

Evaluating the Cost of Genomic Testing for Biomarker-Driven Therapies in Oncology

Supplementary Material

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Supplementary Table 1. SGT prevalence for select tumor types

Tumor type	Marker	Prevalence	ESCAT tier
Adv. NonSq-NSCLC	EGFR	15.00%	I
	ALK – Fusions	5.00%	I
	MET - Mutations ex 14 skipping	3.00%	I
	BRAF – Mutations	2.00%	I
	ROS1 – Fusions	1.50%	I
	RET – Fusions	1.50%	I
	KRAS - Mutations (p.G12C)	12.00%	I
	NTRK – Fusions	0.30%	I
	MSI-H/dMMR	4.50%	I
	FGFR1/2/3 – Fusions	1.30%	I
	FGFR1/2/3 – Mutations	4.51%	I
	TMB-H	29.00%	I
	MET - Focal amplifications	5.00%	II
	ERBB2 - Hotspot mutations	3.00%	II
	NRG1 - Fusions	1.00%	II
Sq-NSCLC	NTRK- Fusions	1.62%	I
mBC	PIK3CA - Hotspot mutations	35.00%	I
	ERBB2 - Amplifications	17.50%	I
	BRCA1/2 - Germline pathogenic/likely pathogenic variants	4.00%	I
	ESR1 - Mutations	35.00%	I
	NTRK - Fusions	0.30%	I
	MSI-H/dMMR	0.63%	I
	RET - Fusions	0.36%	I
	BRAF - Mutations	6.20%	I
	FGFR1/2/3 - Fusions	0.39%	I
	FGFR1/2/3 - Mutations	1.85%	I
	TMB-H	9.40%	I
	PTEN - Mutations/deletions	7.00%	I/II
	AKT (p. E17K) - Mutations	5.00%	I/II
	ERBB2 - Hotspot mutations	4.00%	II
	BRCA1/2 - Somatic mutations	3.00%	II
	PALB2 - Germline pathogenic/likely pathogenic variants	1.00%	II
mCRC	BRAF- Mutations	8.50%	I
	MSI-H/dMMR	4.50%	I

	KRAS - Mutations	4.00%	I
	NTRK - Fusions	0.30%	I
	RET - Fusions	0.36%	I
	FGFR1/2/3 - Fusions	0.77%	I
	FGFR1/2/3 - Mutations	4.51%	I
	ERBB2 - Amplifications	2.00%	II
	POLE - Mutations	1.00%	II
Adv. Prostate	BRCA1/2 - Germline and somatic mutations/deletions	10.00%	I
	NTRK - Fusions	0.30%	I
	MSI-H/dMMR	2.50%	I
	RET - Fusions	0.36%	I
	BRAF - Mutations	6.20%	I
	FGFR1/2/3 - Fusions	0.77%	I
	FGFR1/2/3 - Mutations	4.51%	I
	TMB-H	7.10%	I
	PTEN - Mutations/deletions	40.00%	II
	ATM - Mutations/deletions	6.00%	II
	PALB2 - Mutations/deletions	1.00%	II
mGC	ERBB2 - Amplifications	16.00%	I
	NTRK - Fusions	0.30%	I
	MSI-H/dMMR	6.60%	I
	RET - Fusions	0.10%	I
	BRAF - Mutations	6.20%	I
	FGFR1/2/3 - Fusions	0.77%	I
	FGFR1/2/3 - Mutations	4.51%	I
	TMB-H	44.20%	I
	EGFR - Amplifications	4.00%	II
	MET - Amplifications	3.00%	II
Adv. PDAC	BRCA1/2 - Germline pathogenic/likely pathogenic variants	5.50%	I
	KRAS - Mutations	1.50%	I
	NTRK - Fusions	0.30%	I
	MSI-H/dMMR	1.50%	I
	RET - Fusions	0.36%	I
	BRAF - Mutations	6.20%	I
	FGFR1/2/3 - Fusions	0.77%	I
	FGFR1/2/3 - Mutations	4.51%	I

