

Supplementary Table S1. Lung cancer samples for NGS testing were referred from medical centres and institutions in Malaysia

Locations of referral medical centres and institutions	Samples , N (%)
Klang Valley	304 (64.8%)
Penang	71 (15.1%)
Johor	49 (10.4%)
Malacca	17 (3.6%)
Pahang	5 (1.1%)
Kedah	1 (0.2%)
Kelantan	1 (0.2%)
East Malaysia (Sabah/Sarawak)	21 (4.5%)

Supplementary Table S2. Lung cancer patients smoking habits distributed by sex in Nexus 1 and Nexus 2-3. P-values were obtained using a Chi-square test.

Characteristics	Cohort					
	Nexus 1 (n = 112) n (%)			Nexus 2-3 (n = 201) n (%)		
	Male	Female	<i>p</i> -value	Male	Female	<i>p</i> -value
Non-smoker	15 (20.3)	59 (79.7)	<0.001	62 (47.0)	70 (53.0)	0.002
Smoker + Former smoker	32 (84.2)	6 (15.8)		49 (71.0)	20 (29.0)	

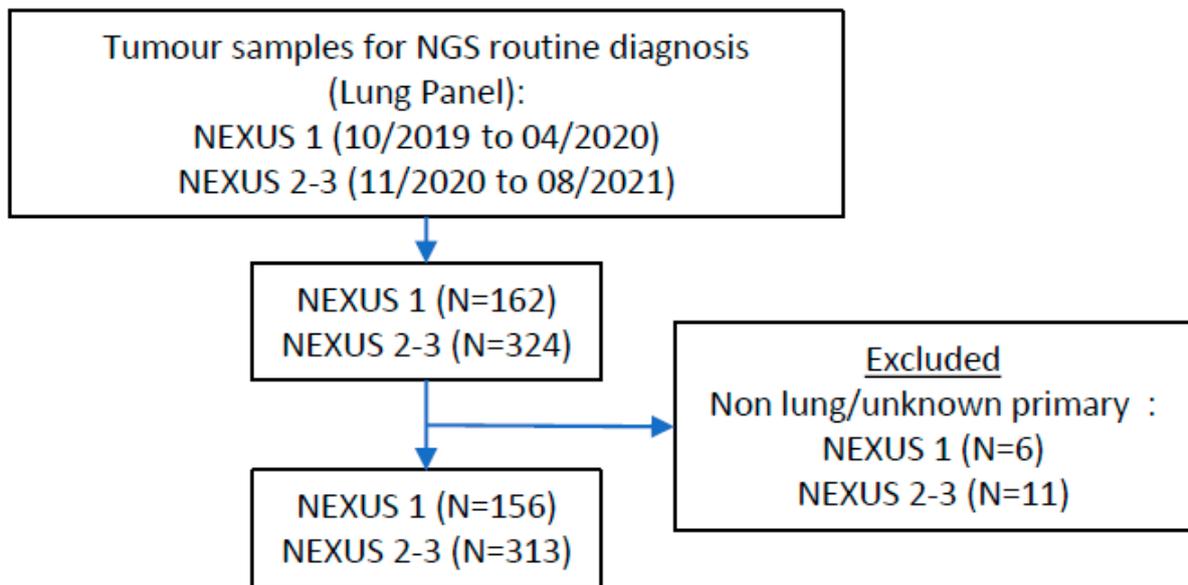
Supplementary Table S3. *EGFR* mutation profile in Nexus1 and Nexus 2-3 cohorts, including the subset of patients that received second-line therapy.

