

# An Autoantibody Test (AABT) to Aid in Early Detection of Lung Cancer in High-Risk Patients is Likely to be Cost-Effective

Peter Boyle<sup>1</sup>, Derek Weycker<sup>2</sup>, Anne Khoo<sup>2</sup>, James R. Jett<sup>3</sup>, Frank C. Detterbeck<sup>4</sup>, Timothy C. Kennedy<sup>5</sup>, Daniel L. Miller<sup>6</sup>, Herbert Fritsche<sup>7</sup>, William C. Wood<sup>6</sup>, Geoffrey Hamilton-Fairley<sup>8</sup>, John F. R. Robertson<sup>9</sup>, John Edelsberg<sup>2</sup>

<sup>1</sup>International Prevention Research Institute (IPRI), Lyon, France; <sup>2</sup>Policy Analysis Inc. (PAI), Brookline, MA; <sup>3</sup>Mayo Clinic, Rochester, MN; <sup>4</sup>Yale University, New Haven, CT; <sup>5</sup>University of Colorado Cancer, Denver, CO;

<sup>6</sup>Emory University, Atlanta, GA; <sup>7</sup>MD Anderson Cancer Center, Houston, TX; <sup>8</sup>Oncimmune Ltd., Nottingham, England; <sup>9</sup>The University of Nottingham, Nottingham, England

## BACKGROUND

- Lung cancer (LC) is most common cause of cancer death in US, in part because it typically is not diagnosed until advanced stages
- Trials suggest screening with computed tomography (CT) may yield favorable shift in LC stage at diagnosis, although a survival benefit has not been convincingly shown
- AABT—*Early*CDT-Lung (Oncimmune Ltd)—to aid in LC detection recently developed:
  - AABT comprises panel of 6 tumor-related antigens found to be present in LC several years before any tumor can be detected
- Thus, although less sensitive than CT, AABT can detect smaller, less-advanced cancers; it also has greater specificity than CT
- Patients with AABT+ (and CT+) are more likely to have LC and thus may be more aggressively evaluated and treated, which may yield tangible (eg, survival) benefits

## STUDY OBJECTIVE

- To estimate cost-effectiveness of screening high-risk patients for LC with AABT, using techniques of decision-analytic modeling

## STUDY METHODS

### Model Description

- Model depicts clinical and economic consequences of alternative strategies for LC screening in cohort of 100,000 previously unscreened high-risk patients

- Model considers a single “prevalence-round” screening exam

- Screening strategies include:

- AABT followed by CT if positive (AABT→CT)

- AABT plus CT (AABT+CT)

- CT alone

- No Screening

- Patients assumed to be 60 years of age and at high-risk of having previously undetected LC due to current or former smoking:

- NSCLC—aggressive and indolent types—and SCLC considered

- Patients classified into one of four groups—true-positive, true-negative, false-positive, false-negative—based on LC+ vs LC- and screening+ vs screening-

- True-positives undergo further diagnostic evaluation followed by LC treatment:

- Diagnostic tests employed, and their scheduling, depend on whether AABT and/or CT are positive, and nodule size

- Detection of aggressive NSCLC/SCLC by CT screening yields earlier stage and smaller tumor (NSCLC stage 1), which confer survival benefits (vs no screening):

- LC detected with AABT assumed, on average, to be smaller and less advanced, which results in stage, size, and survival benefits

- Detection of indolent NSCLC by screening (“overdiagnosis bias”) generates additional costs but confers no survival benefit

## Model Description (Cont.)

- True-negatives undergo no further diagnostic evaluation
- False-positives undergo additional evaluation that ultimately rules out diagnosis
- False-negatives with aggressive NSCLC/SCLC are correctly diagnosed, on average, 12 months following screening and subsequently undergo LC treatment:
  - Cancer assumed to have same size/stage as that detected in clinical practice, and thus to be more advanced than that for true-positives
  - Most patients with false-negative indolent NSCLC are never diagnosed
- Costs include: initial screening (all patients); follow-up diagnostic evaluation (true-positives and false-positives); LC treatment (true-positives and false-negatives)
- Study perspective: healthcare system
- Future benefits and costs (2008US\$) discounted at 3% per year

## Model Estimation

- LC prevalence estimated assuming a three-year “look-forward period”:
  - AABT+ could result from tumor detectable by CT at time of screening or from one so small it would not be detectable by CT for up to three years
- CT sensitivity/specificity calculated from “prevalence-screen” perspective based on results of Mayo Clinic study<sup>1-3</sup>; for AABT, estimates based on published data<sup>4,5</sup>

