primary Endpoints Using The Computer-Assisted LCSS In A Large Multi-National Docetaxel-Based Trial In Non-Small Cell Lung Cancer (NSCLC): The Asia-Pacific QL Trial**

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Topic: NSCLC - Advanced Disease / Elderly and Quality of Life

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Keywords: Docetaxel, QOL (Quality of Life), Non Small Cell Lung Cancer (NSCLC), NSCLC

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## 1. Backgrounds

AP QL Study in Lung Cancer - Background -

**Prospective evaluation of quality of life (QL) and Patient Reported Outcomes (PROs) using the computer-assisted LCSS as primary endpoints in a large multi-national docetaxel-based trial in Non-Small Cell Lung Cancer (NSCLC): the Asia-Pacific QL trial**

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### HRQL as the Primary Endpoint - Background: Quality of Life and "PROs" as Endpoints -

- Few large trials have focused on QL as the primary endpoint in NSCLC although improvement in QL and symptoms are widely considered to be key goals of treatment and in the evaluation of new approaches; however, barriers in accomplishing HRQL assessment are common.
  - In a survey of 260 medical oncologists<sup>1</sup>, 80% supported the concept of evaluating quality of life and symptoms, but many fewer were able to do so in their practices.
  - Barriers included:
    - Lack of knowledge or availability of validated HRQL instruments
    - Insufficient resources within their practices
    - The belief that not enough time was available for HRQL assessment
- Overcoming stated barriers:
  - We recently reported on a trial to approach these problems<sup>2</sup>, the "COMET" study which used the validated LCSS instrument and converted it to a computer-assisted hand-held pocket PC (PDA):
    - Of the 146 patients and 33 doctors and nurses, nearly all found performing the assessments to be highly acceptable, could save time with the visit, and required less than 3 minutes to complete
    - These results form the basis of the current trial testing if a large international group would find the electronic LCSS-QL acceptable, and to investigate if it could affect clinical decision-making

Refs: <sup>1</sup> Morris et al, *Quality of Life Research* 1998; <sup>2</sup> Gralla et al, *Proc ASCO* 2006

### HRQL as the Primary Endpoint - Background: Survival and Response Endpoints -

- Survival, response and quality of life improvements are major goals in treating advanced NSCLC
  - Survival: Enhancing survival for all treated patients with advanced NSCLC beyond that achieved with third generation chemotherapy regimens has proven to be difficult in this highly symptomatic cancer
    - Overall survival in the 11 to 13 month range is the best reported to date
    - Variable results have been reported with the addition of cetuximab (positive results of the FLEX trial were not confirmed with the BMS 099 study)
    - Variable results have been reported with the addition of bevacizumab (positive results with ECOG 4599 were not found in the AVAIL trial)
  - Response is often considered to be an unreliable endpoint for large, randomized clinical trials in NSCLC, related to:
    - A lack of clarity in understanding the worth of response if it does not result in survival or quality of life improvement (including symptomatic benefit)
    - Response evaluation appears to be more accurate with advanced imaging
      - However, this results in greater cost and patient inconvenience, thus limiting the frequency of imaging
      - The predictive prognostic accuracy of even PET scanning has not been established at this time in patients with NSCLC

## HRQL as the Primary Endpoint- Objectives -

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- To demonstrate the feasibility of HRQL assessment (see also Hollen et al, at this meeting)
  - Can quality of life and symptoms be assessed practically in busy oncologic practices in patients receiving chemotherapy and have the data available immediately?
    - Will computer assistance with a hand-held pocket pc (PDA) be practical in 43 practices in 8 countries?
    - Will patients, nurses and physicians complete regular assessments?
    - Do the complications of advanced NSCLC allow regular evaluation?
- To evaluate the effect of chemotherapy on HRQL for all patients being treated
  - In that major response to chemotherapy occurs in only the minority of patients with advanced NSCLC with the most effective regimens, what is the impact on the whole group of patients treated?
  - Prior studies generally have not evaluated or reported the impact on all patients
- To evaluate the effect of chemotherapy on HRQL by response to treatment
  - Is there value in major response to chemotherapy in NSCLC such that patients with response report better symptom control or quality of life than those with stable disease or progression?
  - Does HRQL benefit predict response or better survival?
  - If so, could prospective HRQL evaluation help identify at an early time in treatment those patients benefitting from chemotherapy, and those who are not?

