SUPPLEMENTAL MATERIAL

Supplemental Table 1. Search strategies.

Line #	Database (platform): MEDLINE (Ovid)
1	COVID-19.rx,px,ox. or severe acute respiratory syndrome coronavirus 2.os.
2	("COVID-19" or COVID19 or "COVID 2019" or "novel coronavirus" or "SARS-CoV" or "SARS-CoV-2" or "SARS2" or "2019-nCoV" or ncov19 or ncov-19 or "2019-novel CoV" or sarscov2 or sarscov-2 or Sars-coronavirus2 or Sars-coronavirus-2 or SARS-like coronavirus* or coronavirus-19).ti,ab,kf.
3	(coronavirus* or "corona virus*").ti,kf.
4	Coronavirus Infections/
5	or/1-4
6	20191201:20301231.(dt).
7	5 and 6 [COVID-19, SARS-COV-2]
8	limit 7 to english language
9	exp Neoplasms/
10	(cancer* or carcinom* or tumor* or tumour* or neoplas* or malignan* or metasta* or myeloma* or leuk?emia* or lymphoma* or sarcoma* or melanoma* or oncolog*).ti,ab,kf.
11	9 or 10 [Cancer]
12	8 and 11
13	(checkpoint adj3 (inhibitor* or modulator* or antibod* or block*)).ti,kf,rn.
14	(checkpoint and (inhibitor* or modulator* or antibod* or block*)).nm.
15	(checkpoint adj3 (inhibitor* or modulator* or antibod* or block*)).ab.
16	(("cytotoxic T lymphocyte associated" adj3 "4") or "CTLA 4" or CTLA4).ti,kf,rn.
17	("Cytotoxic t-lymphocyte antigen" adj3 "4").ti,kf,rn.
18	("Cytotoxic t-lymphocyte antigen" or "cytotoxic T lymphocyte associated").nm.
19	(ipilimumab or "MDX CTLA 4" or Yervoy or "MDX 010" or MDX010 or "BMS-734016" or BMS734016).mp.
20	("Programmed Cell Death 1" or PD1 or "PD 1").ti,kf,rn,nm.
	(pembrolizumab or Keytruda or Lambrolizumab or "Merck 3475" or Merck3475 or "MK 3475" or MK3475 or "Sch 900475" or Sch900475 or "HSDB 8257").mp.
22	(nivolumab or "BMS 936558" or BMS936558 or "MDX 1106" or MDX1106 or "ONO 4538" or ONO4538 or Opdivo).mp.
23	("AMP 514" or AMP514 or MEDI0680 or "MEDI 0680").mp.
24	("programmed death ligand 1" or "PD L1" or PDL1 or "B7-H1" or B7HI).ti,kf,rn,nm.
25	(atezolizumab or Tecentriq or MPDL3280A or "MPDL 3280A" or RO5541267 or RO-5541267 or RG 7446 or RG7446 or "CD274 ANTIGEN" or "CD274 protein").mp.
26	(durvalumab or imfinzi or "MEDI 4736" or MEDI4736).mp.
27	(avelumab or Bavencio or MSB0010718C or "MSB 0010718C" or MSB0010682).mp.
28	("BMS 936559" or BMS936559 or MDX1105 or "MDX 1105").mp.

29	(Cemiplimab or libtayo or REGN2810 or "REGN 2810").mp.
30	or/13-29
31	12 and 30 [COVID-19 + cancer patients + immunotherapy (checkpoint inhibitors)]
Line #	Database (Platform): Embase (Ovid)
1	("COVID-19" or COVID19 or "COVID 2019" or "novel coronavirus" or "SARS-CoV" or "SARS-CoV-2" or "SARS2" or "2019-nCoV" or ncov19 or ncov-19 or "2019-novel CoV" or sarscov2 or sarscov-2 or Sars-coronavirus2 or Sars-coronavirus-2 or SARS-like coronavirus* or coronavirus-19).ti,ab,kw.
2	(coronavirus* or "corona virus*").ti.
3	severe acute respiratory syndrome/
4	coronavirus infection/
5	"coronavirus disease 2019"/
6	or/1-5
7	limit 6 to english language
8	limit 7 to dc=20191201-20221231
9	exp malignant neoplasm/
10	(cancer* or neoplas* or tumo?r* or leuk?emia* or lymphoma* or melanoma* or carcinoma* or sarcoma* or oncolog*).ti,ab,kw.
11	9 or 10
12	8 and 11
13	(immun* adj3 checkpoint adj3 (inhibitor* or modulator* or antibod* or block*)).ti,hw,kw.
14	(("cytotoxic T lymphocyte associated" adj3 "4") or "CTLA 4" or CTLA4).ti,kw,hw.
15	("Cytotoxic t-lymphocyte antigen" adj3 "4").ti,kw,hw.
16	(ipilimumab or "MDX CTLA 4" or Yervoy or "MDX 010" or MDX010 or "BMS-734016" or BMS734016).ti,ab,hw,kw,du,tn.
17	("Programmed Cell Death 1" or PD1 or "PD 1").ti,kw,hw,du,tn.
18	(pembrolizumab or Keytruda or Lambrolizumab or "Merck 3475" or Merck3475 or "MK 3475" or MK3475 or "Sch 900475" or Sch900475 or "HSDB 8257").ti,ab,kw,hw,du,tn.
19	(nivolumab or "BMS 936558" or BMS936558 or "MDX 1106" or MDX1106 or "ONO 4538" or ONO4538 or Opdivo).ti,ab,kw,hw,du,tn.
20	("programmed death ligand 1" or "PD L1" or PDL1 or "B7-H1" or B7HI).ti,kw,hw.
21	(atezolizumab or Tecentriq or MPDL3280A or "MPDL 3280A" or RO5541267 or RO-5541267 or RG 7446 or RG7446 or "CD274 ANTIGEN" or "CD274 protein").ti,ab,kw,hw,du,tn.
22	(avelumab or Bavencio or MSB0010718C or "MSB 0010718C" or MSB0010682).ti,ab,kw,hw,du,tn.
23	(Cemiplimab or libtayo or REGN2810 or "REGN 2810").ti,ab,kw,hw,du,tn.
24	(durvalumab or imfinzi or "MEDI 4736" or MEDI4736).ti,ab,kw,hw,du,tn.
25	or/13-24
26	12 and 25

Supplemental Table 2. Characteristics of the participants included in the studies

