An Improved *Early*CDT™-Lung Test Can Be Used To Aid The Detection of Lung Cancer

C. Chapman[1], A. Murray[2], L. Peek[3], P. Boyle[4], J. Allen[2], C. Parsy-Kowalska[2], P. Maddison[5], G. Healey[2], J. Robertson[1,2]

[1]Division of Surgery, University of Nottingham, Nottingham, UK; [2]Oncimmune Ltd., Nottingham, UK; [3]Oncimmune LLC, DeSoto, KS, USA; [4]IPRI, Lyon, France; [5]Department of Neurology, Nottingham NHS Trust, Nottingham UK.   email: caroline.chapman@nottingham.ac.uk

PURPOSE

A humoral immune response in the form of autoantibodies to tumor-associated antigens has been reported in individuals with evidence of solid tumors.

These autoantibodies have been shown to be present in the circulation of individuals with lung cancer, and in some cases up to 5 years before the cancer presented clinically (1-3). These antibodies may therefore represent the earliest marker of carcinogenesis.

*Early*CDT™-Lung detects autoantibodies to a panel of six tumor-associated antigens (TAAs) with a sensitivity of 40% and a specificity of 90%. *Early*CDT-Lung has been shown to aid in the detection of both early-stage and late-stage disease in high-risk individuals.

The addition of **two lung cancer associated antigens** to this test was investigated.

The positivity rate for each antigen by histological subtype and stage of disease are presented.

METHODS

Patients with lung cancers (N=235) and age, gender and smoking matched controls had autoantibodies to eight tumor-associated antigens measured on serum samples taken post-diagnosis but prior to treatment.

Patient Details and Clinical Characteristics

	ALL Lung Cancers	NSCLC	SCLC	Other
Group - n	235	178	53	4
Median age (range)	65 (42-85)	66 (43-85)	62 (42-80)	72 (53-81)
Male % (n)	73% (171)	78% (138)	59% (31)	50% (2)

Stages:
NSCLC (n):
Stage I (87), Stage II (54), Stage III (16), Stage IV (6), unknown (15)

SCLC (n):
Limited Disease (26), Extensive disease (14), unknown (13)

The antigens comprised those in the *Early*CDT-Lung test (p53, NY-ESO-1, CAGE, GBU4-5, SOX2 and Annexin I) with the addition of MAGE A4 and Hu-D.

The presence of autoantibodies was evaluated using a semi-automated enzyme-linked immunosorbent assay (ELISA) method where optical densities (OD) were converted to calibrated reference units (RU) (1).

Full assay details are described elsewhere (1).

REFERENCES

1. Murray *et al* Technical Validation of an autoantibody test for lung cancer. Ann Oncol. 2010;21:1687
2. Boyle *et al* Clinical Validation of an autoantibody test for lung cancer. Ann Oncol. 2010 Jul 30 [Epub]
3. Zhong *et al* Profiling tumor-associated antibodies for early detection of non-small cell lung cancer. J Thor Oncol 2006;1:51

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RESULTS

The addition of MAGE A4 and Hu-D to the *Early*CDT-lung panel improved the sensitivity of the assay for the detection of lung cancer by **7%** with a loss in specificity of only **1%.**

The positivity rates for the panel by stage of disease for non-small cell lung cancer (NSCLC) and for extensive vs limited disease for small cell lung cancer (SCLC) were similar for all stages.

The positivity rate for individual autoantibody assays ranged in NSCLC from 2%-10% and in SCLC from 6%-21% with specificity for each antigen being >96%.