## 2. Methods

AP QL Study in Lung Cancer

- Patients and Methods -

## AP QL Study in Lung Cancer - Patients and Methods -

- All patients received a docetaxel-based chemotherapy regimen (combination or single agent) with every 3-week cycles.
- Docetaxel + platinum regimens are among the best studied combinations for advanced NSCLC in terms of survival and response (*i.e.* the 1200 patient TAX 326 trial<sup>3</sup>). This large existing data base provides context for the current HRQL primary endpoint study. The choice of the specific regimen was at the discretion of the investigator.
- The LCSS-QL quality of life / PRO electronic questionnaire was completed by the patient at the clinic using the pocket PC handheld PDA at the following times:
  - At baseline
  - Every 3 weeks thereafter
  - A total of 7 LCSS-QL evaluations were performed
- Each trial site required only 1 pocket PC for LCSS-QL completion
- Response to chemotherapy (for best response achieved) was assessed at 6 and 9 weeks after starting chemotherapy and at the completion of chemotherapy
- All LCSS-QL data were digitally recorded and were sent electronically to the central database. Additionally, immediate graphic results of patients' HRQL scores over time were provided by this technology.

Refs: <sup>3</sup> Fossella et al *JCO* 2003

## AP QL Study in Lung Cancer - Patients and Methods: LCSS-QL Questionnaire -

- **Practical**

- Designed for clinical trials and patient management, especially for serial quality of life and symptom measurement
- Requires only 2 to 4 minutes for administration with high patient and staff acceptance
- Requires less than 3 minutes for patients to learn to use
- Electronic, PDA computerized format eliminates the need for data transcription and provides an immediate graphic printout. High patient and staff acceptance<sup>4</sup>

- **Patient form: Visual analogue scales (9 questions)**

- **Optional Observer form\*: 5-point categorical scale (6 questions)**

- **The LCSS is well-tested and frequently used (in trials on 6 continents)**

- Good psychometric properties for lung cancer<sup>5</sup>

- **Available in more than 50 languages**

- Standard methodology involving multiple bilingual translators for forward - backward translations, then patient pilot-testing. Good cross-cultural psychometrics

# AP QL Study in Lung Cancer

- Patients and Methods: LCSS-QL Questionnaire -



Arc, Joan 05/12/1921  
LCSS: Observer Scale

**Pain**

100 None

75 present but either no medications required or only non-narcotic, non codeine type oral agents; pain control satisfactory or reasonable

50 codeine or codeine-containing oral medications needed; pain control satisfactory or reasonable

Marked narcotic oral agents required; pain

Back Next

TOSHIBA

Arc, Joan 05/12/1921  
LCSS: Patient Scale

How much pain do you have?

None      As much as it could be

Next

### 3. Results

Results panels are viewed by clicking > read more.

## AP QL Study in Lung Cancer- Inclusion Criteria -

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- Pathologically or cytologically determined NSCLC
- No prior chemotherapy
- Stage IIIB or IV extent
- Performance status: KPS 70 -100% or ECOG 0-1
- Life expectancy estimated to be greater than three months
- Hematologic and metabolic parameters suitable for chemotherapy
- Ability to read one of the languages available on the electronic LCSS (English, Simplified Chinese, Traditional Chinese, Korean, Thai, Hindi, Tamil, Kannada, Malay)
- Signed, written consent form
- Contactable by telephone
- Able to return for follow-up visits

## AP QL Study in Lung Cancer - Patient Characteristics -

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<b>AGE:</b>	
Median (Range)	58 (26 – 81)
<b>GENDER:</b>	
Male	72%
<b>Stage:</b>	
IIIB	23%
IV	77%
<b>PERFORMANCE STATUS: KPS</b>	
90 - 100%	65%
80%	30%
70%	5%
<b>PERFORMANCE STATUS: ECOG</b>	
0	33%
1	67%

