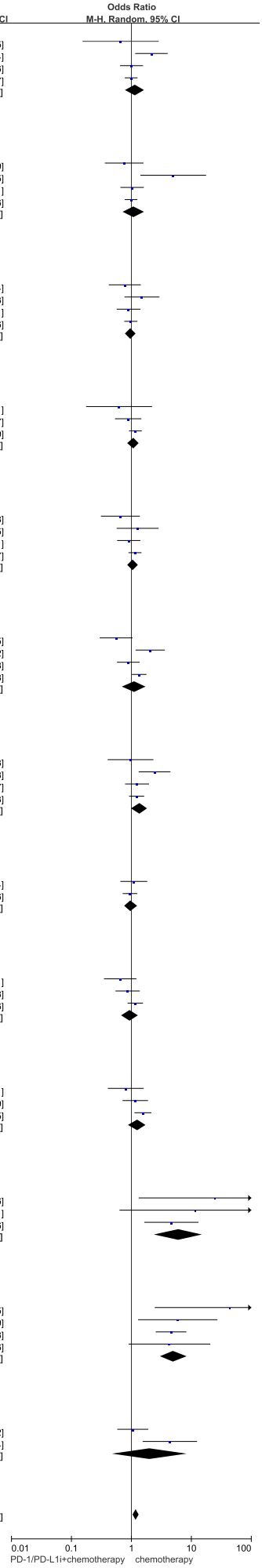
Study or Subgroup	PD-1/PD-L1i+chemotherapy Events	Total	chemotherapy Events	Total	Weight	Odds Ratio M-H, Random, 95% CI
1.10.1 Anemia						
GeparNuevo study 2019	87	92	79	82	0.6%	0.66 [0.15, 2.85]
I-SPY2 Trial 2020	23	69	34	181	2.1%	2.16 [1.16, 4.04]
IMpassion031 2020	63	164	64	167	2.9%	1.00 [0.64, 1.56]
KEYNOTE-522 2020	430	781	215	389	4.0%	0.99 [0.78, 1.27]
Subtotal (95% CI)		**1106**		**819**	**9.6%**	**1.14 [0.80, 1.63]**
Total events	603		392			
Heterogeneity: Tau² = 0.06; Chi² = 5.75, df = 3 (P = 0.12); I² = 48%						
Test for overall effect: Z = 0.74 (P = 0.46)						
1.10.2 Neutropenia						
GeparNuevo study 2019	71	92	67	82	1.7%	0.76 [0.36, 1.59]
I-SPY2 Trial 2020	7	69	4	181	0.8%	5.00 [1.41, 17.65]
IMpassion031 2020	59	164	59	167	2.9%	1.03 [0.66, 1.61]
KEYNOTE-522 2020	365	781	183	389	4.0%	0.99 [0.77, 1.26]
Subtotal (95% CI)		**1106**		**819**	**9.4%**	**1.09 [0.73, 1.64]**
Total events	502		313			
Heterogeneity: Tau² = 0.09; Chi² = 6.78, df = 3 (P = 0.08); I² = 56%						
Test for overall effect: Z = 0.43 (P = 0.67)						
1.10.3 Nausea						
GeparNuevo study 2019	54	92	53	82	2.1%	0.78 [0.42, 1.44]
I-SPY2 Trial 2020	55	69	131	181	1.9%	1.50 [0.77, 2.93]
IMpassion031 2020	106	164	112	167	2.9%	0.90 [0.57, 1.41]
KEYNOTE-522 2020	490	781	246	389	4.0%	0.98 [0.76, 1.26]
Subtotal (95% CI)		**1106**		**819**	**10.9%**	**0.98 [0.80, 1.19]**
Total events	705		542			
Heterogeneity: Tau² = 0.00; Chi² = 2.23, df = 3 (P = 0.53); I² = 0%						
Test for overall effect: Z = 0.24 (P = 0.81)						
1.10.4 Alopecia						
GeparNuevo study 2019	85	92	78	82	0.8%	0.62 [0.18, 2.21]
IMpassion031 2020	123	164	129	167	2.6%	0.88 [0.53, 1.47]
KEYNOTE-522 2020	471	781	220	389	4.0%	1.17 [0.91, 1.49]
Subtotal (95% CI)		**1037**		**638**	**7.4%**	**1.09 [0.87, 1.35]**
Total events	679		427			
Heterogeneity: Tau² = 0.00; Chi² = 1.71, df = 2 (P = 0.43); I² = 0%						
Test for overall effect: Z = 0.76 (P = 0.45)						
1.10.5 Fatigue						
GeparNuevo study 2019	70	92	68	82	1.7%	0.66 [0.31, 1.38]
I-SPY2 Trial 2020	60	69	152	181	1.5%	1.27 [0.57, 2.85]
IMpassion031 2020	59	164	64	167	2.9%	0.90 [0.58, 1.41]
KEYNOTE-522 2020	321	781	147	389	4.0%	1.15 [0.90, 1.47]
Subtotal (95% CI)		**1106**		**819**	**10.1%**	**1.06 [0.86, 1.29]**
Total events	510		431			
Heterogeneity: Tau² = 0.00; Chi² = 2.67, df = 3 (P = 0.45); I² = 0%						
Test for overall effect: Z = 0.53 (P = 0.60)						
1.10.6 Diarrhea						
GeparNuevo study 2019	26	92	34	82	2.1%	0.56 [0.30, 1.05]