Exons	Genetic alterations*	Cohort			
		Nexus 1		Nexus 2-3	
		All patients n = 156 n (%)	Second-line n = 6 n (%)	All patients n = 313 n (%)	Second-line n = 33 n (%)
Exon 15	p.G598V			1 (0.3)	1 (3.0)
Exon 18	p.E709A			2 (0.6)	
	p.E709K			2 (0.6)	
	p.E709V			1 (0.3)	
	p.G719S			2 (0.6)	
	p.G719A	1 (0.6)		6 (1.9)	
	p.G719C	1 (0.6)			
	p.G724S			1 (0.3)	
Exon 19	p.L747P			1 (0.3)	1 (3.0)
	p.L747S			2 (0.6)	
	p.A750P			3 (1.0)	1 (3.0)
	p.K757R			1 (0.3)	
	Exon 19 deletion(s)	28 (17.9)	4 (66.7)	66 (21.1)	12 (36.4)
Exon 20	p.R776H	1 (0.6)			
	p.S768I			4 (1.3)	
	p.T790M		3 (50.0)	4 (1.3)	4 (12.1)
	p.C797S			5 (1.6)	5 (15.2)
	Exon 20 insertion(s)	5 (3.2)		3 (1.0)	
Exon 21	p.L833V			2 (0.6)	
	p.L858R	33 (21.2)	2 (33.3)	51 (16.3)	12 (36.4)
	p.K860I	1 (0.6)			
	p.L861Q	2 (1.3)		2 (0.6)	
	p.A871X	1 (0.6)			

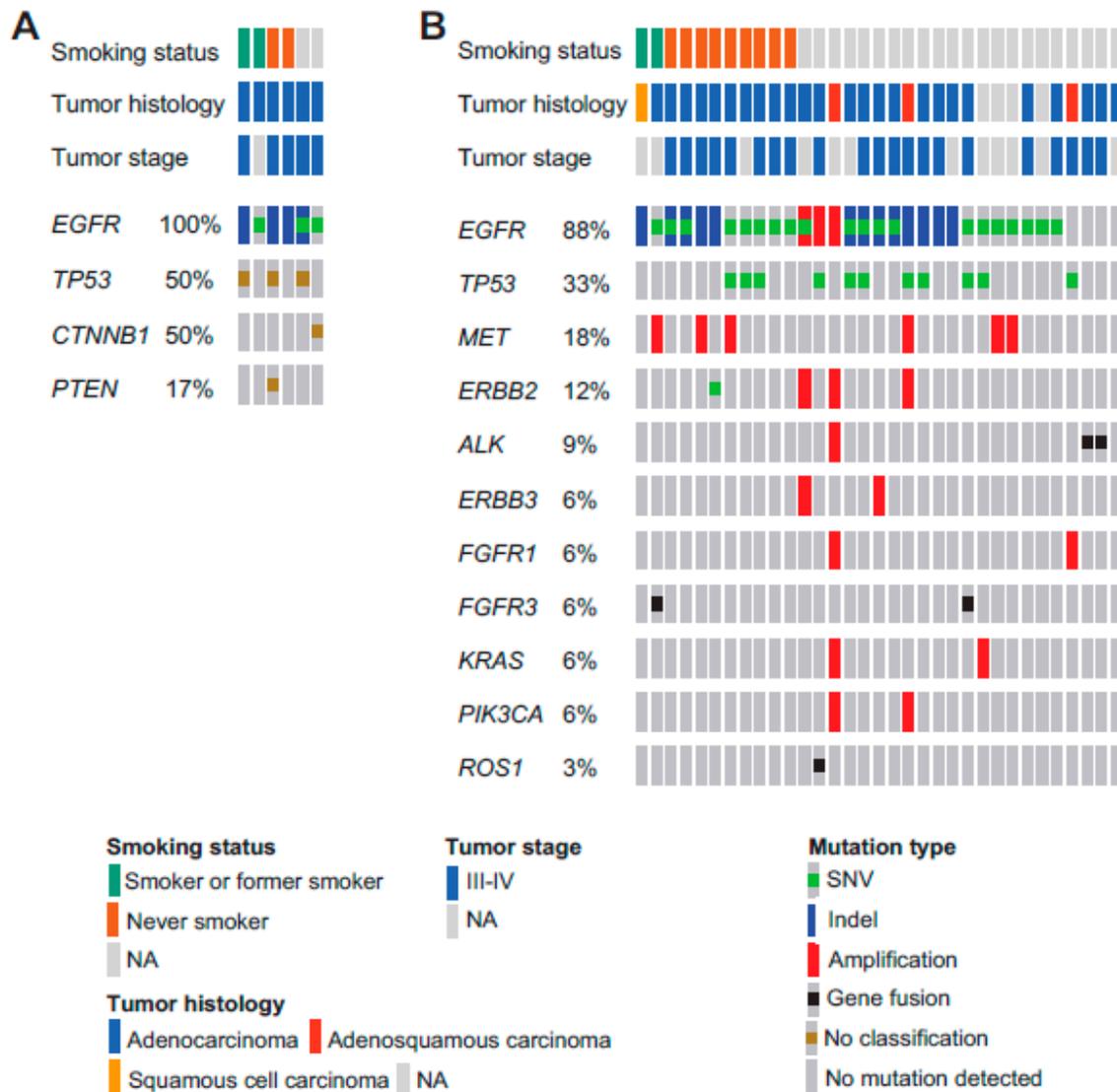
*Genetic alterations are listed from top to bottom of table according to *EGFR* forward strand 5' to 3'