**AP QL Study in Lung Cancer (N = 243)**

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	<b>Patient's Primary Language</b>	<b>LCSS Language Used</b>
<b>CHINESE</b>	<b>42%</b>	
- Simplified		<b>22%</b>
- Traditional		<b>20%</b>
<b>Korean</b>	<b>35%</b>	<b>35%</b>
<b>Thai</b>	<b>14%</b>	<b>14%</b>
<b>English</b>	<b>7%</b>	<b>8%</b>
<b>Hindi</b>	<b>1%</b>	<b>1%</b>
<b>Malay</b>	<b>1%</b>	

## AP QL Study in Lung Cancer - Patient Data Analyzed by Study Visit and Chemotherapy Response Evaluation Status -

### AP QL Study in Lung Cancer

- Patient Data Analyzed by Study Visit and Chemotherapy Response Evaluation Status -

	Baseline LCSS Evaluation	LCSS Evaluation at Baseline and at 6 Weeks	LCSS Evaluation at Baseline and at 9 Weeks
Patients with:	243*	186	146
Patients with <i>Response Evaluation</i> and with:	-----	134	100

**Median time for patients to complete the LCSS-QL: 4 minutes**

- This is an ongoing study; many patients have not reached the 6 and 9 week evaluation points

**92% of QL and PRO planned assessments were completed**

- No patient declined to complete the LCSS-QL due to being "too ill"

**AP QL Study in Lung Cancer - Chemotherapy Factors (N = 243) -**

**AP QL Study in Lung Cancer  
- Chemotherapy Factors (N = 243) -**

<b>CHEMOTHERAPY:</b>	
<b>Docetaxel + Cisplatin</b>	<b>52%</b>
<b>Docetaxel + Carboplatin</b>	<b>30%</b>
<b>Docetaxel + other</b>	<b>2%</b>
<b>Docetaxel (single agent)</b>	<b>16%</b>
<b>Median Dose Given:</b>	
<b>Docetaxel</b>	<b>100 mg (60 mg / M<sup>2</sup>)</b>
<b>Cisplatin</b>	<b>110 mg (66 mg / M<sup>2</sup>)</b>
<b>Carboplatin</b>	<b>450 mg (271 mg / M<sup>2</sup>)</b>
<b>Number of Cycles Received:</b>	
<b>Median</b>	<b>4</b>
<b>Mean (range)</b>	<b>4 (1 – 13)</b>

**HRQL Evaluation after 3 Chemotherapy Cycles (at 9 Weeks)- Assessment of All Patients Receiving Chemotherapy - (n = 146 NSCLC)**