	PALB2 - Germline pathogenic/likely pathogenic variants	3.50%	II
	NRG1 - Fusions	7.00%	II
Adv. HCC	NTRK - Fusions	0.30%	I
	MSI-H/dMMR	2.00%	I
	RET - Fusions	0.10%	I
	BRAF - Mutations	41.20%	I
	FGFR1/2/3 - Fusions	0.77%	I
	FGFR1/2/3 - Mutations	4.51%	I
	TMB-H	3.50%	I
Adv. CC	IDH1 - Mutations	13.00%	I
	FGFR2 - Fusions	10.00%	I
	ERBB2 - Amplifications	15.00%	I
	KRAS - Mutations	1.00%	I
	BRAF - Mutations	50.00%	I
	NTRK - Fusions	0.30%	I
	MSI-H/dMMR	2.00%	I
	RET - Fusions	0.36%	I
	ERBB2 - Mutations	4.00%	II
Adv. Ovarian	BRCA1/2 - Variants	16.00%	I
	BRCA1/2 - Somatic pathogenic/likely pathogenic variants	6.00%	I
	HRD	47.50%	I
	NTRK - Fusions	0.30%	I
	MSI-H/dMMR	24.50%	I
	RET - Fusions	0.36%	I
	BRAF - Mutations	1.70%	I
	FGFR1/2/3 - Fusions	0.30%	I
	FGFR1/2/3 - Mutations	0.80%	I
	TMB-H	1.60%	I
Adv. soft-tissue sarcomas	ALK - Fusions	1.20%	I
	COL1A1-PDGFB - Fusions	0.02%	I
	INI1/SMARCB1 - Mutations/deletions	1.40%	I
	NTRK1/2/3 - Fusions	0.30%	I
	MSI-H/dMMR	1.00%	I
	RET - Fusions	0.36%	I
	BRAF - Mutations	6.20%	I
	FGFR1/2/3 - Fusions	0.77%	I

	FGFR1/2/3 - Mutations	4.51%	I
	TSC1/2 - Mutations	3.00%	II
Adv. GIST	KIT Mutations/insertions/deletions/indels	85.00%	I
	PDGFRA Mutations/insertions/deletions/indels	12.50%	I
	PDGFRA Exon 18 D842V mutations	5.00%	I
	NTRK - Fusions	0.30%	I
	MSI-H/dMMR	1.00%	I
	RET - Fusions	0.36%	I
	BRAF - Mutations (p.V600E)	1.00%	I
	FGFR1/2/3 - Fusions	0.77%	I
	FGFR1/2/3 - Mutations	1.00%	I
Adv. Thyroid	RET - Mutations	0.90%	I
	RET - Fusions	7.00%	I
	BRAF - Mutations	0.60%	I
	NTRK - Fusions	0.30%	I
	MSI-H/dMMR	2.50%	I
	FGFR1/2/3 - Fusions	0.77%	I
	FGFR1/2/3 - Mutations	4.51%	I
	TMB-H	2.70%	I
Unfavorable CUP	NTRK - Fusions	0.30%	I
	RET - Fusions	0.01%	I
	BRAF - Mutations	0.12%	I
	FGFR1/2/3 - Fusions	0.02%	I
	FGFR1/2/3 - Mutations	0.09%	I
	TMB-H	14.67%	I
	ALK - Fusions	1.00%	II

Adv.: advanced; Adv. CC: advanced cholangiocarcinoma; Adv. GIST: advanced gastrointestinal stromal tumor; Adv. HCC: advanced hepatocellular carcinoma; Adv. NonSq-NSCLC: advanced non-squamous non-small cell lung cancer; Adv. PDAC: advanced pancreatic ductal adenocarcinoma; CUP: cancer of unknown primary; ESCAT: ESMO Clinical Actionability of molecular Targets; mBC: metastatic breast cancer; mCRC: metastatic colorectal cancer; mGC: metastatic gastric cancer; Sq-NSCLC: squamous non-small cell lung cancer.