Study ID	Country	Age	Cancer types	Types of ICI	Interval between last ICI dose and COVID-19 diagnosis	Funding
			Prospectiv	ve cohorts		
Mandala 2021 ²²	Italy	66.5 mean (SD 12.1)	melanoma, lung, renal cell carcinoma	anti-PD-1, anti- PD-L1, anti- CTLA4	median 23.5 (IQR 14-42) days	None
Nichetti 2020 ²⁵	Italy	62 median (IQR 54.5-71)	breast, colorectal, gastric, head and neck, lung, melanoma, pancreatic, prostate, renal, sarcoma, urothelial, neuroendocrine	pembrolizumab nivolumab	median 50 days	None
Yarza 2020 ³²	Spain	66	kidney, lung, colorectal, upper gastrointestinal, bladder, breast, gynecological, prostate, thyroid, head and neck, sarcoma.	NR	within 28 days	None
			Retrospect	ive cohorts		
Albiges 2020 ¹⁰	France	61 median (IQR 52- 71)	breast, gynecological, head and neck, gastrointestinal, genitourinary, thoracic, dermatology, others. Mature B cell neoplasm, acute	NR	within 90 days	NR

			myeloid leukemia, Hodgkin lymphoma.			
Assaad 2020 ⁹	France	63.8 mean (SD 2.2)	breast, colorectal, soft tissue sarcomas, renal cell carcinoma, pancreas, uterine, bone, peritoneal, esophagus, adrenal, anal carcinoma, ovarian, prostate, testis adenocarcinoma, glioma, duodenum, parotid, maxillary sinuses, supraglottis, thymoma, bladder carcinoma	anti-PD-1, anti- PD-L1	within 30 days	NetSARC (INCA & DGOS) and RREPS (INCA & DGOS), RESOS (INCA & DGOS) and LYRICAN (INCA-DGOS-INSERM 12563), Institut Convergence PLASCAN (17- CONV-0002), Association DAM's,Ensemble contre Le GIST, Eurosarc (FP7-278,742), la Fondation ARC, Infosarcome, InterSARC (INCA), LabEx DEvweCAN (ANR- 10-LABX-0061), Ligue de L'Ain contre le Cancer, La Ligue contre le Cancer, EURACAN (EC 739,521)
Dai 2020 ¹²	United States	64 median	lung, gastrointestinal, breast, thyroid, blood cancer, cervix, esophagus	anti-PD-1	within 40 days	None
Garassino 2020 ¹³	Italy	68 median (IQR 61.8-75)	thoracic malignancy	NR	within 60 days	None
Gonzalez- Cao 2020 ²³	Spain	69 median (range 6 - 94)	melanoma	anti-PD-1	undergoing cancer treatment	NR
Grivas 2021 ¹⁴	United States	70 median (IQR 60- 79)	breast, prostate, thoracic, lower gastrointestinal, genitourinary, gynecological, upper gastrointestinal,	NR	within 90 days	Vanderbilt Institute for Clinical and <u>Translational Research</u> grant support

			endocrine, skin cancer, head and neck, sarcoma, nervous system, lymphoid neoplasms, multiple myeloma, myeloid neoplasm	and DD 1 and		
Gulati 2021 ¹⁵	United States	66	NR	anti-PD-1, anti- PD-L1, anti- CTLA4	within 1 year	NIH
Hwang 2021 ¹⁶	United States	66 median (IQR 55- 75)	hematological, breast, genitourinary, lung, gastrointestinal, abdominal, gynecological, CNS and brain, skin, head and neck,	NR	within 30 days	None
Jee 2021 ¹⁷	United States	NR	breast, colorectal, renal, bladder, melanoma, cervical, uterine, esophageal, stomach, hepatocellular carcinoma.	anti-PD-1, anti- PDL1, anti- CTLA4	within 90 days	NIH
Klebanov 2021 ¹⁸	United States	66.6 mean (SD 12)	hematological, solid	pembrolizumab, nivolumab, atezolizumab, ipilimumab, cemiplimab, avelumab, durvalumab	NR	NR
Lara 2020 ¹⁹	United States	64 median (IQR 51- 73)	gynecological	pembrolizumab, nivolumab, NC318	within 50 days	NIH
Lin 2021 ²⁰	United States	65 median (range 31-94)	breast, gynecological, gastrointestinal, lung, head and neck, genitourinary, brain, osteosarcoma, hematological	atezolizumab, durvalumab, pembrolizumab, nivolumab	within 30 days	NR

Luo 2020 ²¹	United States	68 median (IQR 61- 75)	lung	anti-PD-1	within 45 days	NR
Moritz 2021 ³⁸	Germany	65 median (IQR 26- 88)	melanoma	anti-PD-1	median 17 days (range 0-51)	None
Pinato 2020 ²⁶	United Kingdom	68 mean (SD 12.8)	head and neck, lung, gastrointestinal, breast, gynecologic, genitourinary, lymphoma/leukemia	NR	mean 19.3 days (SD 33.3)	None
Robilotti 2020 ⁷	United States	60	leukemia, lymphoma, myeloma, breast, colorectal, lung, prostate	pembrolizumab, nivolumab, atezolizumab, avelumab, durvalumab, ipilimumab, nivolumab + ipilimumab	within 90 days	NR
Trojaniello 2021 ³⁹	Italy	NR	skin cancer	cemiplimab, nivolumab, pembrolizumab, ipilimumab	undergoing ICI treatment	None
Tyan 2020 ³¹	United States	tes 72 median (range 45-83) thoracic, melanoma and non- melanoma skin cancer, gastrointestinal, hematologic		atezolizumab, durvalumab, pembrolizumab, nivolumab, ipilimumab	median 29 days	NR
			Case r	reports		

Buyansky 2021 ¹¹	Canada	62	squamous cell carcinoma	durvalumab	10 days	Fonds de Recherche du Québec en Santé
Ramos- Ruperto 2021 ²⁷	Switzerland	76	lung cancer	pembrolizumab	undergoing ICI treatment	NR
Rolfo 2020 ²⁸	Colombia	1. 62 2. 58	lung	1. ipilimumab + nivolumab 2. pembrolizumab	2 days	NR
Serra-Garcia 2021 ²⁹	Spain	48	basal cell carcinoma	cemiplimab	NR	None

NR = not reported; NA = not applicable; ICI = immune checkpoint inhibitor; IQR = interquartile range; SD = standard deviation; anti-PD-1= programmed cell death protein 1 inhibitors; anti-PD-L1= programmed death-ligand 1 inhibitors; anti-CTLA4 = cytotoxic T lymphocyte-associated protein 4 inhibitor

			election		Comparability		Outcome			Total quality score
Author	Representativen ess of exposed cohort	Selection of non- exposed cohort	Ascertainment of exposure	Demonstration that outcome of interest was not present at start of study, OR baseline assessment	Adjust for the most important risk factors	Adjust for other risk factors	Assessment of outcome	Follow-up length	Loss to follow-up rate	
Albiges 2020	☆	☆	☆	☆	☆			☆	☆	7
Assaad 2020	☆	☆	☆	☆	☆	☆		☆	☆	8
Dai 2020	☆	☆	☆	☆	☆	☆		☆	☆	8
Garassino 2020	☆	☆	☆	☆	☆		☆	☆	☆	8
Gonzalez-Cao 2020	*	☆	☆				*	☆	☆	6
Grivas 2021	*	\$		\$	☆	☆	☆	\$		7
Gulati 2021	☆	☆	☆	☆				☆	☆	6
Hwang 2021	☆	☆	☆	☆	☆	☆	☆	☆	☆	9
Jee 2021	☆	☆	☆	☆				☆	☆	6
Klebanov 2021			☆	☆	☆				☆	4
Lara 2020	☆	☆	☆		☆		☆	☆	☆	7
Lin 2021	☆	☆	☆		*	☆	☆	☆	☆	8
Luo 2020	☆	☆	☆	☆			☆		☆	6
Mandala 2021	☆	☆	☆	☆			☆	☆	☆	7
Moritz 2021	*		☆				☆		\$	4
Nichetti 2020	*	☆	☆	*			☆	☆	☆	7
Pinato 2020	*		☆		☆			\$	*	5
Robilotti 2020	*	☆	☆	☆	☆		☆	☆	☆	8
Trojaniello 2021	☆		☆	☆			\$		☆	5
Tyan 2020	*	☆			☆		*	☆	☆	6
Yarza 2020	☆	☆	☆	☆	☆	☆	☆	☆	☆	9