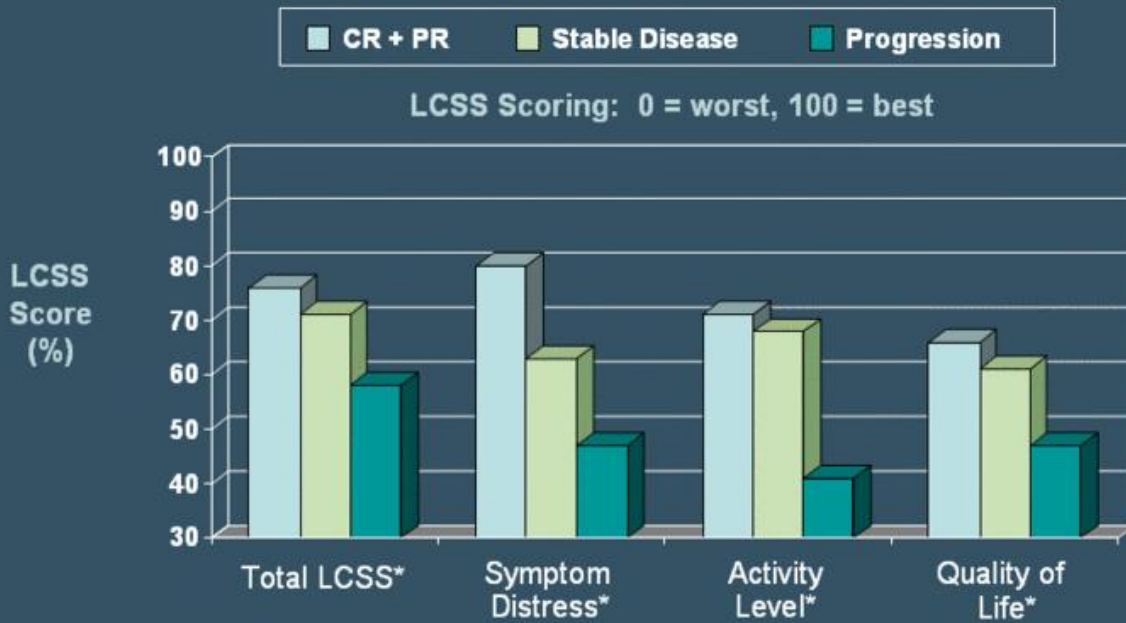
**HRQL Evaluation after 3 Chemotherapy Cycles (at 9 Weeks)  
- Assessment of All Patients Receiving Chemotherapy - (n = 146 NSCLC)**

	<b>Baseline Median*</b>	<b>Median at 9 Weeks*</b>
<b>THORACIC SYMPTOMS:</b>		
Cough	72%	81%
Dyspnea	76%	78%
Hemoptysis	95%	96%
<b>GENERAL SYMPTOMS:</b>		
Pain	80%	82%
Fatigue	69%	69%
Appetite	77%	75%
<b>SUMMARY ITEMS:</b>		
Symptom Distress	64%	68%
Activity Level	68%	66%
Quality of Life	59%	62%

\* LCSS Scoring: 0 = worst, 100 = best

**Results After 2 Cycles of Chemotherapy (At 6 weeks) By Response Category: Summary Items (n = 134 Patients)**

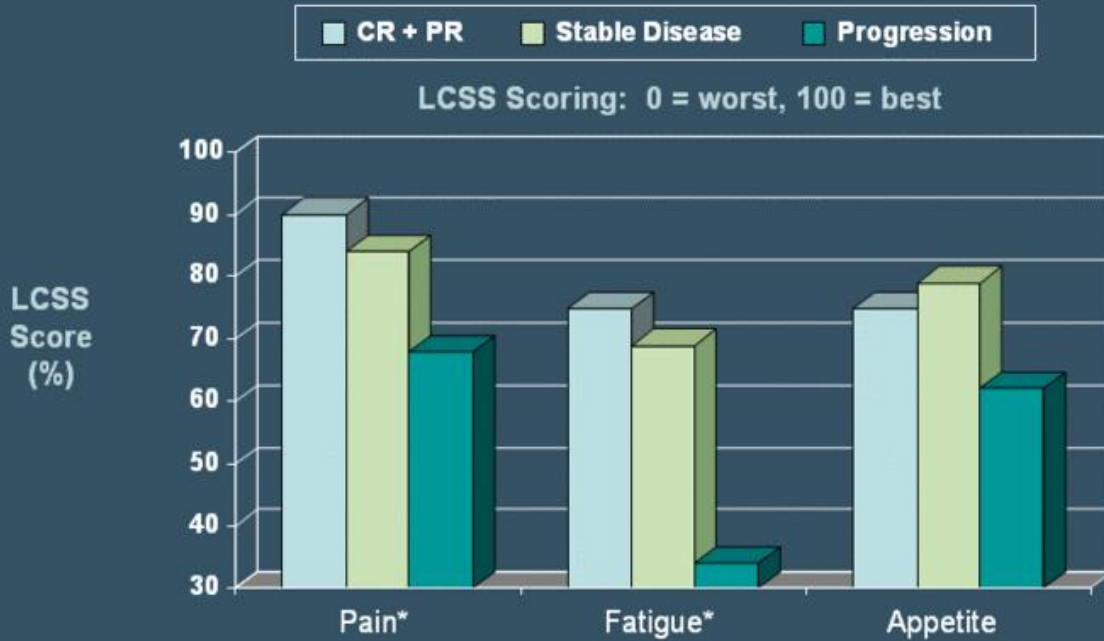
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**Results After 2 Cycles of Chemotherapy (At 6 weeks) By Response Category: General Symptoms (n = 134 Patients)**

