Supplementary

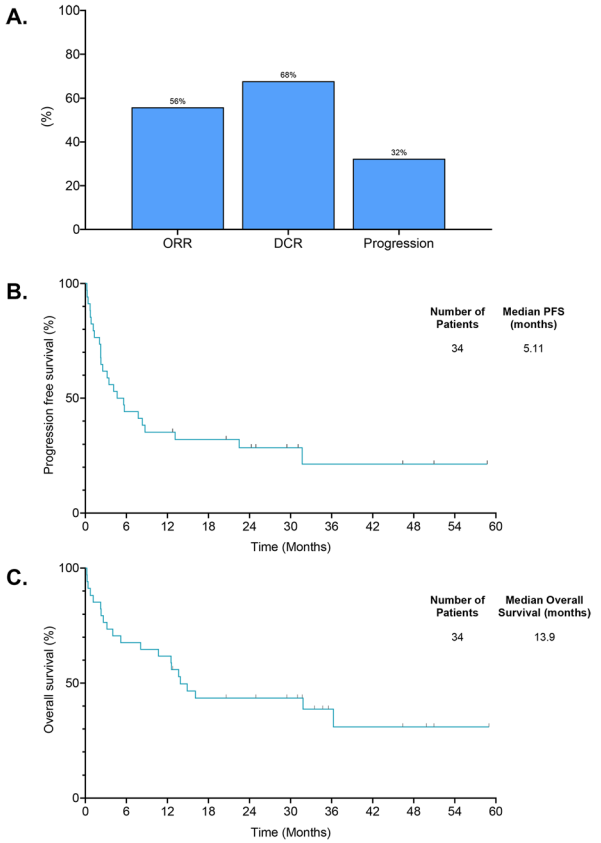

Figure S1 Efficacy of immunotherapy in overall population. (A) ORR, DCR and progression. (B) Kaplan Meier plot for PFS. (C) Kaplan Meier plot for OS. ORR, objective response rate; DCR, disease control rate; PFS, progression-free survival; OS, overall survival.

Table S1 Mutational status of the population study

Variables	Total (n=34)
NGS, n (%)	
Not performed	2 (5.9)
Oncogenic mutation, n (%)	
Mutated	20 (58.8)
KRAS mutation	15 (44.1)
KRAS G12C	9 (26.5)
KRAS non-G12C	6 (17.6)
MET ex.14 skipping mutation	5 (14.7)
BRAF non-V600E	3 (8.8)
Co-alterations, n (%)	
EGFR	
EGFR amplification	2 (5.9)
KRAS	
KRAS amplification	1 (2.9)
TP53	11 (32.4)
PTEN	2 (5.9)
AKT1	1 (2.9)
MAP2K1	1 (2.9)
CDKN2A	1 (2.9)
TERT	1 (2.9)
PIK3CA	1 (2.9)

NGS, next-generation sequencing.

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Table S2 Characteristics of MET exon 14 mutated patients

No.	Sex	Age at diagnosis (years)	Tabagism [pack years]	Exon 14 mutation (NM_001127500)	Co-mutation	PD-L1 TC (%)	First line treatment	Number of cycles (first line)	Best response (first line)	PFS (first line) (months)	Cause of first-line treatment discontinuation	TKI treatment after first line?[†]	Overall survival (months)
1	Male	78	Former smoker [20]	c.3082G>C; p.?	No	75	Pembrolizumab	43	Partial response	31.7	Progression	No	Alive at the end of follow-up (34.8)
2	Female	71	Non-smoker	c.3028G>A; p.?	No	70	Pembrolizumab	1	Progression	0.7	Progression	No	10.7
3	Male	71	Smoker [50]	c.3028+1G>T; p.?	No	100	Pembrolizumab	2	Progression	0.9	Progression	Yes (crizotinib, partial response, death by peritonitis complicating a perforated ulcer)	2.6
4	Male	69	Smoker [40]	c.3028G>A; p.?	BRAF exon 15: c.1801A>G; p.Lys601Glu	100	Pembrolizumab	5	Stabilisation	3.5	Deceased. Myocarditis, possible imputability to pembrolizumab	No	5.2
5	Male	68	Former smoker [20]	c.2942-19_2961del; p.?	No	10	Pembrolizumab, carboplatin, pemetrexed	4	Stabilisation	2.3	Deceased. Severe SARS-COV2 pneumonia	No	3.2

[†], during the follow-up period, no other therapy targeting MET than crizotinib was available in France (except for clinical trials). PD-L1, programmed cell death 1 ligand 1; PFS, progression-free survival; TKI, tyrosine kinase inhibitor; SARS-COV2, severe acute respiratory syndrome coronavirus 2.