Supplemental Table 3. Risk of bias of cohort studies. Newcastle Ottawa Scale

Study ID	Outcome	ICI events/total (%)	Chemotherapy events/total (%)	ICI + chemotherapy events/total (%)	Targeted therapy events/total (%)	No treatment events/total (%)	Hormone therapy events/total (%)	No ICI treatment events/total (%)	Adjusted analysis OR (CI95%)
Albiges 2020 ¹⁰	Clinical Worsening	3/19 (16.8)	26/66 (39.4)	-	7/30 (23.3)	-	-	-	NR
202010	Mortality	3/19 (16.8)	18/66 (27.3)	-	2/30 (6.7)	-	-	-	NR
Assaad 2020 ⁹	Mortality	0/3 (0)	0/16 (0)	-	-	5/26 (19.2)	-	-	NR
	Mortality	2/6 (33.3)	1/12 (8.3)	1/3 (33.3)	0/4 (0)	-	-	-	NR
Dai 2020 ¹²	Severe COVID-19	4/6 (66.7)	-	-	-	-	-	-	NR
	ICU admission	-	-	-	-	-	-	-	NR
Garassino 2020 ¹³	Hospital admission	26/34 (76.5)	35/48 (72.9)	16/20 (80)	17/28 (60.7)	42/52 (80.8)	-	-	NR
202013	Mortality	11/33 (33.3)	22/46 (47.8)	-	8/28 (28.6)	13/49 (26.5)	-	-	NR
Gonzalez- Cao 2020 ¹⁴	Mortality	3/22 (13.6)	-	-	2/16 (12.5)	4/12 (33.3)	-	-	NR
	Mortality	39/248 (15.7)	144/802 (18)	-	104/693 (15)	374/2807 (13.3)	47/483 (9.7)	-	0.91 (0.56- 1.47)
	ICU Admission	15/248 (6)	29/802 (3.6)	-	34/693 (4.9)	142/2807 (5.1)	20/483 (4.1)	-	NR
Grivas 2021 ¹⁴	Hospital Admission	75/248 (30.2)	293/802 (36.5)	-	243/693 (35.1)	953/2807 (34)	149/483 (30.8)	-	NR
	Mechanical ventilation	11/248 (4.4)	31/802 (3.9)	-	48/693 (6.9)	167/2807 (5.9)	24/483 (5)	-	NR
	Severe COVID-19	-	-	-	-	-	-	-	0.86 (0.64- 1.16)
Gulati 2021 ¹⁵	Venous thromboem bolism (VTE)	23/199 (11.6)	-	-	62/675 (9.2)	-	26/363 (7.2)	-	NR

Supplemental Table 4. Results of individual cohort studies

Hwang 2021 ¹⁶	Mortality	6/12 (50)	12/39 (30.8)	-	12/63 (19)	152/1175 (12.9)	-	-	5.22 (1.2- 22.3)*
Jee 2021 ¹⁷	Respiratory failure or death	14/51 (27.5)	14/38 (36.8)	-	-	-	-	-	NR
Klebanov	COVID-19 infection	22/1545 (1.4)	-	-	-	-	-	213/20418 (1)	1.38 (0.89- 2.13)
2021 ¹⁸	Mortality	9/22 (40.9)	-	-	-	-	-	61/213 (28.6)	1.60 (0.78- 3.29)
Lara 2020 ¹⁹	Severe COVID-19	3/8 (37.5)	6/35 (17.1)	-	2/13 (15.4)	-	0/9 (0)	-	NR
Lin 2021 ²⁰	Hospital Admission	5/10 (50)	16/35 (45.7)	-	-	-	-	-	NR
	Hospital Admission	18/26 (69.2)	18/26 (69.2)	12/14 (85.7)	7/10 (70)	-	-	-	1.20 (0.33- 4.23)
Luo 2020 ²¹	ICU/Intuba tion/DNI	7/26 (26.9)	11/26 (42.3)	6/14 (42.9)	5/10 (50)	-	-	-	0.83 (0.24- 2.82)
	Mortality	5/26 (19.2)	9/26 (34.6)	4/14 (28.6)	1/10 (10)	-	-	-	1.13 (0.25- 5.03)
	COVID-19 infection	52/159 (32.7)	13/50 (26)	-	24/84 (28.6)	-	-	-	NR
	Hospital admission	7/52 (13.5)	1/13 (7.7)	-	-	-	-	-	NR
Mandala 2021 ²²	Mortality	6/52 (11.5)	2/13 (15.4)	-	-	-	-	-	NR
2021	Serious	9/52 (17.3)	2/13 (15.4)						
	adverse events	4/107 (3.7) no SARS- CoV-2	1/37 (2.7) no SARS-CoV-2	-	-	-	-	-	NR
	Mortality	0/13 (0)	-	-	-	-	-	-	NR
Moritz	ICU Admission	2/13 (15.4)	-	-	-	-	-	-	NR
2021 ³⁸	COVID-19 infection	13/652 (2)	-	-	-	-	-	-	NR
	irAEs	0/13 (0)	-	-	-	-	-	-	NR
	Mortality	2/4 (50)	2/5 (40)	-	-	-	2/2 (100)	-	NR

Nichetti 2020 ²⁵	COVID-19 infection	4/493 (493)	-	-	-	-	-	7/822 (0.85)	NR
Pinato 2020 ²⁶	Mortality	NA	-	-	-	-	-	-	HR 0.80 (0.46- 1.40)**
D 1'1 #'	Hospital admission	-	-	-	-	-	-	-	2.66 (1.05- 6.54)
Robilotti 2020 ⁷	Severe respiratory illness	-	-	-	-	-	-	-	2.22 (1.06- 4.65)
Trojaniello	Severe COVID-19	1/17 (5.9)	-	-	-	-	-	-	NR
2021 ³⁹	irAEs	0/17 (0)							
	Mortality	7/25 (28)	-	-	-	-	-	9/25 (36)	0.36 (0.07- 1.87)
Tyan 2020 ³¹	Hospital admission	19/25 (76)	-	-	-	-	-	24/25 (96)	NR
	ICU admission	5/25 (20)	-	-	-	-	-	10/25 (40)	NR
	Respiratory failure	4/8 (50)	19/36 (52.8)	-	2/7 (28.6)	-	6/7 (85.7)	-	NR
Yarza 2020 ³²	ARDS	3/8 (37.5)	7/36 (19.4)	-	1/7 (14.3)	-	4/7 (57.1)	-	NR
2020	Mortality	-	-	-	-	-	-	-	0.15 (0.01- 1.65)