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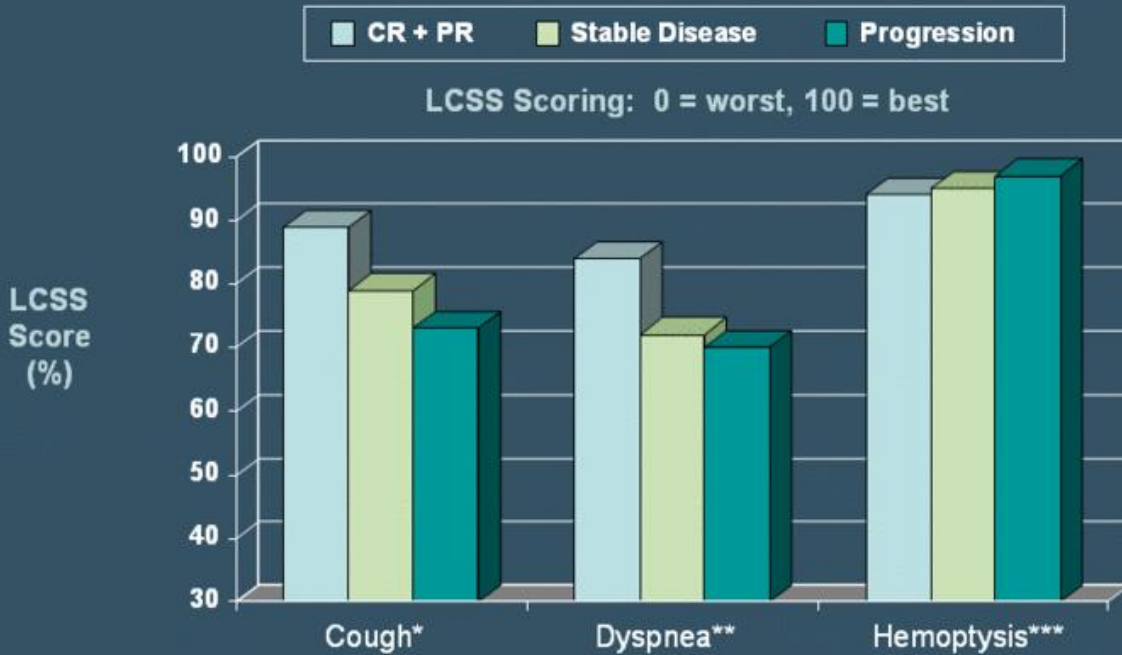


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Note: At 8 weeks (n = 100) patients with progression had even poorer scores for all symptoms

## Results After 2 Cycles of Chemotherapy (At 6 weeks) By Response Category: Thoracic Symptoms (n = 134 Patients)

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\*  $p < 0.05$  CR+PR versus Stable Disease or Prog; \*\*  $p < 0.05$  CR+PR versus Stable Disease (CR+PR = 39%, SD = 45%, Progression = 16%) \*\*\* Note: Hemoptysis present in very few patients at any time  
Note: At 9 weeks (n = 100) patients with progression had poorer scores for cough (61%,  $p < 0.05$ ), hemoptysis (81%,  $p < 0.05$ ), and dyspnea (61%, NS) when compared with those with CR + PR and / or Stable Disease

#### 4. Conclusions

AP QL Study In Lung Cancer

- Conclusions -

# AP QL Study In Lung Cancer - Conclusions -

### Feasibility:

- The LCSS-QL was feasible and highly acceptable to health care professionals and to patients receiving chemotherapy when completed on an every 3 week basis:
  - It required less than 4 minutes of patient time for completion
  - The LCSS-QL completion rate was 92%
  - Patients were enlisted from 8 countries at 43 sites and completed the LCSS-QL in 6 languages