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Table S3 First-line immunotherapy for NSCLC

Study	Treatment	Type	PD-L1 (%)	Groups	ORR (%)	PFS (months)	OS (months)
This study (immunotherapy or immunotherapy + chemotherapy)							
Birsen *et al.*	IO or IO CT	PSC	–	IO	52.0	3.4	13.1
				IO CT	64.0	8.7	16.1
Immunotherapy versus chemotherapy							
Keynote-024 (update)	Pembrolizumab or CT	NSCLC	≥50	IO	46.1	7.7	26.3
				CT	31.1	5.5	13.4
CheckMate-026	Nivolumab or CT	NSCLC	≥5	IO	26.0	4.2	14.4
				CT	33.0	5.9	13.2
Impower-110	Atezolizumab or CT	NSCLC	≥1	IO	40.2	8.2	18.9
				CT	28.6	5.0	14.7
Empower-Lung1	Cemiplimab or CT	NSCLC	≥50	IO	39.0	8.2	NR
				CT	20.0	5.7	14.2
Immunotherapy + chemotherapy versus chemotherapy							
KEYNOTE-189	Pembrolizumab + chemotherapy or CT	Non-squamous NSCLC	–	IO CT	48.3	9.0	22
				CT	19.9	4.9	10.6
IMpower-132	Atezolizumab + chemotherapy or CT	Non-squamous NSCLC	–	IO CT	47.0	7.6	17.5
				CT	32.0	5.2	13.6
ORIENT-11	Sintilimab + CT or CT	Non-squamous NSCLC	–	IO CT	51.9	8.9	NR
				CT	29.8	5.0	NR
RATIONALE-304	Tislelizumab + CT or CT	Non-squamous NSCLC	–	IO CT	57.4	9.7	NR
				CT	36.9	7.6	NR
CameL	Camrelizumab + CT or CT	Non-squamous NSCLC	–	IO CT	55.1	11.0	27.1
				CT	32.9	6.5	19.8
KEYNOTE-407	Pembrolizumab + chemotherapy or CT	Squamous NSCLC	–	IO CT	62.2	8.0	17.2
				CT	38.8	5.1	11.6
IMpower-131	Atezolizumab + chemotherapy or CT	Squamous NSCLC	–	IO CT	49.7	6.3	14.2
				CT	41.0	5.6	13.5
ORIENT-12	Sintilimab + CT or CT	Squamous NSCLC	–	IO CT	44.7	5.5	NR
				CT	35.4	4.9	NR
RATIONALE-307	Tislelizumab + CT or CT	Squamous NSCLC	–	IO CT	72.5	7.6	NR
				CT	49.6	5.5	NR
CameL-sq	Camrelizumab + CT or CT	Squamous NSCLC	–	IO CT	64.8	8.5	NR
				CT	36.7	4.9	14.5
Double immunotherapy versus chemotherapy							
CHECKMATE-9LA	Nivolumab + ipilimumab + CT or CT	NSCLC	–	dIO	38	6.4	15.8
				CT	25	5.3	11.0
CHECKMATE 227	Nivolumab + ipilimumab + CT or nivolumab or CT	NSCLC	≥1	IO	36	5.1	17.1
				dIO	28	4.2	15.7
				CT	30	5.6	14.9

NSCLC, non-small cell lung cancer; PD-L1, programmed cell death 1 ligand 1; ORR, objective response rate; PSC, pulmonary sarcomatoid carcinomas; OS, overall survival; IO, immunotherapy; CT, chemotherapy; dIO, double immunotherapy; NR, non-reached.

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Table S4 Studies investigating the efficacy of immunotherapy in patients with metastatic PSC

Author	Publication year	Treatment line	Type of treatment	Type of study	Number of patients	Median OS (months)	Median PFS (months)	ORR (%)	DCR (%)
Birsen *et al.*	This study	First line	Pembrolizumab alone or pembrolizumab + platinum doublet or nivolumab + ipilimumab	Retrospective	34	13.9	5.11	55.8	67.6
Domblides *et al*.	2020	Second-line or subsequent-line	Nivolumab alone or Pembrolizumab alone or Atezolizumab alone	Retrospective	37	12.7	4.89	29.7	56.8
Inomata *et al*.	2023	First-line (63.6%) or subsequent-line (36.4%)	Nivolumab alone or pembrolizumab alone or platinum doublet + pembrolizumab or platinum doublet + atezolizumab or nivolumab + ipilimumab	Retrospective	22	NR	9.6	NA	NA
Kim *et al*.	2020	First-line	Durvalumab + tremelimumab	Prospective (phase II)	18	15.4	5.9	26.7	60.0
Lee *et al*.	2020	First-line (4.1%) or subsequent-line (95.9%)	Nivolumab alone or pembrolizumab alone or atezolizumab alone	Retrospective	49	22.2	7.2	49.0	NA
Qian *et al*.	2022	First-line	Sintilimab alone or camrelizumab alone or anlotinib + tislelizumab or anlotinib + camrelizumab or anlotinib + sintilimab or anlotinib + pembrolizumab	Retrospective	21	22.8	9.2	57.2	81.0
Zhou *et al*.	2022	First-line (85.7%) or subsequent-line (14.3%)	ICI alone or chemotherapy + ICI or chemotherapy + ICI + bevacizumab	Retrospective	42	NR	10.3	73.8	92.9
Chu *et al*.	2023	First-line	Camrelizumab + famitinib	Prospective	15	18.2	7.8	46.7	86.7

PSC, pulmonary sarcomatoid carcinomas; ICI, immune checkpoint inhibitor; OS, overall survival; PFS, progression-free survival; ORR, overall response rate; DCR, disease control rate; NR, non-reached; NA, non-available.

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