ICU = intensive care unit; ARDS: acute respiratory distress syndrome; DNI = do not intubate; NR = not reported; irAE = immune related adverse event; HR = hazard ratio; <math>CI = confidence interval

*The comparison group was cancer patients without treatment

**univariable analysis

FOREST PLOT

Supplemental Figure 1. Comparison ICI versus no cancer treatment

	ICI		No cancer tre	atment		Risk Ratio		Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI		M-H, Random, 95% Cl
2.1.1 Mortality								
Assad 2020	0	3	5	26	6.0%	0.61 [0.04, 9.11]		
Garassino 2020 👘	11	33	13	49	24.3%	1.26 [0.64, 2.46]		
Gonzalez-Cao 2020	3	22	4	12	15.4%	0.41 [0.11, 1.53]		_
Grivas 2021	34	238	374	2807	28.8%	1.07 [0.77, 1.48]		- + -
Hwang 2021	6	12	152	1175	25.6%	3.87 [2.15, 6.94]		;;^*
Subtotal (95% CI)		308		4069	100.0%	1.29 [0.62, 2.69]		
Total events	.54		548					
Heterogeneity: Tau ² =	0.46; Chi	²≓19.2	4, df = 4 (P = 0.	0007); I ^z =	79%			
Test for overall effect:	Z=0.68 (P = 0.50))					
2.1.2 ICU admission								
Grivas 2021	:15	248	142	2807	100.0%	1.20 [0.71, 2.00]		
Subtotal (95% CI)		248		2807	100.0%	1.20 [0.71, 2.00]		*
Total events	. 15		142					
Heterogeneity: Not ap	oplicable							
Test for overall effect:	Z=0.68 (P = 0.50	0)					
2.1.3 Hospital admis	sion							
Garassino 2020	26	34	42	52	42.3%	0.95 [0.75, 1.19]		₽
Grivas 2021	75	248	953	2807	57.7%	0.89 [0.73, 1.08]		
Subtotal (95% CI)		282		2859	100.0%	0.91 [0.79, 1.06]		•
Total events	101		995					
Heterogeneity: Tau ² =	0.00; Chi	² = 0.20	, df = 1 (P = 0.6	6); I ² = 0%				
Test for overall effect:	Z=1.18 (P = 0.24	4)					
								, , , , , , , , , , , , , , , , , , ,
							0.01	0.1 1 10 10
								Favours ICI Favours control