### The impact of chemotherapy on HRQL in all patients:

- For the whole group of patients, HRQL and symptoms remained stable or modestly improved for all parameters 9 weeks after starting docetaxel-based chemotherapy:
  - Meta-analysis has noted survival advantage for the whole group of patients treated with chemotherapy. This study demonstrates that this survival benefit is associated with at least stable HRQL, even though fewer than half of patients experience a major response. These results demonstrate that both benefits need to be emphasized in clinical decisions.

### The impact of chemotherapy on HRQL by response to treatment:

- After only 2 cycles of these docetaxel-based regimens, clear differences in HRQL and symptoms could be seen between those achieving major response contrasted to patients with progression
- HRQL and symptom control were generally better for those with major response as opposed to patients with stable disease

### These findings indicate that prospective evaluation of HRQL:

- Is feasible in patients receiving chemotherapy for NSCLC
- Can assist in clinical decision making, enhancing earlier evaluation of the efficacy of chemotherapy. This may also allow for better resource utilization regarding imaging and continuation of chemotherapy
- Can benefit from further testing to investigate whether HRQL can predict the likelihood of major response or survival advantage based on the rapidity or magnitude of change
- The Asia Pacific QL trial will continue accrual to 710 patients to allow for better definition of all findings

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## 5. Mediafiles

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## HRQL as the Primary Endpoint - Objectives -

- To demonstrate the feasibility of HRQL assessment (see also Hollen et al, at this meeting)
  - Can quality of life and symptoms be assessed practically in busy oncologic practices in patients receiving chemotherapy and have the data available immediately?
    - Will computer assistance with a hand-held pocket pc (PDA) be practical in 43 practices in 8 countries?
    - Will patients, nurses and physicians complete regular assessments?
    - Do the complications of advanced NSCLC allow regular evaluation?
- To evaluate the effect of chemotherapy on HRQL for all patients being treated
  - In that major response to chemotherapy occurs in only the minority of patients with advanced NSCLC with the most effective regimens, what is the impact on the whole group of patients treated?
  - Prior studies generally have not evaluated or reported the impact on all patients
- To evaluate the effect of chemotherapy on HRQL by response to treatment
  - Is there value in major response to chemotherapy in NSCLC such that patients with response report better symptom control or quality of life than those with stable disease or progression?
  - Does HRQL benefit predict response or better survival?
  - If so, could prospective HRQL evaluation help identify at an early time in treatment those patients benefitting from chemotherapy, and those who are not?

**Prospective evaluation of quality of life (QL) and Patient Reported Outcomes (PROs) using the computer-assisted LCSS as primary endpoints in a large multi-national docetaxel-based trial in Non-Small Cell Lung Cancer (NSCLC): the Asia-Pacific QL trial**

