CURRENT ONCOLOGY
A Canadian Cancer Research Journal

Supplemental Materials for

Comprehensive genomic profiling for non-small cell lung cancer: health and budget impact

K.M. Johnston PhD, B. Sheffield MD, S. Yip MD, P. Lakzadeh MSc, C. Qian MSc, J. Nam MSc.

Listing of Supplemental Material(s):

Supplementary Appendix

Appendix 1: Details of testing efficacy calculations

For conventional genetic testing, genetic alterations considered were: EGFR, ALK, ROS1, BRAF, MET, HER2, RET, KRAS, noting that testing and treatment for MET, HER2, and RET were not considered applicable in Canada. The prevalence of mutations was reported in the literature by squamous and non-squamous histology type as summarized in the table below (Appendix 1Table 1).

Appendix 1 Table 1 Prevalence of alterations under conventional testing

Histology / Locus	Prevalence of alterations using conventional testing	Source	Link
Non-squamous (70%)			
EGFR	17%	Kris 2014	http://jama.jamanetwork.com/article.aspx?articleid=1872815
ALK	3%	Bergethon 2010	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3295572/
ROS1	1%	Gainor 2013	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3720641/
BRAF	2%	Kris 2014	http://jama.jamanetwork.com/article.aspx?articleid=1872815
MET	1%	Kris 2014	http://jama.jamanetwork.com/article.aspx?articleid=1872815
HER2	3%	Kris 2014	http://jama.jamanetwork.com/article.aspx?articleid=1872815
RET	1%	Gainor 2013	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3720641/
KRAS	25%	Kris 2014	http://jama.jamanetwork.com/article.aspx?articleid=1872815
Squamous (30%)			

MET	6%	Heist 2012	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3404741/

The distribution of squamous (30%) and non-squamous (70%) NSCLC is from key statistics of lung cancer reported by American Cancer Society (http://www.cancer.org/cancer/lungcancer-non-smallcell/detailedguide/non-small-cell-lung-cancer-what-is-non-small-cell-lung-cancer).

The prevalence of mutations is calculated as a weighted average of the prevalence among non-squamous cancer and squamous cancer (Appendix 1 Table 2):

Appendix 1 Table 2 Calculation of detection rates in the total NSCLC population for those tested conventionally

Histology / Locus	Prevalence of alterations under conventional testing calculation	Prevalence of alterations under conventional testing in total NSCLC population
Non-squamous (70%); **Squamous (30%)**		
EGFR	17%*.7	11.9%
ALK	3%*.7	2.1%
ROS1	1%*.7	0.7%
BRAF	2%*.7	1.4%
MET	1%*.7+6.2*.3	2.6%
HER2	3%*.7	2.1%
RET	1%*.7	0.7%
KRAS	25%*.7	17.5%

Among patients receiving Foundation Medicine, detection rates were based on literature reporting detection rates specifically for Foundation Medicine testing (Appendix 1 Table 3).

Appendix 1 Table 3 Prevalence of alterations with Foundation Medicine testing

Locus	Prevalence of alterations with Foundation Medicine	Source	Link
Non-squamous (70%)			
EGFR	20%	Suh 2016	http://theoncologist.alphamedpress.org/cgi/pmidlookup?view=long&pmid=27151654
ALK	4.1%	Suh 2016	http://theoncologist.alphamedpress.org/cgi/pmidlookup?view=long&pmid=27151654
ROS1	1.5%	Suh 2016	http://theoncologist.alphamedpress.org/cgi/pmidlookup?view=long&pmid=27151654

BRAF	5.7%	Suh 2016	http://theoncologist.alphamedpress.org/cgi/pmidlookup?view=long&pmid=27151654
MET	5.6%	Suh 2016	http://theoncologist.alphamedpress.org/cgi/pmidlookup?view=long&pmid=27151654
HER2	6.0%	Suh 2016	http://theoncologist.alphamedpress.org/cgi/pmidlookup?view=long&pmid=27151654
RET	2.4%	Suh 2016	http://theoncologist.alphamedpress.org/cgi/pmidlookup?view=long&pmid=27151654
KRAS	32%	Suh 2016	http://theoncologist.alphamedpress.org/cgi/pmidlookup?view=long&pmid=27151654
Squamous (30%)			
MET	6%	Heist et al. review (2012)	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3404741/

The prevalence of mutations is calculated as a weighted average of the prevalence among non-squamous cancer and squamous cancer (Appendix 1 Table 4):

Appendix 1 Table 4 Calculation of detection rates in the total NSCLC population for those tested with Foundation Medicine

Histology / Locus	Prevalence of alterations under Foundation Medicine testing	Prevalence of alterations under Foundation Medicine testing in total NSCLC population
Non-squamous (70%); Squamous (30%)		
EGFR	20%*.7	14%
ALK	4.1%*.7	2.9%
ROS1	1.5% *.7	1%
BRAF	5.7%*.7	4%
MET	5.6%*.7+6.2%*.3	5.8%
HER2	6.0%*.7	4.2%
RET	2.4%*.7	1.7%
KRAS	32%*.7	22.4%

The average number of tests per person by reference and adoption scenarios (Appendix 1 Table 5):

Appendix 1 Table 5 Average number of tests per person by reference and adoption scenarios (50% uptake for FoundationOne in all adoption scenarios).