ELISA Scatter Plots - Examples
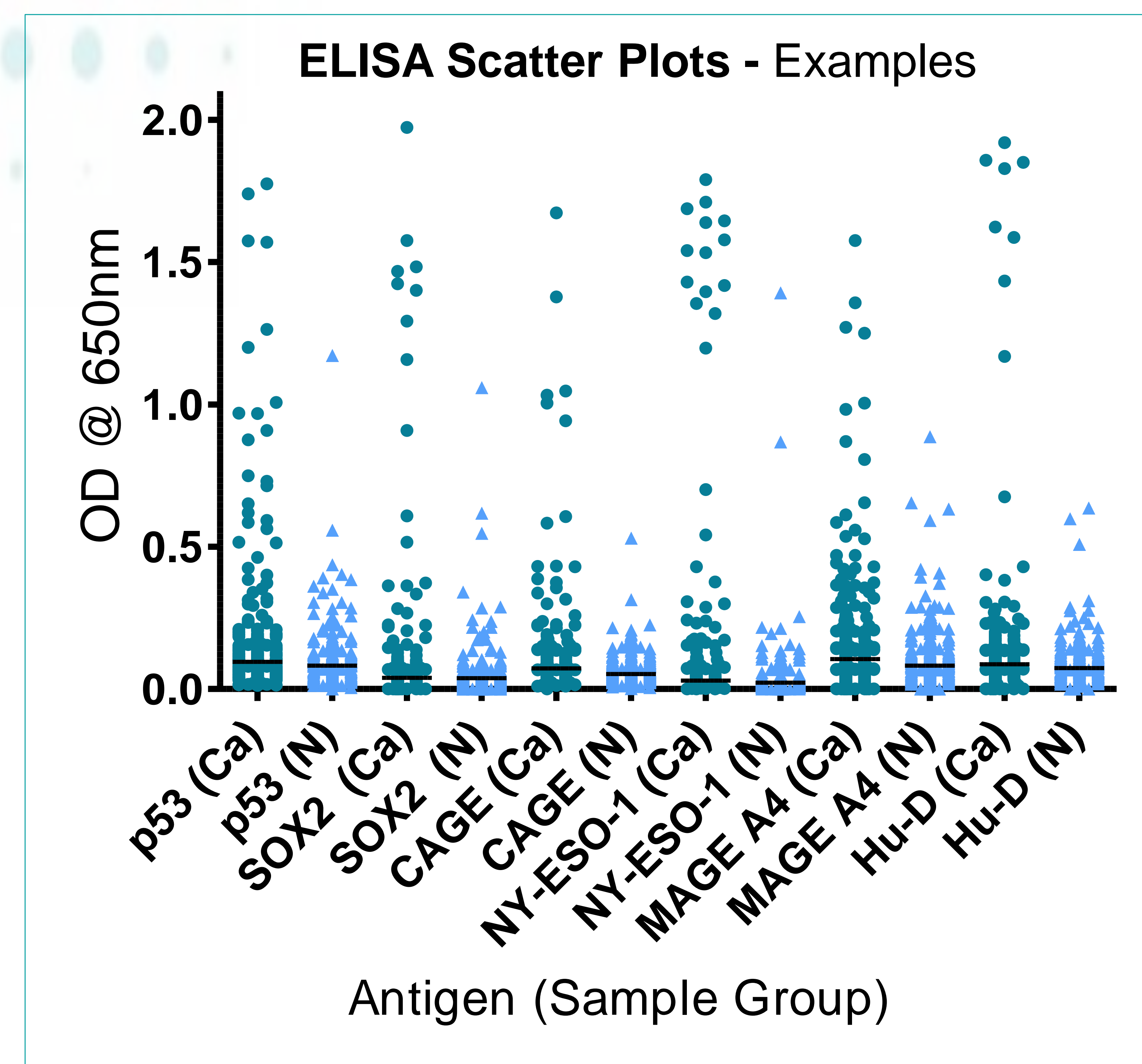
Frequency of Autoantibodies to Individual TAAs

GROUP		p53	SOX2	CAGE	NY-ESO-1	GBU4-5	Annexin I	MAGE A4	Hu-D
All Lung Cancers	%+ve (95% CI)	10 (7, 15)	8 (5, 12)	11 (8, 16)	11 (7, 15)	4 (2, 7)	7 (4, 11)	9 (6, 13)	5 (2, 8)
NSCLC	%+ve (95% CI)	9 (5, 14)	4 (2, 9)	10 (6, 15)	10 (6, 16)	2 (0, 5)	7 (4, 11)	10 (6, 16)	2 (0, 5)
SCLC	%+ve (95% CI)	15 (7, 28)	21 (11, 34)	17 (8, 30)	13 (5, 25)	9 (3, 21)	8 (2, 18)	6 (1, 16)	15 (7, 28)
Matched Normals	%+ve (95% CI)	2 (1, 5)	3 (1, 5)	2 (0, 4)	2 (0, 4)	2 (1, 5)	3 (1, 7)	2 (1, 5)	0 (0, 2)
Specificity	%	98	97	98	98	98	97	98	>99

%+ve with 95% confidence interval (x,y) in each patient group

CLINICAL IMPLICATIONS

The presence of autoantibodies in individuals with lung cancer may provide an early indication of disease for high-risk individuals, when the chance of successful treatment would be greatest.