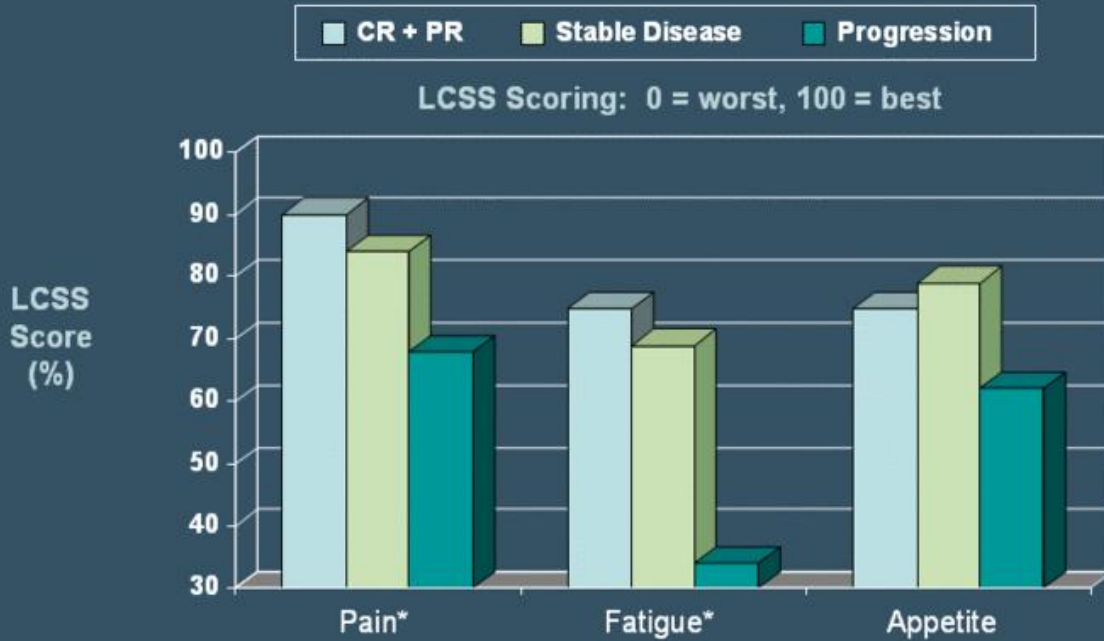
**Prospective evaluation of quality of life (QL) and Patient Reported Outcomes (PROs) using the computer-assisted LCSS as primary endpoints in a large multi-national docetaxel-based trial in Non-Small Cell Lung Cancer (NSCLC): the Asia-Pacific QL trial**



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**Results After 2 Cycles of Chemotherapy (At 6 weeks) By Response Category: General Symptoms (n = 134 Patients)**

**Results After 2 Cycles of Chemotherapy (At 6 weeks) By Response Category:  
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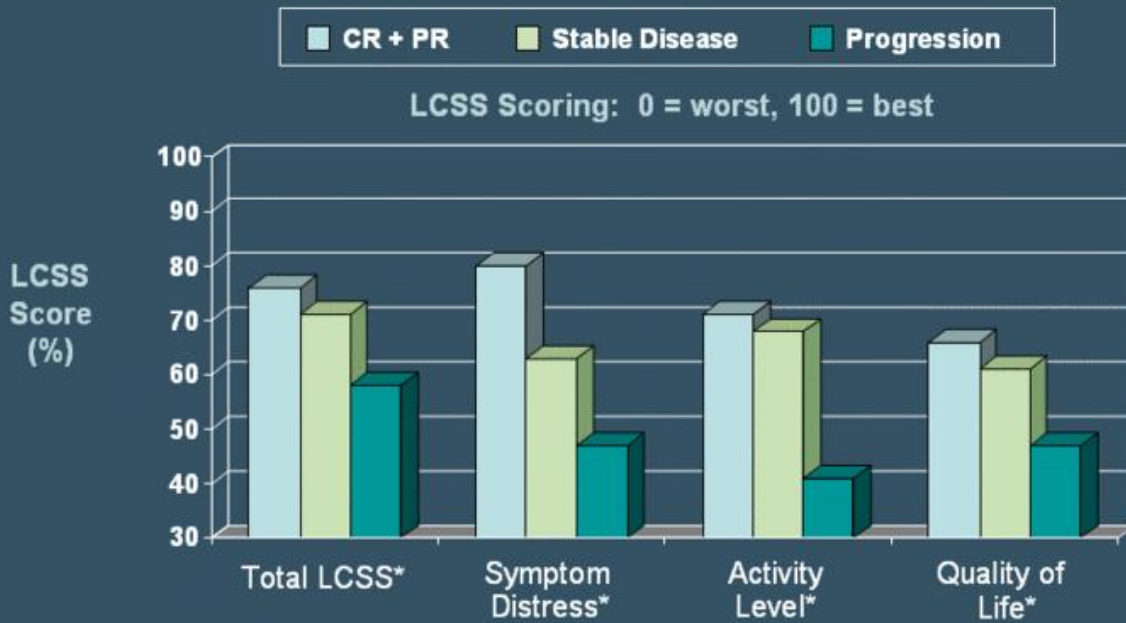