Sources: ESMO 2024 (1); OncologyPRO Educational Portal (2); Olivares-Hernández et al., 2022 (3); Wang et al., 2014 (4); Kang et al., 2022 (5); Ricciuti et al., 2022 (6); ESMO 2020 (7); My Cancer Genome website (8-14); Vidula et al., 2022 (15); Kazandjian et al., 2024 (16); Chen et al., 2021 (17); Saridogan et al., 2023 (18); Hu et al., 2024 (19); Guan et al., 2021 (20); Shi et al., 2021 (21); Luchini

et al., 2021 (22); Mukai et al., 2021 (23); Souleymane et al., 2022 (24); Yang et al., 2024 (25); Penn and Alvarez, 2023 (26); Zhao et al., 2019 (27); Campos et al., 2018 (28); Lin et al., 2021 (29); Zhang et al., 2024 (30); Aster Insights website (31); Cooper and Hong, 2022 (32); Yiong et al., 2023 (33); Liu et al., 2020 (34); OncLive website (35); Villano, 2023 (36); Serrano et al., 2023 (37); Genutis et al., 2019 (38); Thyroid.org website (39); Shao et al., 2020 (40); Cancer.org website (41).

Supplementary Table 1. NGS prevalence for ESCAT I and II biomarkers in select tumor types

Tumor type	Prevalence (%)
Adv. NonSq-NSCLC	86.93
Sq-NSCLC	1.62
mBC	70.44
mCRC	59.51
Adv. Prostate	37.77
mGC	79.22
Adv. PDAC	69.71
Adv. HCC	9.45
Adv. CC	41.67
Adv. Ovarian	66.94
Adv. soft-tissue sarcomas	13.44
Adv. GIST	12.65
Adv. Thyroid	69.09
Unfavorable CUP	16.20

Adv.: advanced; Adv. CC: advanced cholangiocarcinoma; Adv. GIST: advanced gastrointestinal stromal tumor; Adv. HCC: advanced hepatocellular carcinoma; Adv. NonSq-NSCLC: advanced non-squamous non-small cell lung cancer; Adv. PDAC: advanced pancreatic ductal adenocarcinoma; CUP: cancer of unknown primary; ESCAT: ESMO Clinical Actionability of molecular Targets; mBC: metastatic breast cancer; mCRC: metastatic colorectal cancer; mGC: metastatic gastric cancer; NGS: next-generation sequencing; Sq-NSCLC: squamous non-small cell lung cancer.

Sources: Kang et al., 2023 (5); Ricciuti et al., 2022 (6); TCGA dataset (42).

Supplementary Table 3. Sequential SGT for biomarkers in select tumor types

Tumor type	Marker	SGT1	SGT2
Adv. NonSq-NSCLC	EGFR	PCR/qPCR	
	ALK – Fusions	IHC	FISH
	MET - Mutations ex 14 skipping	PCR/qPCR	
	BRAF – Mutations	PCR/qPCR	

	ROS1 – Fusions	PCR/qPCR	
	RET – Fusions	FISH	
	KRAS - Mutations (p.G12C)	PCR/qPCR	
	NTRK – Fusions	FISH	
	MSI-H/dMMR	IHC	PCR/qPCR
	FGFR1/2/3 – Fusions	PCR/qPCR	
	FGFR1/2/3 – Mutations	PCR/qPCR	
	TMB-H	PCR/qPCR	
	MET - Focal amplifications	PCR/qPCR	
	ERBB2 - Hotspot mutations	PCR/qPCR	
	NRG1 - Fusions	FISH	
Sq-NSCLC	NTRK- Fusions	FISH	
mBC	PIK3CA - Hotspot mutations	PCR/qPCR	
	ERBB2 - Amplifications	FISH	
	BRCA1/2 - Germline pathogenic/likely pathogenic variants	PCR/qPCR	
	ESR1 – Mutations	PCR/qPCR	
	NTRK - Fusions	FISH	
	MSI-H/dMMR	IHC	PCR/qPCR
	RET - Fusions	FISH	
	BRAF - Mutations	PCR/qPCR	
	FGFR1/2/3 - Fusions	PCR/qPCR	
	FGFR1/2/3 - Mutations	PCR/qPCR	
	TMB-H	PCR/qPCR	
	PTEN - Mutations/deletions	IHC	PCR/Qpcr
	AKT (p. E17K) - Mutations	PCR/qPCR	
	ERBB2 - Hotspot mutations	FISH	
	BRCA1/2 - Somatic mutations	PCR/qPCR	
mCRC	PALB2 - Germline pathogenic/likely pathogenic variants	PCR/qPCR	
	BRAF- Mutations	PCR/qPCR	
	MSI-H/dMMR	IHC	PCR/qPCR
	KRAS - Mutations	PCR/qPCR	
	NTRK - Fusions	FISH	
	RET - Fusions	FISH	
	FGFR1/2/3 - Fusions	PCR/qPCR	
	FGFR1/2/3 - Mutations	PCR/qPCR	
	ERBB2 - Amplifications	FISH	
	POLE - Mutations	PCR/qPCR	