Supplemental Figure 2. Comparison ICI versus chemotherapy

Study or Subaroup	ICI		Chemoth			Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Random, 95% Cl
1.1.1 Mortality							
Algibes 2020	3	19	18	66	5.1%	0.58 [0.19, 1.76]	
Assad 2020	0	3	0	16		Not estimable	
Dai 2020	2	6	1	12	1.3%	4.00 [0.45, 35.79]	
Garassino 2020	11	33	22	46	19.0%	0.70 [0.39, 1.23]	— • +
Grivas 2021	34	238	144	802	50.4%	0.80 [0.56, 1.12]	-8
Hwang 2021	6	12	12	39	11.4%	1.63 [0.78, 3.39]	
Luo 2020	5	26	9	26	6.9%	0.56 [0.22, 1.43]	-
Mandala 2021	6	52	2	13	2.9%	0.75 [0.17, 3.30]	
Nichetti 2020	2	4	2	5	3.0%	1.25 [0.29, 5.35]	
Subtotal (95% CI)		393		1025	100.0%	0.84 [0.65, 1.07]	•
Total events	69		210				
Heterogeneity: Tau ² :	= 0.00; Chi	i ^z = 7.08	6, df = 7 (P	= 0.42);	I ² = 1%		
Test for overall effect	c Z = 1.41 ((P = 0.1	6)				
1.1.2 ICU admission							
Grivas 2021	15	248	29	802	53.2%	1.67 [0.91, 3.07]	+
Luo 2020	7	26	11	26	46.8%	0.64 [0.29, 1.38]	
Subtotal (95% CI)		274		828	100.0%	1.06 [0.41, 2.75]	
Total events	22		40				
Heterogeneity: Tau ² :	= 0.34; Chi	i ^z = 3.70	3, df = 1 (P	= 0.05);	l² = 73%		
Test for overall effect	c Z = 0.13 ((P = 0.9	0)				
1.1.3 Hospital admis	ssion						
Garassino 2020	26	34	35	48	32.3%	1.05 [0.81, 1.35]	+
			293	802	47.3%	0.83 [0.67, 1.02]	-
Grivas 7071	75	/48					
Grivas 2021 L in 2021	75 5	248 10			41%	1 03 0 51 2 10	+
Lin 2021	5	10	16	33	4.1% 15.9%	1.03 [0.51, 2.10] 1.00 [0.70, 1.44]	-+
Lin 2021 Luo 2020	5 18	10 26		33 26	15.9%	1.00 [0.70, 1.44]	
Lin 2021 Luo 2020 Mandala 2021	5	10	16 18	33 26 13		1.00 [0.70, 1.44] 1.75 [0.24, 13.00]	
Lin 2021 Luo 2020 Mandala 2021 Subtotal (95% CI)	5 18 7	10 26 52	16 18 1	33 26 13	15.9% 0.5%	1.00 [0.70, 1.44]	•
Lin 2021 Luo 2020 Mandala 2021 Subtotal (95% Cl) Total events	5 18 7 131	10 26 52 370	16 18 1 363	33 26 13 922	15.9% 0.5% 100.0%	1.00 [0.70, 1.44] 1.75 [0.24, 13.00]	•
Lin 2021 Luo 2020 Mandala 2021 Subtotal (95% CI)	5 18 7 131 = 0.00; Chi	10 26 52 370 i ² = 3.02	16 18 1 363 2, df = 4 (P	33 26 13 922	15.9% 0.5% 100.0%	1.00 [0.70, 1.44] 1.75 [0.24, 13.00]	
Lin 2021 Luo 2020 Mandala 2021 Subtotal (95% CI) Total events Heterogeneity: Tau ² : Test for overall effect	5 18 7 131 = 0.00; Chi t: Z = 0.95 (10 26 52 370 i ² = 3.02	16 18 1 363 2, df = 4 (P	33 26 13 922	15.9% 0.5% 100.0%	1.00 [0.70, 1.44] 1.75 [0.24, 13.00]	
Lin 2021 Luo 2020 Mandala 2021 Subtotal (95% CI) Total events Heterogeneity: Tau ² : Test for overall effect 1.1.4 Severe COVID	5 18 7 131 = 0.00; Chi t: Z = 0.95 (- 19	10 26 52 370 (P = 0.3	16 18 1 363 2, df = 4 (P 4)	33 26 13 922 = 0.55);	15.9% 0.5% 100.0% I [*] = 0%	1.00 [0.70, 1.44] 1.75 [0.24, 13.00] 0.93 [0.81, 1.08]	
Lin 2021 Luo 2020 Mandala 2021 Subtotal (95% CI) Total events Heterogeneity: Tau ² : Test for overall effect 1.1.4 Severe COVID Algibes 2020	5 18 7 131 = 0.00; Chi t: Z = 0.95 (-19 3	10 26 52 370 (P = 0.3 (P = 0.3	16 18 1 2, df = 4 (P 4) 26	33 26 13 922 = 0.55); 66	15.9% 0.5% 100.0% ² = 0% 30.8%	1.00 [0.70, 1.44] 1.75 [0.24, 13.00] 0.93 [0.81, 1.08] 0.40 [0.14, 1.18]	
Lin 2021 Luo 2020 Mandala 2021 Subtotal (95% CI) Total events Heterogeneity: Tau ² : Test for overall effect 1.1.4 Severe COVID Algibes 2020 Lara 2020	5 18 7 131 = 0.00; Chi t: Z = 0.95 (- 19 3 3	10 26 52 370 (P = 0.3 (P = 0.3 19 8	16 18 1 2, df = 4 (P 4) 26 6	33 26 13 922 = 0.55); 66 35	15.9% 0.5% 100.0% ² = 0% 30.8% 29.0%	1.00 [0.70, 1.44] 1.75 [0.24, 13.00] 0.93 [0.81, 1.08] 0.40 [0.14, 1.18] 2.19 [0.69, 6.93]	
Lin 2021 Luo 2020 Mandala 2021 Subtotal (95% CI) Total events Heterogeneity: Tau ² : Test for overall effect 1.1.4 Severe COVID Algibes 2020 Lara 2020 Yarza 2020	5 18 7 131 = 0.00; Chi t: Z = 0.95 (-19 3	10 26 52 370 (P = 0.3 (P = 0.3 19 8 8	16 18 1 2, df = 4 (P 4) 26	33 26 13 922 = 0.55); 66 35 36	15.9% 0.5% 100.0% ² = 0% 30.8% 29.0% 40.2%	1.00 [0.70, 1.44] 1.75 [0.24, 13.00] 0.93 [0.81, 1.08] 0.40 [0.14, 1.18] 2.19 [0.69, 6.93] 0.95 [0.44, 2.02]	
Lin 2021 Luo 2020 Mandala 2021 Subtotal (95% CI) Total events Heterogeneity: Tau ² : Test for overall effect 1.1.4 Severe COVID - Algibes 2020 Lara 2020 Yarza 2020 Subtotal (95% CI)	5 18 7 131 = 0.00; Chi t: Z = 0.95 (- 19 3 3 4	10 26 52 370 (P = 0.3 (P = 0.3 19 8	16 18 1 2, df = 4 (P 4) 26 6 19	33 26 13 922 = 0.55); 66 35 36	15.9% 0.5% 100.0% ² = 0% 30.8% 29.0%	1.00 [0.70, 1.44] 1.75 [0.24, 13.00] 0.93 [0.81, 1.08] 0.40 [0.14, 1.18] 2.19 [0.69, 6.93]	
Lin 2021 Luo 2020 Mandala 2021 Subtotal (95% CI) Total events Heterogeneity: Tau ² : Test for overall effect 1.1.4 Severe COVID - Algibes 2020 Lara 2020 Yarza 2020 Subtotal (95% CI) Total events	5 18 7 131 = 0.00; Chi t: Z = 0.95 (- 19 3 3 4 10	10 26 52 370 ₽ = 3.02 (P = 0.3 19 8 8 35	16 18 1 2, df = 4 (P 4) 26 6 19 51	33 26 13 922 = 0.55); 66 35 36 137	15.9% 0.5% 100.0% ² = 0% 30.8% 29.0% 40.2% 100.0%	1.00 [0.70, 1.44] 1.75 [0.24, 13.00] 0.93 [0.81, 1.08] 0.40 [0.14, 1.18] 2.19 [0.69, 6.93] 0.95 [0.44, 2.02]	
Lin 2021 Luo 2020 Mandala 2021 Subtotal (95% CI) Total events Heterogeneity: Tau ² : Test for overall effect 1.1.4 Severe COVID - Algibes 2020 Lara 2020 Yarza 2020 Subtotal (95% CI) Total events Heterogeneity: Tau ² :	5 18 7 131 = 0.00; Chi t: Z = 0.95 (- 19 3 3 4 10 = 0.36; Chi	10 26 52 370 (P = 0.3 (P = 0.3 19 8 8 35 (² = 4.8 ⁴)	16 18 1 2, df = 4 (P 4) 26 6 19 51 1, df = 2 (P	33 26 13 922 = 0.55); 66 35 36 137	15.9% 0.5% 100.0% ² = 0% 30.8% 29.0% 40.2% 100.0%	1.00 [0.70, 1.44] 1.75 [0.24, 13.00] 0.93 [0.81, 1.08] 0.40 [0.14, 1.18] 2.19 [0.69, 6.93] 0.95 [0.44, 2.02]	
Lin 2021 Luo 2020 Mandala 2021 Subtotal (95% CI) Total events Heterogeneity: Tau ² : Test for overall effect 1.1.4 Severe COVID - Algibes 2020 Lara 2020 Yarza 2020 Subtotal (95% CI) Total events	5 18 7 131 = 0.00; Chi t: Z = 0.95 (- 19 3 3 4 10 = 0.36; Chi	10 26 52 370 (P = 0.3 (P = 0.3 19 8 8 35 (² = 4.8 ⁴)	16 18 1 2, df = 4 (P 4) 26 6 19 51 1, df = 2 (P	33 26 13 922 = 0.55); 66 35 36 137	15.9% 0.5% 100.0% ² = 0% 30.8% 29.0% 40.2% 100.0%	1.00 [0.70, 1.44] 1.75 [0.24, 13.00] 0.93 [0.81, 1.08] 0.40 [0.14, 1.18] 2.19 [0.69, 6.93] 0.95 [0.44, 2.02]	
Lin 2021 Luo 2020 Mandala 2021 Subtotal (95% CI) Total events Heterogeneity: Tau ² : Test for overall effect 1.1.4 Severe COVID - Algibes 2020 Lara 2020 Yarza 2020 Subtotal (95% CI) Total events Heterogeneity: Tau ² :	5 18 7 131 = 0.00; Chi t: Z = 0.95 (- 19 3 3 4 10 = 0.36; Chi	10 26 52 370 (P = 0.3 (P = 0.3 19 8 8 35 (² = 4.8 ⁴)	16 18 1 2, df = 4 (P 4) 26 6 19 51 1, df = 2 (P	33 26 13 922 = 0.55); 66 35 36 137	15.9% 0.5% 100.0% ² = 0% 30.8% 29.0% 40.2% 100.0%	1.00 [0.70, 1.44] 1.75 [0.24, 13.00] 0.93 [0.81, 1.08] 0.40 [0.14, 1.18] 2.19 [0.69, 6.93] 0.95 [0.44, 2.02]	
Lin 2021 Luo 2020 Mandala 2021 Subtotal (95% CI) Total events Heterogeneity: Tau ² : Test for overall effect 1.1.4 Severe COVID Algibes 2020 Lara 2020 Yarza 2020 Subtotal (95% CI) Total events Heterogeneity: Tau ² :	5 18 7 131 = 0.00; Chi t: Z = 0.95 (- 19 3 3 4 10 = 0.36; Chi	10 26 52 370 (P = 0.3 (P = 0.3 19 8 8 35 (² = 4.8 ⁴)	16 18 1 2, df = 4 (P 4) 26 6 19 51 1, df = 2 (P	33 26 13 922 = 0.55); 66 35 36 137	15.9% 0.5% 100.0% ² = 0% 30.8% 29.0% 40.2% 100.0%	1.00 [0.70, 1.44] 1.75 [0.24, 13.00] 0.93 [0.81, 1.08] 0.40 [0.14, 1.18] 2.19 [0.69, 6.93] 0.95 [0.44, 2.02]	