Table 1. Estimated values of selected model parameters

Model Parameter	Value		Reference
	NSCLC	SCLC	
<b>Disease Characteristics</b>			
Prevalence of Lung Cancer, %	3.20%	0.56%	1-3, 6, 7
Type of Lung Cancer, %	85%	15%	7
<b>Screening Test Characteristics</b>			
<b>CT</b>			
Sensitivity	47%	47%	1-3
Specificity	49%	49%	
<b>AABT</b>			
Sensitivity	40%	40%	4, 5
Specificity	90%	90%	
<b>Stage Shift vs No Screening, %</b>			
CT	50%	25%	8 (NSCLC), Expert Opinion (SCLC)
AABT→CT	80%	40%	Expert Opinion
AABT+CT	67.6%	34.3%	Derived
<b>Size Shift (Stage 1) vs No Screening, mm</b>			
CT	16.0	---	2
AABT→CT	18.0	---	Expert Opinion
AABT+CT	17.2	---	Derived
Overdiagnosis Bias, %	27%	---	9
<b>Costs</b>			
<b>Initial Screen</b>			
CT	\$301	\$301	10
AABT	\$300	\$300	Assumed
<b>LC Treatment</b>			
11			
Initial Year (Stage 1 - 4)	\$35,871 - \$50,346	\$50,346	
Continuing Years (Annual)	\$4,576	\$4,576	
Last Year of Life (Stage 1 - 4)	\$46,295 - \$78,623	\$78,623	

## Analyses

- Cost-effectiveness calculated as ratio of difference in expected costs to difference in expected quality-adjusted life-years (QALYs) between:
  - AABT→CT vs No Screening and CT alone, respectively
  - AABT+CT vs No Screening and CT alone, respectively
  - CT vs No Screening

## RESULTS

### Outcomes

- Of 2,901 cases of aggressive NSCLC/SCLC, 1,161 (true-positives) would be detected with AABT→CT, 1,979 with AABT+CT, and 1,363 with CT alone; false-positives would total 9,623 (AABT→CT), 53,794 (AABT+CT), and 49,079 (CT alone)

Table 2. Classification from screening for lung cancer in a hypothetical population of 100,000 current/former smokers

	No Screening	CT	AABT→CT	AABT+CT
True Negatives	96,234	47,155	86,611	42,440
False Positives	---	49,079	9,623	53,794
True Positives	---	1,770	1,507	2,569
NSCLC	---	1,505	1,281	2,184
Aggressive	---	1,098	935	1,594
Indolent	---	407	346	590
SCLC	---	265	226	385
False Negatives	3,766	1,996	2,259	1,197
NSCLC	3,202	1,697	1,921	1,018
Aggressive	2,337	1,239	1,402	743
Indolent	865	458	519	275
Detected	123	0	0	0
Undetected	742	458	519	275
SCLC	564	299	338	179

- Compared with no screening, screening would increase costs by \$497 (AABT→CT), \$1242 (AABT+CT), and \$802 (CT alone) per patient, and yield an additional 0.04 (AABT→CT), 0.05 (AABT+CT), and 0.03 (CT alone) QALYs per patient

Table 3. Outcomes from screening for lung cancer in a hypothetical population of 100,000 current/former smokers\*

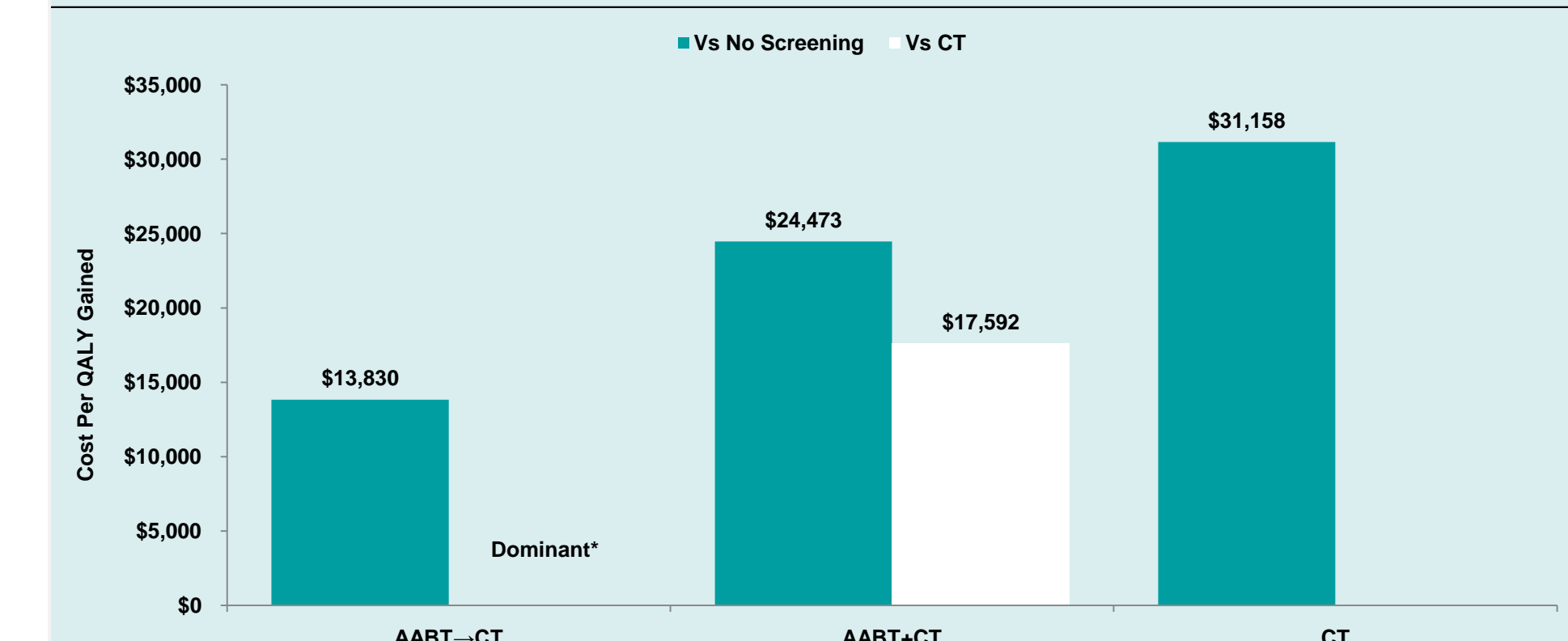
	No Screening	CT	AABT→CT	AABT+CT
Life-Years	1,506	1,510	1,511	1,513
Quality-Adjusted Life-Years	1,303	1,306	1,307	1,308
Cost	\$230,947	\$311,162	\$280,676	\$355,165
Screening	\$0	\$30,051	\$33,345	\$60,051
Diagnostic Follow-up	\$10,481	\$51,227	\$23,018	\$61,011
Treatment	\$220,466	\$229,883	\$224,313	\$234,103