Adv. Prostate	BRCA1/2 - Germline and somatic mutations/deletions	PCR/qPCR	
	NTRK - Fusions	FISH	
	MSI-H/dMMR	IHC	PCR/qPCR
	RET - Fusions	FISH	
	BRAF - Mutations	PCR/qPCR	
	FGFR1/2/3 - Fusions	PCR/qPCR	
	FGFR1/2/3 - Mutations	PCR/qPCR	
	TMB-H	PCR/qPCR	
	PTEN - Mutations/deletions	IHC	PCR/qPCR
	ATM - Mutations/deletions	PCR/qPCR	
	PALB2 - Mutations/deletions	PCR/qPCR	
mGC	ERBB2 - Amplifications	FISH	
	NTRK - Fusions	FISH	
	MSI-H/dMMR	IHC	PCR/qPCR
	RET - Fusions	FISH	
	BRAF - Mutations	PCR/qPCR	
	FGFR1/2/3 - Fusions	PCR/qPCR	
	FGFR1/2/3 - Mutations	PCR/qPCR	
	TMB-H	PCR/qPCR	
	EGFR - Amplifications	PCR/qPCR	
	MET - Amplifications	PCR/qPCR	
Adv. PDAC	BRCA1/2 - Germline pathogenic/likely pathogenic variants	PCR/qPCR	
	KRAS - Mutations	PCR/qPCR	
	NTRK - Fusions	FISH	
	MSI-H/dMMR	IHC	PCR/qPCR
	RET - Fusions	FISH	
	BRAF - Mutations	PCR/qPCR	
	FGFR1/2/3 - Fusions	PCR/qPCR	
	FGFR1/2/3 - Mutations	PCR/qPCR	
	PALB2 - Germline pathogenic/likely pathogenic variants	PCR/qPCR	
	NRG1 - Fusions	FISH	
Adv. HCC	NTRK - Fusions	FISH	
	MSI-H/dMMR	IHC	PCR/qPCR
	RET - Fusions	FISH	
	BRAF - Mutations	PCR/qPCR	
	FGFR1/2/3 - Fusions	PCR/qPCR	

	FGFR1/2/3 - Mutations	PCR/qPCR	
	TMB-H	PCR/qPCR	
Adv. CC	IDH1 - Mutations	PCR/qPCR	
	FGFR2 - Fusions	FISH	
	ERBB2 - Amplifications	FISH	
	KRAS - Mutations	PCR/qPCR	
	BRAF - Mutations	PCR/qPCR	
	NTRK - Fusions	FISH	
	MSI-H/dMMR	IHC	PCR/qPCR
	RET - Fusions	FISH	
	ERBB2 - Mutations	PCR/qPCR	
Adv. Ovarian	BRCA1/2 - Variants	PCR/qPCR	
	BRCA1/2 - Somatic pathogenic/likely pathogenic variants	PCR/qPCR	
	HRD	PCR/qPCR	
	NTRK - Fusions	FISH	
	MSI-H/dMMR	IHC	PCR/qPCR
	RET - Fusions	FISH	
	BRAF - Mutations	PCR/qPCR	
	FGFR1/2/3 - Fusions	PCR/qPCR	
	FGFR1/2/3 - Mutations	PCR/qPCR	
	TMB-H	PCR/qPCR	
Adv. soft-tissue sarcomas	ALK - Fusions	IHC	FISH
	COL1A1-PDGFB - Fusions	FISH	
	INI1/SMARCB1 - Mutations/deletions	PCR/qPCR	
	NTRK1/2/3 - Fusions	FISH	
	MSI-H/dMMR	IHC	PCR/qPCR
	RET - Fusions	FISH	
	BRAF - Mutations	PCR/qPCR	
	FGFR1/2/3 - Fusions	PCR/qPCR	
	FGFR1/2/3 - Mutations	PCR/qPCR	
	TSC1/2 - Mutations	PCR/qPCR	
Adv. GIST	KIT Mutations/insertions/deletions/indels	PCR/qPCR	
	PDGFRA Mutations/insertions/deletions/indels	PCR/qPCR	
	PDGFRA Exon 18 D842V mutations	PCR/qPCR	