\*  $p < 0.05$  CR + PR, and Stable Disease versus Progressive Disease (CR+PR = 39%, SD = 45%, Progression = 16%)

Note: At 8 weeks (n = 100) patients with progression had even poorer scores for all symptoms

**Results After 2 Cycles of Chemotherapy (At 6 weeks) By Response Category: Summary Items (n = 134 Patients)**

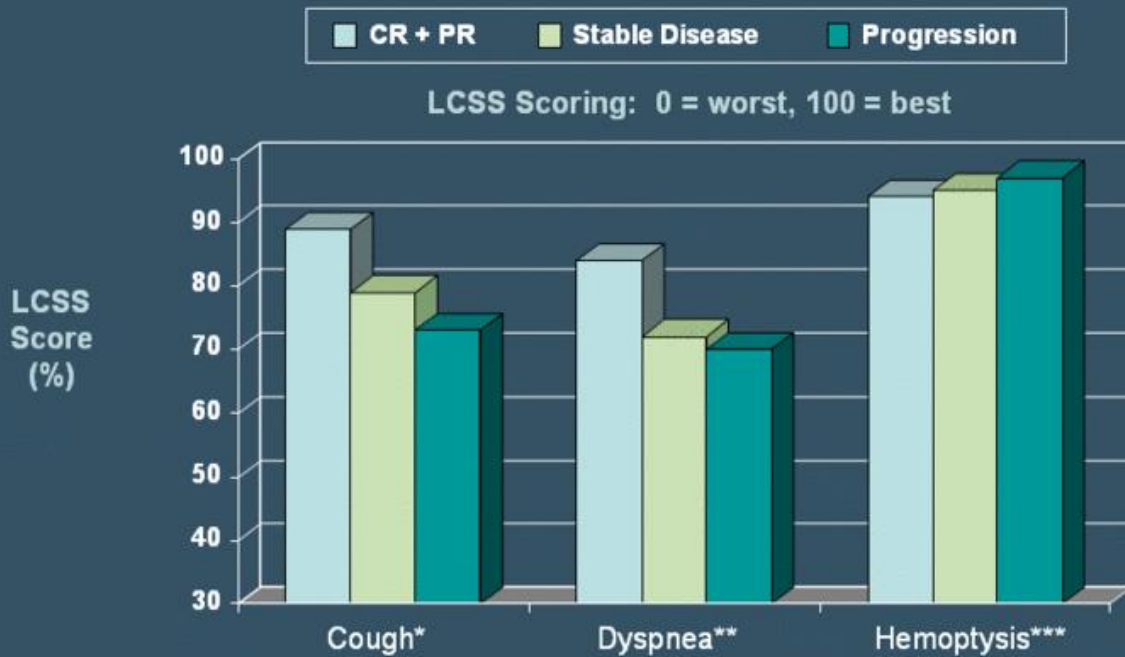
**Results After 2 Cycles of Chemotherapy (At 6 weeks) By Response Category:  
Summary Items (n = 134 Patients)**



\*  $p < 0.05$  CR + PR, and Stable Disease versus Progressive Disease (CR+PR = 39%, SD = 45%, Progression = 16%)

**Results After 2 Cycles of Chemotherapy (At 6 weeks) By Response Category: Thoracic Symptoms (n = 134 Patients)**

**Results After 2 Cycles of Chemotherapy (At 6 weeks) By Response Category:  
Thoracic Symptoms (n = 134 Patients)**



\*  $p < 0.05$  CR+PR versus Stable Disease or Prog; \*\*  $p < 0.05$  CR+PR versus Stable Disease (CR+PR = 39%, SD = 45%, Progression = 16%) \*\*\* Note: Hemoptysis present in very few patients at any time

Note: At 9 weeks (n = 100) patients with progression had poorer scores for cough (61%,  $p < 0.05$ ), hemoptysis (81%,  $p < 0.05$ ), and dyspnea (61%, NS) when compared with those with CR + PR and / or Stable Disease