Supplemental Figure 3. Comparison ICI versus targeted therapy

	ICI		Targeted th	егару		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Random, 95% Cl
3.1.1 Mortality							
Algibes 2020	3	19	2	30	3.4%	2.37 [0.44, 12.89]	
Dai 2020	2	6	0	4	1.3%	3.57 [0.21, 59.39]	
Garassino 2020	11	33	8	28	15.8%	1.17 [0.55, 2.49]	
Gonzalez-Cao 2020	3	22	2	16	3.5%	1.09 [0.21, 5.79]	
Grivas 2021	34	238	104	693	52.6%	0.95 [0.67, 1.36]	-=
Hwang 2021	6	12	12	63	15.7%	2.63 [1.23, 5.62]	- _
Luo 2020	5	26	1	10	2.4%	1.92 [0.26, 14.49]	
Yarza 2020	4	8	2	7	5.3%	1.75 [0.45, 6.82]	
Subtotal (95% CI)		364		851	100.0%	1.28 [0.93, 1.75]	•
Total events	68		131				
Heterogeneity: Tau ² =	= 0.02; Chi	² = 7.48	, df = 7 (P = 0).38); I z =	6%		
Test for overall effect:	: Z = 1.51 (P = 0.10	3)				
3.1.2 Hospital admis	sion						
Garassino 2020	26	34	17	28	30.8%	1.26 [0.89, 1.79]	
Grivas 2021	75	248	243	693	48.9%	0.86 [0.70, 1.07]	- -
Luo 2020	18	26	7	10	20.4%	0.99 [0.61, 1.60]	
Subtotal (95% CI)		308		731	100.0%	1.00 [0.77, 1.28]	•
Total events	119		267				
Heterogeneity: Tau ² =).17); I² =	43%		
Test for overall effect:	Z = 0.03 (P = 0.98	3)				
3.1.3 venous thromb	oembolis	m					
3.1.3 venous thromb Gulati 2021	ooembolis 23	m 199	62	675	100.0%	1.26 [0.80, 1.98]	
			62		100.0% 100.0%	1.26 [0.80, 1.98] 1.26 [0.80, 1.98]	
Subtotal (95% CI)		199	62 62				-
Gulati 2021 Subtotal (95% CI) Total events	23 23	199					-
Gulati 2021 Subtotal (95% CI) Total events Heterogeneity: Not ap	23 23 oplicable	199 199	62				-
Gulati 2021 Subtotal (95% CI) Total events Heterogeneity: Not ap Test for overall effect:	23 23 oplicable : Z = 1.00 (199 199	62				-
Gulati 2021 Subtotal (95% CI) Total events Heterogeneity: Not ap Test for overall effect: 3.1.4 Severe COVID-7	23 23 oplicable : Z = 1.00 (199 199	62				
Gulati 2021 Subtotal (95% CI) Total events Heterogeneity: Not ap Test for overall effect: 3.1.4 Severe COVID- Algibes 2020	23 23 oplicable : Z = 1.00 (19	199 199 P = 0.32	62 2)	675	100.0%	1.26 (0.80, 1.98)	
Gulati 2021 Subtotal (95% CI) Total events Heterogeneity: Not ap Test for overall effect: 3.1.4 Severe COVID- Algibes 2020 Lara 2020	23 23 oplicable : Z = 1.00 (19 3	199 199 P = 0.32	62 2) 7	675 30	100.0% 41.2%	1.26 (0.80, 1.98) 0.68 (0.20, 2.30)	
Gulati 2021 Subtotal (95% CI) Total events Heterogeneity: Not ar Test for overall effect: 3.1.4 Severe COVID-4 Algibes 2020 Lara 2020 Yarza 2020	23 23 oplicable : Z = 1.00 (19 3 3	199 199 P = 0.32 19 8	62 2) 7 2	675 30 13 7	100.0% 41.2% 25.5%	1.26 (0.80, 1.98) 0.68 (0.20, 2.30) 2.44 (0.51, 11.57)	
Gulati 2021	23 23 oplicable : Z = 1.00 (19 3 3	199 199 P = 0.32 19 8 8	62 2) 7 2	675 30 13 7	100.0% 41.2% 25.5% 33.3%	1.26 [0.80, 1.98] 0.68 [0.20, 2.30] 2.44 [0.51, 11.57] 1.75 [0.45, 6.82]	
Gulati 2021 Subtotal (95% CI) Total events Heterogeneity: Not ap Test for overall effect: 3.1.4 Severe COVID-4 Algibes 2020 Lara 2020 Yarza 2020 Subtotal (95% CI)	23 23 23 29 27 27 27 27 27 27 27 27 27 27 27 27 27	199 199 P = 0.32 19 8 35 ² = 1.92	62 2) 7 2 2 11 , df = 2 (P = 0	675 30 13 7 50	100.0% 41.2% 25.5% 33.3% 100.0%	1.26 [0.80, 1.98] 0.68 [0.20, 2.30] 2.44 [0.51, 11.57] 1.75 [0.45, 6.82]	
Gulati 2021 Subtotal (95% CI) Total events Heterogeneity: Not ap Test for overall effect: 3.1.4 Severe COVID-4 Algibes 2020 Lara 2020 Yarza 2020 Subtotal (95% CI) Total events Heterogeneity: Tau ² =	23 23 23 29 27 27 27 27 27 27 27 27 27 27 27 27 27	199 199 P = 0.32 19 8 35 ² = 1.92	62 2) 7 2 2 11 , df = 2 (P = 0	675 30 13 7 50	100.0% 41.2% 25.5% 33.3% 100.0%	1.26 [0.80, 1.98] 0.68 [0.20, 2.30] 2.44 [0.51, 11.57] 1.75 [0.45, 6.82]	
Gulati 2021 Subtotal (95% CI) Total events Heterogeneity: Not ap Test for overall effect: 3.1.4 Severe COVID-4 Algibes 2020 Lara 2020 Yarza 2020 Subtotal (95% CI) Total events Heterogeneity: Tau ² =	23 23 23 29 27 27 27 27 27 27 27 27 27 27 27 27 27	199 199 P = 0.32 19 8 35 ² = 1.92	62 2) 7 2 2 11 , df = 2 (P = 0	675 30 13 7 50	100.0% 41.2% 25.5% 33.3% 100.0%	1.26 [0.80, 1.98] 0.68 [0.20, 2.30] 2.44 [0.51, 11.57] 1.75 [0.45, 6.82]	