	NTRK - Fusions	FISH	
	MSI-H/dMMR	IHC	PCR/qPCR
	RET - Fusions	FISH	
	BRAF - Mutations (p.V600E)	PCR/qPCR	
	FGFR1/2/3 - Fusions	PCR/qPCR	
	FGFR1/2/3 - Mutations	PCR/qPCR	
Adv. Thyroid	RET - Mutations	FISH	
	RET - Fusions	FISH	
	BRAF - Mutations	PCR/qPCR	
	NTRK - Fusions	FISH	
	MSI-H/dMMR	IHC	PCR/qPCR
	FGFR1/2/3 - Fusions	PCR/qPCR	
	FGFR1/2/3 - Mutations	PCR/qPCR	
	TMB-H	PCR/qPCR	
Unfavorable CUP	NTRK - Fusions	FISH	
	RET - Fusions	FISH	
	BRAF - Mutations	PCR/qPCR	
	FGFR1/2/3 - Fusions	PCR/qPCR	
	FGFR1/2/3 - Mutations	PCR/qPCR	
	TMB-H	PCR/qPCR	
	ALK - Fusions	IHC	FISH

Adv.: advanced; Adv. CC: advanced cholangiocarcinoma; Adv. GIST: advanced gastrointestinal stromal tumor; Adv. HCC: advanced hepatocellular carcinoma; Adv. NonSq-NSCLC: advanced non-squamous non-small cell lung cancer; Adv. PDAC: advanced pancreatic ductal adenocarcinoma; CUP: cancer of unknown primary; ESCAT: ESMO Clinical Actionability of molecular Targets; FISH: fluorescence in situ hybridization; IHC: immunohistochemistry; mBC: metastatic breast cancer; mCRC: metastatic colorectal cancer; mGC: metastatic gastric cancer; NGS: next-generation sequencing; PCR: polymerase chain reaction; qPCR: quantitative polymerase chain reaction; Sq-NSCLC: squamous non-small cell lung cancer. SGT: single-gene test.

Sources: ESMO 2020 (7); ESMO 2024 (1).

Supplementary Table 4. Diagnostic yield, PSI, and NNP using sequential SGT or NGS to achieve a comprehensive genomic profile in select tumor types