	Reference scenario: Conventional testing	Adoption scenario 1: FoundationOne CDx replacing all reflex test	Adoption scenario 2: FoundationOne CDx replacing panel	Adoption scenario 3: FoundationOne CDx after negative reflex + panel	Adoption scenario 4: FoundationOne Liquid only
	Reference scenario 1: Single-gene testing only				
Number of single-gene tests per-person	3.4	2.2	Not applicable	Not applicable	3.4

Number of hotspot panels per-person	0	0			0
Number of Foundation Medicine tests per-person	0	0.5			0.05
	Reference scenario 2: Single-gene testing followed by hotspot panel				
Number of single-gene tests per-person	2.5	1.7	2.5	2.5	2.5
Number of hotspot panels per-person	0.8	0.4	0.4	0.8	0.8
Number of Foundation Medicine tests per-person	0	0.5	0.4	0.4	0.05

Appendix 2: Details of infrastructure cost calculations

The costs of conventional testing vary by specific test and method used (e.g. in-house versus external laboratory). To comprehensively capture all relevant costs, a structured interview was conducted to collect relevant costing inputs from a large genomics laboratory in British Columbia. Based on tis, annual operating budget, and allocation of capital and staffing costs were taken into consideration to appropriately adjust for the volume of laboratory work associated with NSCLC specifically.

Specifically, the following components were collected: estimated annual purchasing cost of all equipment used for NSCLC testing, annual NSCLC-specific operational costs consisting of equipment maintenance, material, labor, and other costs comprise reporting, shipping, software updates, and test validation and calibration costs. Testing-related costs were further broken down into specific testing methods of IHC, FISH, PCR, AC-based NGS, and HC-based NGS.

All costs and calculations are summarized below in Appendix 2 Table 1 & Table 2:

Appendix 2 Table 1 Test-specific costs

	CAPITAL COST		**EQUIPMENT MAINTENANCE COST**		**MATERIAL COST**
	TOTAL	***NSCLC***	***TOTAL***	***NSCLC***	
IHC	$ 29,479.17	$ 2,210.94	$ 10,000.00	$ 750.00	$ 52,000.00
FISH	$ 39,479.17	$ 39.48	$ 13,750.00	$ 13.75	
PCR	$ 20,145.83	$ 241.75	$ 6,500.00	$ 78.00	
AC-BASED NGS	$ 69,479.17	$ -	$ 25,000.00	$ -	$ -
HC-BASED NGS	$ 69,479.00	$ 16,675.00	$ 25,000.00	$ 6,000.00	$ 1,274,000.00
TOTAL ANNUAL CAPITAL COST ATTRIBUTABLE TO NSCLC		**$ 19,167.00**		**$ 6,841.75**	**$ 1,326,000.00**

Appendix 2 Table 2 Non-test specific costs

	OPERATIONAL COST - LABOUR COST (ANNUAL)	
	TOTAL	***NSCLC***
TECHNICIANS/ADMIN STAFF	$ 1,600,000	$ 240,000
ADMIN STAFF	$ 320,000	$ 48,000
MANAGEMENT STAFF	$ 360,000	$ 54,000
MEDICAL/SCIENTIFIC STAFF	$ 950,000	$ 142,500
PATHOLOGISTS	$ 118,750	$ 17,813
TOTAL ANNUAL LABOUR COST ATTRIBUTABLE TO NSCLC		$ 502,313
	OPERATIONAL COST - OTHER COSTS (ANNUAL)	
	TOTAL	***NSCLC***
TEST VALIDATION	$ 6,700	$ 670
TEST CALIBRATION	$ -	
SOFTWARE UPDATES	$ 2,000	$ 300
SHIPPING	$ 130,000	$ 130,000
REPORTING	$ 105,000	$ 15,750
OTHER	$ -	$ -
TOTAL ANNUAL MAINTENANCE COST ATTRIBUTABLE TO NSCLC		$ 146,050

Total costs are summarized below in Appendix 3 Table 3:

Appendix 2 Table 3 Summarized costs

	OPERATIONAL COST - MATERIALS ONLY	**ALL OTHER COSTS**	**NUMBER OF TESTS ANNUALLY**	**ESTIMATED COST PER TEST**
IHC	$ 52,000.00	$ 674,371.42	390	$ 652.08
NGS	$ 1,274,000.00		1300	$ 1,918.75