Supplemental	Figure 4.	Comparison	ICI versus no	ICI. aOR
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Study of Subarrup	lasiodas Datis)	er.	Mainht	Odds Ratio	Odds Ratio
Study or Subgroup	log[Odds Ratio]	35	weight	IV, Random, 95% CI	IV, Random, 95% Cl
9.1.1 Mortality					
Grivas 2021	-0.09		46.1%	0.91 [0.56, 1.49]	
Luo 2020	0.12	0.76	10.4%	1.13 [0.25, 5.00]	
Tyan 2020	-1.02	0.84	8.7%	0.36 [0.07, 1.87]	e
Yarza 2020	-1.89	1.3	3.9%	0.15 [0.01, 1.93]	
Subtotal (95% CI)			69.2%	0.82 [0.53, 1.29]	◆
Heterogeneity: Tau ² =	= 0.00: Chi ² = 3.01.	df = 3	(P = 0.39)); ² = 0%	
Test for overall effect			```		
9.1.2 Interval betwee Klebanov 2021 Subtotal (95% CI)		0.37	19 not re 30.8% 30.8%	- 1.60 [0.77, 3.30]	
Heterogeneity: Not ap	pplicable				
Test for overall effect	: Z = 1.27 (P = 0.20))			
Total (95% CI)			100.0%	0.95 [0.57, 1.60]	+
Heterogeneity: Tau ² =	= 0.09; Chi ² = 5.35.	df = 4	(P = 0.25)); I² = 25%	
Test for overall effect			•		
Test for subgroup dif	• • •		= 1 (P = 0	13) I≧= 57 3%	Favours ICI Favours control
restror subgroup an	101011000. Off $= 2.0$	54, ui -	-10 = 0.	.107.1 - 01.070	

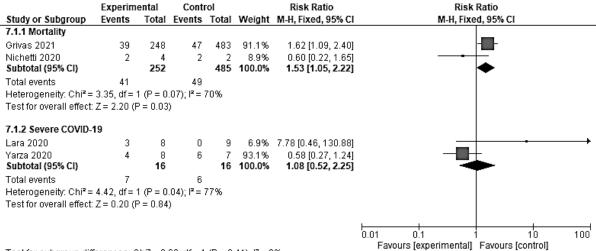
ICI=immune checkpoint inhibitor; aOR=adjusted odds ratio

Supplemental Figure 5.a. Comparison ICI versus hormone therapy. Metanalysis using random effects model

	Experim	ental	Contr	ol		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Random, 95% Cl
7.1.1 Mortality							
Grivas 2021	39	248	47	483	61.0%	1.62 [1.09, 2.40]	-8-
Nichetti 2020	2	4	2	2	39.0%	0.60 [0.22, 1.65]	
Subtotal (95% CI)		252		485	100.0%	1.10 [0.42, 2.90]	
Total events	41		49				
Heterogeneity: Tau ² :	= 0.36; Chi ^a	'= 3.35,	df = 1 (P	= 0.07)); I ² = 70%		
Test for overall effect	:Z=0.19(P	P = 0.85)				
7.1.2 Severe COVID	19						
Lara 2020	3	8	0	9	40.2%	7.78 [0.46, 130.88]	
Yarza 2020	4	8	6	7	59.8%	0.58 [0.27, 1.24]	-8+
Subtotal (95% CI)		16		16	100.0%	1.65 [0.08, 33.66]	
Total events	7		6				
Heterogeneity: Tau ² :	= 3.81; Chi ^a	= 4.42,	df = 1 (P	= 0.04); l ^z = 77%	6	
Test for overall effect	: Z = 0.33 (F	^o = 0.74)				
							Favours [experimental] Favours [control]
Test for subgroup dit	fforoncoe: (`hi₹ – 0	06 df - 1	(P - 0)	901 = 12 - 0	196	r avouro (experimental) i avouro (control)

Test for subgroup differences: $Chi^2 = 0.06$, df = 1 (P = 0.80), $I^2 = 0\%$

Supplemental Figure 5.b. Comparison ICI versus hormone therapy. Metanalysis using fixed effects model



Test for subgroup differences: $Chi^2 = 0.68$, df = 1 (P = 0.41), $I^2 = 0\%$

Supplemental Figure 6.a. Comparison ICI versus chemotherapy + ICI. Metanalysis using random	
effects model	

	Experim	ental	Cont	rol		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% Cl
8.1.1 Mortality							
Dai 2020	2	6	1	3	25.4%	1.00 [0.14, 7.10]	ŧ
Luo 2020	5	26	4	14	74.6%	0.67 [0.21, 2.11]	
Subtotal (95% CI)		32		17	100.0%	0.74 [0.28, 2.00]	
Total events	7		5				
Heterogeneity: Tau ² =	= 0.00; Chi ^a	² = 0.12,	df = 1 (P	= 0.73)	; I ² = 0%		
Test for overall effect	: Z = 0.59 (F	P = 0.56	i) .				
	,						
8.1.2 Hospital admis	sion						
Garassino 2020	26	34	16	20	57.4%	0.96 [0.72, 1.27]	
Luo 2020	18	26	12	14	42.6%	0.81 [0.58, 1.13]	-=-
Subtotal (95% CI)		60		34	100.0%	0.89 [0.72, 1.11]	◆
Total events	44		28				
Heterogeneity: Tau ² =	= 0.00; Chi ^a	= 0.56,	df = 1 (P	= 0.45)	; ² = 0%		
Test for overall effect	: Z = 1.05 (F	P = 0.29	ŋ .				
			-				
							0.01 10 10
Test for subgroup dif	foroncoc: (`hi≊ – ∩	12 df - 1	(P – 0	72) 17 - 0	96	Favours [experimental] Favours [control]

Test for subgroup differences: Chi² = 0.12, df = 1 (P = 0.73), l² = 0\%

Supplemental Figure 6.b. Comparison ICI versus chemotherapy + ICI. Metanalysis using fixed effects model