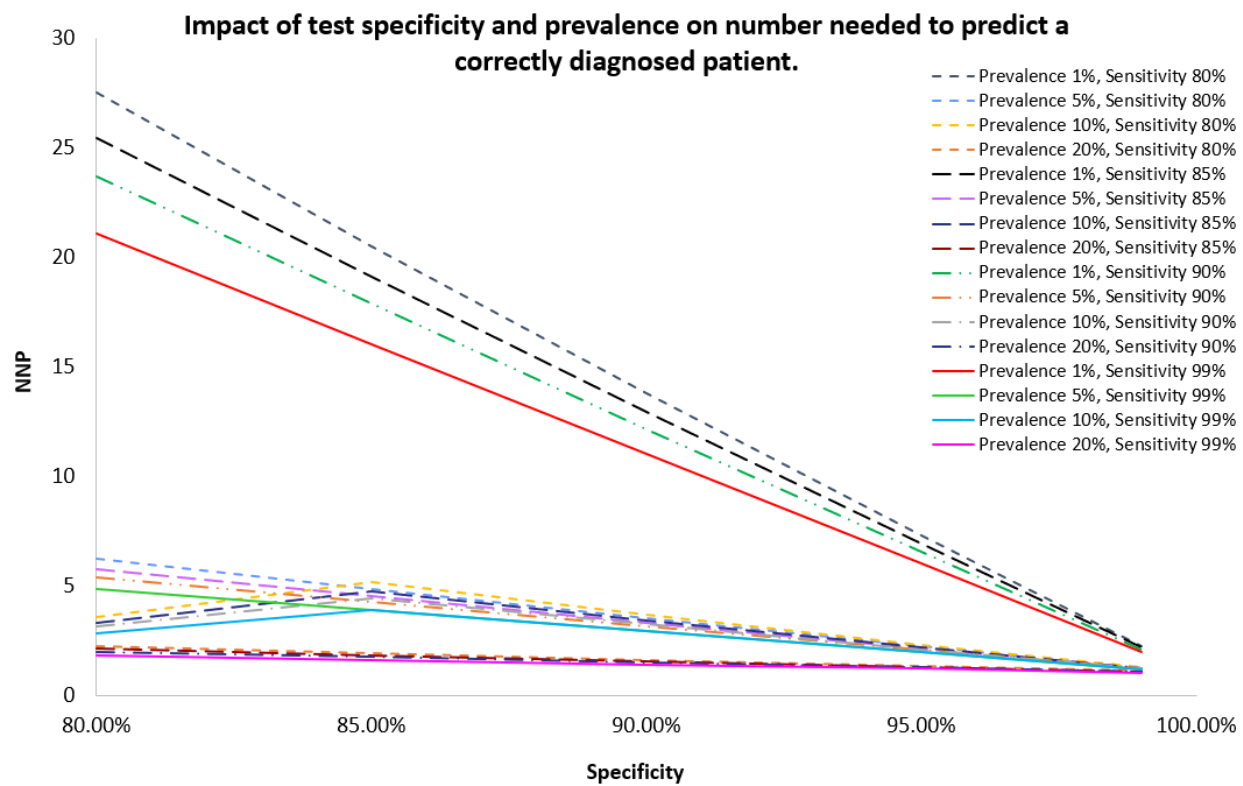
Tumor	Diagnostic yield (%)	PSI (%)	NNP
Adv. NonSq-NSCLC			
SGT	69.65	80.37	1.24

NGS	73.24	46.71	2.14
Sq-NSCLC			
SGT	4.81	29.29	3.41
NGS	4.53	29.60	3.38
mBC			
SGT	81.54	87.18	1.15
NGS	59.97	69.85	1.43
mCRC			
SGT	36.27	57.06	1.75
NGS	51.16	77.68	1.29
Adv. Prostate			
SGT	62.90	82.79	1.21
NGS	33.65	84.79	1.18
mGC			
SGT	68.15	85.36	1.17
NGS	67.04	60.00	1.67
Adv. PDAC			
SGT	40.56	58.68	1.70
NGS	59.38	70.50	1.42
Adv. HCC			

