Supplementary

Table S1 Study participant sites and patients included by site

Sites	N	%
Institut Català d´Oncologia L´Hospitalet de Llobregat (ICO)	26	15.1
Hospital Universitario Central de Asturias	20	11.6
Complejo Hospitalario de Navarra	16	9.3
Hospital Universitari de Sant Joan de Reus	15	8.7
Complexo Hospitalario Universitario de Vigo	14	8.1
Hospital Clínic de Barcelona	14	8.1
Hospital General Universitario Gregorio Marañón	11	6.4
Hospital Universitario Puerta de Hierro Majadahonda	11	6.4
Hospital Universitario 12 de Octubre	9	5.2
Hospital Universitario Virgen de las Nieves	7	4.1
Hospital del Mar	6	3.5
Hospital Clínico Universitario Lozano Blesa	5	2.9
Hospital Virgen del Rocío	5	2.9
Complejo Hospitalario Universitario Insular Materno Infantil de Gran Canaria	4	2.3
Hospital General Universitario de Alicante	3	1.7
Hospital General Universitario de Valencia	3	1.7
Complejo Hospitalario Regional de Málaga	1	0.6
Hospital Universitari Mútua de Terrasa	1	0.6
Hospital Virgen Macarena	1	0.6
Total	172	100.0

Table S2 Description of the tests

Idylla™ *EGFR* Mutation Test (Biocartis)	Oncomine™ Precision Assay (ThermoFisher Scientific)
Quantitative PCRs were run on the Idylla platform with 2 FFPE sections of 10 µm (tissue area between 25–300 mm^2), output data were provided by the Idylla embedded software (Version 4.1.1).	Nucleic acid extraction was performed using the AllPrep DNA/RNA FFPE kit (50) (QIAGEN® GmbH) according to the manufacturer's instructions. DNA and RNA library generation, as well as sequencing, was carried out on the ThermoFisher Ion Torrent Genexus system using the Oncomine precision assay. Point mutations, small insertions and deletions, and CNVs of somatic hotspot region genes, as well as fusion genes and splice variants, were evaluated using Torrent Suite Genexus software version 6.6.2.1 Minimum quality criteria for DNA sequencing was established: average insert size ≥80 bp, average hot spot exon coverage ≥100×, and average sequencing depth and average coverage >2,000×. For RNA, mapped reads on target ≥1,000 and average insert size ≥80 bp. Minimum number of RNA expression controls detected >5 It was required a minimum coverage of 100 reads per base to report a single nucleotide variant (with an allele frequency detection limit of 5%), according to the manufacturer recommendations. Point variants with higher allelic frequency ≥5%, CNVs greater than ≥4 copies, and fusion genes represented by more than ≥3% of reads were reported using *Homo sapiens* GRCh37 build reference sequence

CNV, copy number variants; FFPE, formalin-fixed paraffin-embedded; PCR, polymerase chain reaction.

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Table S3 EGFR mutations covered by the Idylla™ EGFR Mutation Test

EGFR mutation detection	Protein-level changes	Nucleotide-level changes
Exon 18	G719A	c.2156G>C
	G719C	c.2155G>T; c.2154_2155delinsTT
	G719S	c.2155G>A
Exon 19		c.2238_2248delinsGC
		c.2239_2248delinsC
		c.2240_2248del
		c.2239_2247del
	Del12	c.2239_2251delinsC
		c.2240_2251del
		c.2235_2249del
		c.2236_2250del
		c.2239_2253del
		c.2240_2254del
		c.2238_2252del
		c.2237_2251del
		c.2235_2252delinsAAT
		c.2237_2252delinsT
		c.2234_2248del
		c.2236_2253delinsCTA
		c.2237_2253delinsTA
		c.2237_2253delinsTC
		c.2235_2251delinsAG
		c.2236_2253delinsCAA
		c.2230_2249delinsGTCAA
	Del18	c.2240_2257del
		c.2237_2255delinsT
		c.2239_2256del
		c.2236_2253del
		c.2239_2258delinsCA
		c.2237_2254del
		c.2238_2255del
		c.2237_2257delinsTCT
		c.2236_2255delinsAT
		c.2236_2256delinsATC
		c.2237_2256delinsTT
		c.2237_2256delinsTC
		c.2235_2255delinsGGT
	Del21	c.2238_2258del
		c.2236_2256del
	Del24	c.2253_2276del
Exon 20	T790M	c.2369C>T
	S768I	c.2303G>T
	insG	c.2310_2311insGGT
	insASV9	c.2308_2309insGCCAGCGTG
	insASV11	c.2308_2311delinsCCAGCGTGGAT
	insSVD	c.2311_2312insGCGTGGACA
	insH	c.2319_2320insCAC
Exon 21	L858R	c.2573T>G
		c.2573_2574delinsGT
		c.2573_2574delinsGA
	L861Q	c.2582T>A