	Experim	ental	Contr	ol		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	M-H, Fixed, 95% CI
8.1.1 Mortality							
Dai 2020	2	6	1	3	20.4%	1.00 [0.14, 7.10]	
Luo 2020	5	26	4	14	79.6%	0.67 [0.21, 2.11]	
Subtotal (95% CI)		32		17	100.0%	0.74 [0.28, 1.98]	
Total events	7		5				
Heterogeneity: Chi2:	= 0.12, df = 1	1 (P = 0	.73); I ² = I	0%			
Test for overall effect	t: Z = 0.60 (F	P = 0.55)				
8.1.2 Hospital admis	SSION						
Garassino 2020	26	34	16	20	56.4%	0.96 [0.72, 1.27]	
Luo 2020	18	26	12	14	43.6%	0.81 [0.58, 1.13]	-8-
Subtotal (95% CI)		60		34	100.0%	0.89 [0.72, 1.11]	◆
Total events	44		28				
Heterogeneity: Chi2:	= 0.56, df = 1	1 (P = 0	.45); I ^z = I	0%			
Test for overall effect	t: Z = 1.04 (F	P = 0.30)				
							0.01 1 10 10
Taet for subaroun di	fforoncoc: C	hi≊ – 0	10 df - 1	/P = 0	72) 17-0	104	Favours [experimental] Favours [control]

Test for subgroup differences: Chi² = 0.13, df = 1 (P = 0.72), l² = 0%

Sensitivity analysis excluding studies with high risk of bias for the outcome mortality

	ICI		No cancer trea	atment		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Random, 95% Cl
Assad 2020	0	3	5	26	6.8%	0.61 [0.04, 9.11]	
Garassino 2020	11	33	13	49	28.7%	1.26 [0.64, 2.46]	
Grivas 2021	34	238	374	2807	34.3%	1.07 [0.77, 1.48]	-
Hwang 2021	6	12	152	1175	30.2%	3.87 [2.15, 6.94]	
Total (95% CI)		286		4057	100.0%	1.59 [0.73, 3.48]	
Total events	51		544				
Heterogeneity: Tau ² =	0.44; Chi	r = 15.9	98, df = 3 (P = 0.	001); I ^z =	81%		
Test for overall effect:	Z=1.17 ((P = 0.2	24)				0.01 0.1 1 10 100 Favours [experimental] Favours [control]

Supplemental Figure 7. Comparison ICI versus no cancer treatment

ICI= immune checkpoint inhibitor

Supplemental Figure 8. Comparison ICI versus chemotherapy

**	0		1			1.4	
	ICI		Chemothe	erapy		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Random, 95% Cl
Algibes 2020	3	19	18	66	6.0%	0.58 [0.19, 1.76]	
Assad 2020	0	3	0	16		Not estimable	
Dai 2020	2	6	1	12	1.6%	4.00 [0.45, 35.79]	
Garassino 2020	11	33	22	46	21.4%	0.70 [0.39, 1.23]	— = —
Grivas 2021	34	238	144	802	50.7%	0.80 [0.56, 1.12]	-=-
Hwang 2021	6	12	12	39	13.3%	1.63 [0.78, 3.39]	
Mandala 2021	6	52	2	13	3.4%	0.75 [0.17, 3.30]	
Nichetti 2020	2	4	2	5	3.6%	1.25 [0.29, 5.35]	
Total (95% CI)		367		999	100.0%	0.87 [0.66, 1.14]	•
Total events	64		201				
Heterogeneity: Tau ²	= 0.01; Ch	i ² = 6.3 ⁻	1, df = 6 (P =	= 0.39);	I² = 5%		
Test for overall effec	t: Z = 1.01	(P = 0.3	31)				0.01 0.1 1 10 100 Favours [experimental] Favours [control]

Appendix 1

Case reports description

- 1. Buyanski *et al.* reported the case of a 62-year-old patient with poorly differentiated squamous cell carcinoma of unknown primary origin with lymph node metastases and peritoneal carcinomatosis. He was treated with durvalumab (1,500 mg monthly) since 2017. The patient presented a bullous pemphigoid-like eruption and the immunotherapy was discontinued. In 2020 the patient restarted durvalumab. Three weeks after restarting the treatment, the patient was admitted to the hospital for COVID-19. During the hospital stay, the patient developed severe rapidly progressive acute kidney injury with refractory hyperkalemia requiring hemodialysis. Biopsy of the kidney showed severe acute tubulointerstitial nephritis. Prednisone was started and kidney function was recovered. One explanation is and immune regulation dysfunction produced by SARS-CoV-2 exaggerated by the treatment with anti-PD-L1.
- 2. Ramos-Ruperto *et al.* reported the case of a 76-year-old man under treatment with pembrolizumab for lung cancer. He was admitted to the hospital for fever and dyspnea and oxygen saturation lower than 90%. He was diagnosed with COVID-19. After 10 days of respiratory support, the patient was discharged after improvement of fever and oxygenation. Two weeks after discharge the patient returned to the hospital because of daily fever. Blood cultures and viral serology were negative. He evolved with pancytopenia, organomegaly, and elevation of cytokines and ferritin. The diagnosis was hemophagocytic lymphohistiocystosis ad high-dose immunoglobulins were started. The patient improved and discharged from the hospital. The hypothesis was that treatment with anti-PD-1 contributed to hemophagocytic lymphohistocystosis (HLH) in the of context of SARS-CoV-2 infection. HLH related to ICI occur in 0.06% of patients.
- 3. Rolfo *et al.* published 2 case reports of patients with lung cancer treated with ICI who developed atypical skin manifestations. The first case report is a 62-year-old man with stage IV squamous cell lung cancer treated with combination of nivolumab + ipilimumab. He was diagnosed with symptomatic mild COVID-19. The patient developed urticarial popular lesions with minimal erythema located in the lower dorsal, lumbar and gluteal region. Besides, the patient had a burning sensation in the skin and severe joint pain

with reactive polyarthritis. Corticosteroids were administrated and the patient improved the symptoms. The second case was a 58-year-old woman with lung adenocarcinoma treated with chemotherapy + pembrolizumab. The patients presented with respiratory symptoms and was diagnosed with COVID-19. After 48 hours, the patient developed several lesions with targetoid appearance and late-onset painful oral ulcers. The biopsy of skin lesions was consisted with erythema multiforme. The symptoms were controlled with corticosteroids and antihistamines.

4. Serra-Garcia *et al.* reported the case of a 48-year-old woman with history of unresectable facial basal cell carcinoma treated with cemiplimab. She presented at the emergency department with painful digital distal ulcers without any COVID-19 respiratory symptoms. He had necrotic scar and bullae formation on the second, third, and fourth fingertips of the right hand and erythema with a necrotic scar on the fifth fingertip of the left hand. RT-PCR was positive for COVID-19. The lesions worsened to fingertip ischemia and the ICI was stopped. The patient was admitted and received alprostadil. After 1 week the patient improved the lesions and was discharged. It is hypothesized that in this patient with cemiplimab therapy, COVID-19 immune dysregulation could have triggered sever ischemia lesions