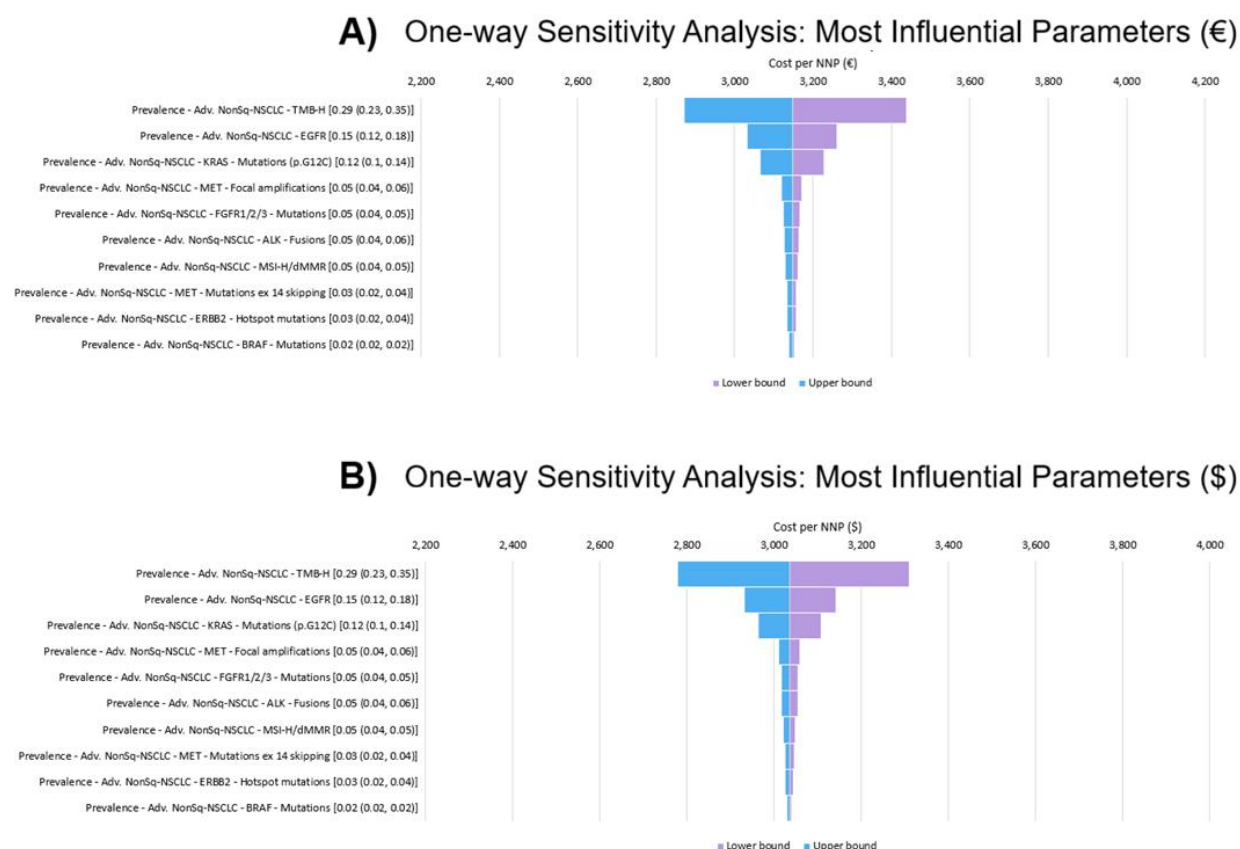
SGT	52.27	83.53	1.20
NGS	10.84	71.31	1.40
Adv. CC			
SGT	72.15	87.34	1.15
NGS	36.79	84.18	1.19
Adv. Ovarian			
SGT	72.47	88.32	1.13
NGS	57.14	72.79	1.37
Adv. soft-tissue sarcomas			
SGT	32.21	48.07	2.08
NGS	14.05	77.58	1.29
Adv. GIST			
SGT	85.94	92.20	1.08
NGS	13.42	76.61	1.31
Adv. Thyroid			
SGT	30.57	50.57	1.98
NGS	58.88	71.04	1.41
Unfavorable CUP			
SGT	27.04	54.12	1.85
NGS	16.28	80.24	1.25

Note: Diagnostic yield is the expected percentage of all ESCAT Tier I and Tier II genetic alterations within the tumor category as found in the ESMO NGS guideline recommendations.

Adv.: advanced; Adv. CC: advanced cholangiocarcinoma; Adv. GIST: advanced gastrointestinal stromal tumor; Adv. HCC: advanced hepatocellular carcinoma; Adv. NonSq-NSCLC: advanced non-squamous non-small cell lung cancer; Adv. PDAC: advanced pancreatic ductal adenocarcinoma; CUP: cancer of unknown primary; mBC: metastatic breast cancer; mCRC: metastatic colorectal cancer; mGC: metastatic gastric cancer; NGS: next-generation sequencing; NNP: number needed to predict; PSI: predictive summary index; SGT: single-gene test; Sq-NSCLC: squamous non-small cell lung cancer.



Supplementary Figure 1. Impact of test specificity and prevalence on number needed to predict a correctly identified patient.



Supplementary Figure 2. One-way sensitivity analysis: cost per NNP in EUR (€) and USD (\$)

Panel A displays the tornado diagram for NNP in EUR (€). Panel B displays results in USD (\$). Upper and lower bounds: 95% CI. Adv.: advanced; NNP: number needed to predict; NonSq-NSCLC: non-squamous non-small cell lung cancer.

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