EGFR, epidermal growth factor receptor.

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Table S4 Adjuvant chemotherapy regimens used according to tumor stage

Tumor stage	CBDCA + paclitaxel		CBDCA + pemetrexed		CBDCA + vinorelbine		CDDP + pemetrexed		CDDP + vinorelbine		Total	
	N	%	N	%	N	%	N	%	N	%	N	%
IA	1	50.0	0	0.0	0	0.0	0	0.0	1	50	2	100.0
IIA	0	0.0	0	0.0	0	0.0	0	0.0	1	100	1	100.0
IIB	7	38.9	0	0.0	4	22.2	3	16.7	4	22.2	18	100.0
IIIA	5	38.5	1	7.7	4	30.8	2	15.4	1	7.7	13	100.0
IIIB	2	66.7	0	0.0	0	0.0	1	33.3	0	0.0	3	100.0
Unknown	0	0.0	0	0.0	0	00	1	100	0	0.0	1	100.0
Total	15	39.5	1	2.6	8	21.1	7	18.4	7	18.4	38	100.0

None of the patients received adjuvant osimertinib since the study was conducted before reimbursement was approved in Spain. CBDCA, carboplatin; CDDP, cisplatin.

Table S5 Correlation between IdyllaTM and Oncomine Precision Assay Data

EGFR mutation test	Oncomine Precision Assay		
	Mutated	No mutated	Total
Mutated	21	0	21
No mutated	4	103	107
Total	25	103	128

Kappa index =0.89. This indicates a high concordance between the Idylla™ *EGFR* mutation test and the Oncomine™ Precision Assay. *EGFR*, epidermal growth factor receptor.

Table S6 Logistic regression of the factors associated with a positive result in the Oncomine Precision Assay

Factors	β	S.E.	Wald	df	Sig.	OR	95% confidence interval	
							Lower	Upper
Age (continuous)	–0.027	0.005	29.984	1	0.000	0.973	0.964	0.983
Gender (Ref: male)	0.890	0.425	4.378	1	0.036	2.435	1.058	5.604

The variable "histology" could not be included in the model as independent variable because all but one cases included in the multivariate analyses had an adenocarcinoma. df, degrees of freedom; OR, odds ratio; S.E., standard error; Sig., significance.

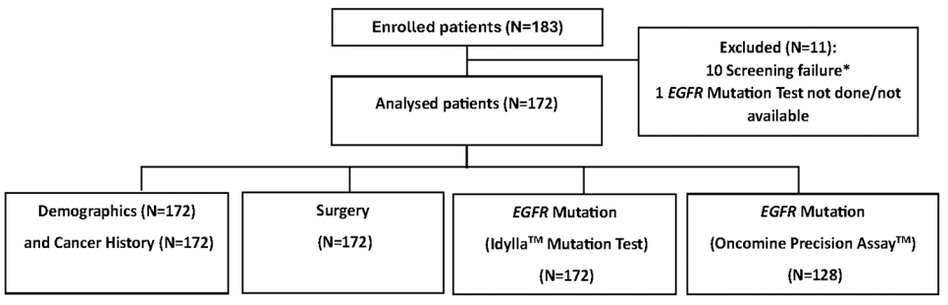

Figure S1 Study flow diagram. *, 10 screening failures: 8 patients had no histological or cytological disease information; 1 patient had no available tumor cells; and 1 patient had duplicate data. *EGFR*, epidermal growth factor receptor.

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