Supplementary Table S4. *RET* and *MET* mutation profile in Nexus 1 and Nexus 2-3 cohorts.

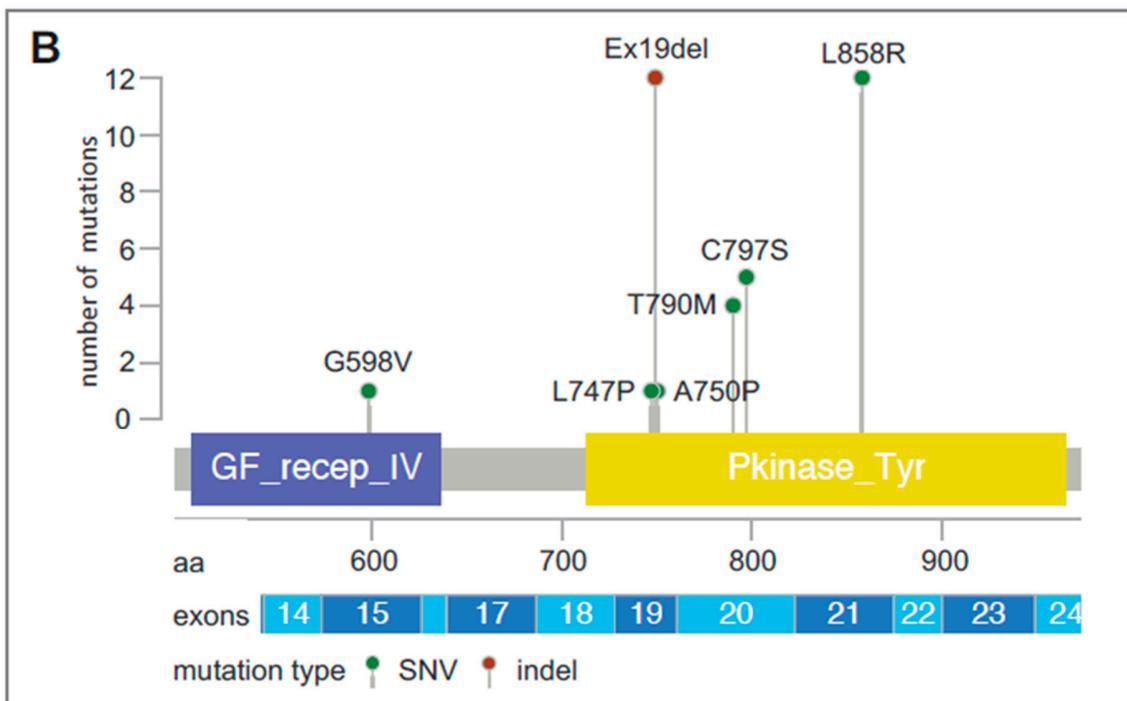
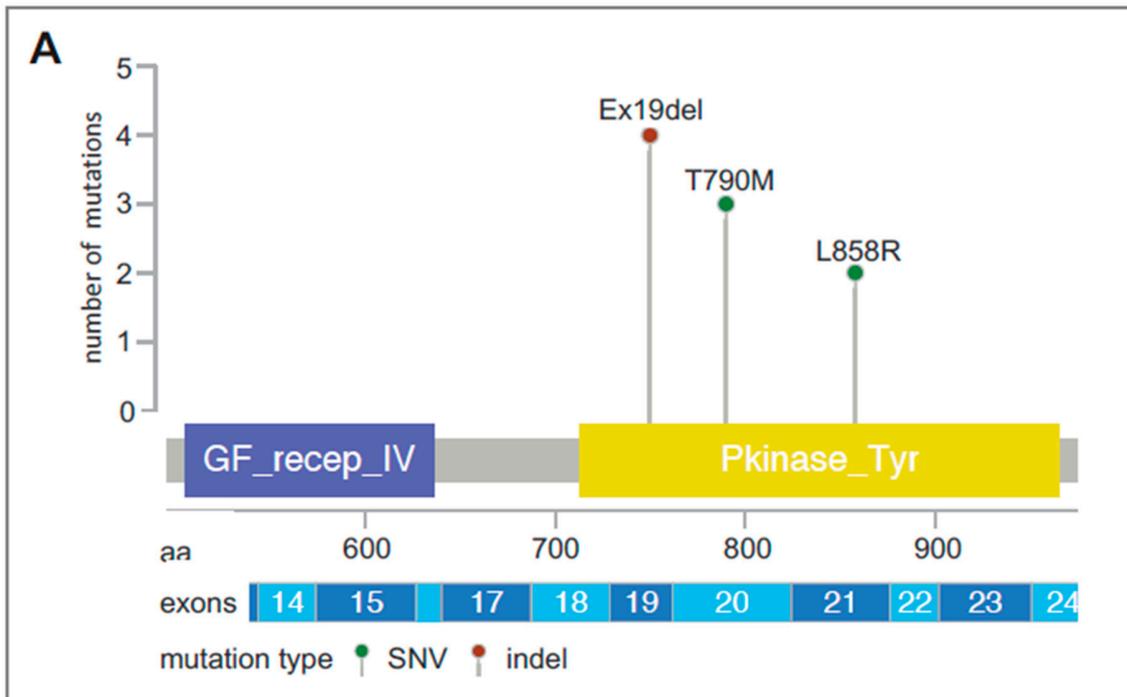
Genetic alterations	Cohort			
	Nexus 1 (n = 156) n (%)		Nexus 2-3 (n = 313) n (%)	
	<i>RET</i>	<i>MET</i>	<i>RET</i>	<i>MET</i>
SNV	–	–	–	2 (0.6)
Fusion	1 (0.6)	–	2 (0.6)	–
Amplification	–	–	–	17 (5.4)
Exon 14 skipping	–	3 (1.9)	–	12 (3.8)
Frameshift	–	–	–	1 (0.3)



Supplementary Figure S1. STARD Flow diagram depicting samples included in analysis.



Supplementary Figure S2. Mutation profiles of lung cancer patients that received second-line therapy in the Nexus 1 (A) and Nexus 2-3 (B) cohorts. Each column represents a patient and each row represents a gene. Patients were clustered according to smoking status; also represented are tumor histology and stage (color-coded in categories I-II and III-IV for improved visualization). The mutated genes are listed on the left side of the diagram, in descending order of frequency, and within the same frequency, in alphabetical order. The color code represents the mutation type, smoking status, tumor histology and tumor stage indicated in the figure legend. NA: not available.



Supplementary Figure S3. *EGFR* mutation profile in the subset of patients that received second-line therapy in the Nexus 1 (A) and Nexus 2-3 (B) cohorts. Diagrams represent the *EGFR* domains where mutations were detected. Ex19del: exon 19 deletion, Ex20ins: exon 20 insertion, GF_recep_IV: growth factor receptor domain IV, Pkinase_Tyr: protein tyrosine kinase, aa: amino acid, SNV: single nucleotide variant, indel: nucleotide(s) insertion or deletion.