Frequency of Autoantibodies to a Panel of TAAs

Sensitivity for Final Panel Specificity of ~90%
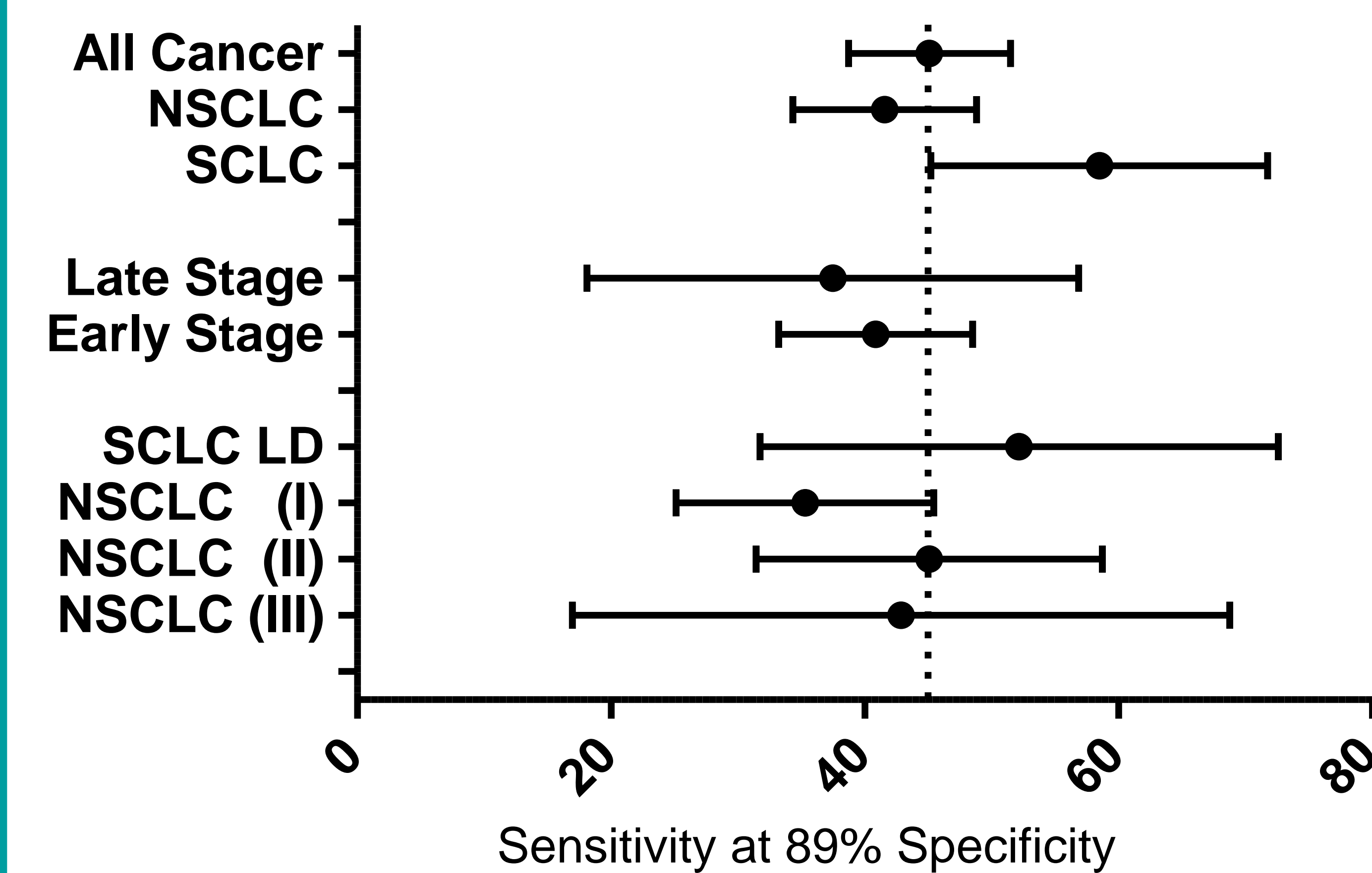Panel of 6 - *Early*CDT-Lung Panel
Panel of 8 - *Early*CDT-Lung + MAGE A4 & Hu-D

Group	n		PANEL of 6	PANEL of 8
All Lung Cancers	235	% +ve 95% CI	38*** (32, 44)	45*** (39, 52)
NSCLC	178	% +ve 95% CI	34*** (27, 41)	42*** (34, 49)
SCLC	53	% +ve 95% CI	53*** (39, 67)	58*** (44, 72)
Matched Normals	235	% +ve 95% CI	10 (6, 14)	11 (7, 16)
Specificity	235	%	90	89

% +ve with 95% confidence interval (x,y) in each patient group. *Denotes p-value relative to normal control results. Chi-squared analysis *** -p<0.001

Forest Plot - Sensitivity by Cancer Stage

Positivity defined as the presence of one or more autoantibodies (panel of 8 Antigens)

CONCLUSIONS

These data confirm that the **addition of two new antigens** to the *Early*CDT-Lung panel **increased the detection of all stages of lung cancer** giving a sensitivity of at least 45%.

The **presence of autoantibodies may provide an early indication of lung cancer**, even in early-stage disease and may be useful in the management of high-risk individuals.

Differences in the autoantibody profiles may in the future be useful in identifying what subtype or stage of lung cancer a patient is most likely to have.