\*Discounted values, in 000s

## RESULTS (CONT.)

### Cost-Effectiveness

Figure. Cost-effectiveness of screening for lung cancer with AABT→CT and AABT+CT versus no screening and versus screening with CT alone, respectively



\*Less costly, more effective

## Sensitivity Analyses

Table 4. Sensitivity analyses on cost per QALY gained

Base-case	AABT→CT vs		AABT+CT vs	
	No Screen	CT	No Screen	CT
Prevalence	\$13,830	Dominant	\$24,473	\$17,592
Age 50 (1.07%)	\$32,329	Dominant	\$55,775	\$39,848
Age 70 (7.88%)	\$13,902	Dominant	\$22,604	\$17,399
<b>Cost of AABT screening</b>				
\$0	\$5,487	Dominant	\$18,563	\$5,598
\$100	\$8,268	Dominant	\$20,533	\$9,596
\$200	\$11,049	Dominant	\$22,503	\$13,594
\$500	\$19,392	Dominant	\$28,413	\$25,588
<b>Sensitivity - AABT</b>				
20%	\$24,413	\$48,272 (CT)	\$28,331	\$24,069
30%	\$17,432	Dominant	\$26,230	\$20,203
60%	\$10,182	Dominant	\$21,685	\$14,271
<b>Specificity - AABT</b>				
80%	\$18,722	Dominant	\$26,496	\$21,697
95%	\$11,384	Dominant	\$23,462	\$15,540
<b>Stage Shift - AABT→CT</b>				
NSCLC 65%, SCLC 40%	\$17,706	---	---	---
NSCLC 50%, SCLC 40%	\$23,718	---	---	---
NSCLC 25%, SCLC 40%	\$47,254	---	---	---
NSCLC 80%, SCLC 0%	\$12,990	---	---	---
<b>Stage Shift - AABT→CT vs CT</b>				
NSCLC 65% vs 50%, SCLC 40% vs 25%	---	Dominant	---	---
NSCLC 50% vs 50%, SCLC 40% vs 25%	---	\$95,654 (CT)	---	---
NSCLC 25% vs 25%, SCLC 40% vs 25%	---	\$273,049 (CT)	---	---
NSCLC 80% vs 50%, SCLC 0% vs 0%	---	Dominant	---	---
<b>Stage Shift - AABT+CT</b>				
NSCLC 50%, SCLC 34.3%	---	---	\$34,042	---
NSCLC 25%, SCLC 34.3%	---	---	\$68,321	---
<b>Stage Shift - AABT+CT vs CT</b>				
NSCLC 50% vs 50%, SCLC 34.3% vs 25%	---	---	---	\$40,119
NSCLC 25% vs 25%, SCLC 34.3% vs 25%	---	---	---	\$78,472

## CONCLUSION AND CLINICAL IMPLICATION

- Screening high-risk patients for LC using AABT, in conjunction with CT, is likely to be cost-effective by current standards in comparison with CT screening or no screening
- Use of AABT in early detection of lung cancer is supported by clinical as well as economic evidence

## REFERENCES

- Swensen, *Am J Respir Crit Care Med* 2002;165:508-13
- Swensen, *Radiology* 2003;226:756-61
- Swensen, *Radiology* 2005;235:259-65
- Boyle, *JCO* 2010;in press
- Murray, *Ann Oncol* 2010;doi:10.1093/annonc/mdp606
- SEER Cancer Statistics Review 1975-2006, NCI website
- Fry, *Cancer* 1996;77:1947-55
- Mahadevia, *JAMA* 2003;289:313-22
- Lindell, *Radiology* 2007;242:555-62
- RBRVS 2008; Chicago, Ill: American Medical Association
- Yabroff, *J Natl Cancer Inst* 2008;100:630-41