I-SPY2 Trial 2020	39	69	70	181	2.4%	2.06 [1.17, 3.62]
IMpassion031 2020	68	164	74	167	3.0%	0.89 [0.58, 1.38]
KEYNOTE-522 2020	230	781	92	389	3.8%	1.35 [1.02, 1.78]
Subtotal (95% CI)		**1106**		**819**	**11.2%**	**1.11 [0.71, 1.74]**
Total events	363		270			
Heterogeneity: Tau² = 0.15; Chi² = 11.70, df = 3 (P = 0.008); I² = 74%						
Test for overall effect: Z = 0.45 (P = 0.65)						
1.10.7 Vomiting						
GeparNuevo study 2019	12	92	11	82	1.4%	0.97 [0.40, 2.33]
I-SPY2 Trial 2020	26	69	36	181	2.2%	2.44 [1.33, 4.48]
IMpassion031 2020	58	164	51	167	2.8%	1.24 [0.79, 1.97]
KEYNOTE-522 2020	199	781	85	389	3.8%	1.22 [0.92, 1.63]
Subtotal (95% CI)		**1106**		**819**	**10.1%**	**1.37 [1.00, 1.86]**
Total events	295		183			
Heterogeneity: Tau² = 0.04; Chi² = 4.70, df = 3 (P = 0.19); I² = 36%						
Test for overall effect: Z = 1.97 (P = 0.05)						
1.10.8 Asthenia						
IMpassion031 2020	38	164	36	167	2.6%	1.10 [0.65, 1.84]
KEYNOTE-522 2020	191	781	99	389	3.8%	0.95 [0.72, 1.26]
Subtotal (95% CI)		**945**		**556**	**6.4%**	**0.98 [0.77, 1.25]**
Total events	229		135			
Heterogeneity: Tau² = 0.00; Chi² = 0.24, df = 1 (P = 0.63); I² = 0%						
Test for overall effect: Z = 0.16 (P = 0.87)						
1.10.9 Constipation						
GeparNuevo study 2019	29	92	34	82	2.1%	0.65 [0.35, 1.21]
IMpassion031 2020	48	164	54	167	2.8%	0.87 [0.54, 1.38]
KEYNOTE-522 2020	185	781	82	389	3.7%	1.16 [0.87, 1.56]
Subtotal (95% CI)		**1037**		**638**	**8.6%**	**0.95 [0.69, 1.30]**
Total events	262		170			
Heterogeneity: Tau² = 0.03; Chi² = 3.21, df = 2 (P = 0.20); I² = 38%						
Test for overall effect: Z = 0.34 (P = 0.73)						
1.10.10 Rash						
GeparNuevo study 2019	21	92	22	82	1.9%	0.81 [0.40, 1.61]
IMpassion031 2020	46	164	42	167	2.7%	1.16 [0.71, 1.89]
KEYNOTE-522 2020	170	781	59	389	3.6%	1.56 [1.12, 2.15]
Subtotal (95% CI)		**1037**		**638**	**8.1%**	**1.25 [0.88, 1.76]**
Total events	237		123			
Heterogeneity: Tau² = 0.04; Chi² = 3.21, df = 2 (P = 0.20); I² = 38%						
Test for overall effect: Z = 1.25 (P = 0.21)						
1.10.11 Hyperthyroidism						
I-SPY2 Trial 2020	4	69	0	181	0.2%	24.94 [1.32, 469.56]
IMpassion031 2020	5	164	0	167	0.2%	11.55 [0.63, 210.61]
KEYNOTE-522 2020	36	781	4	389	1.1%	4.65 [1.64, 13.16]
Subtotal (95% CI)		**1014**		**737**	**1.4%**	**6.04 [2.39, 15.29]**
Total events	45		4			
Heterogeneity: Tau² = 0.00; Chi² = 1.33, df = 2 (P = 0.51); I² = 0%						
Test for overall effect: Z = 3.79 (P = 0.0001)						
1.10.12 Hypothyroidism						
I-SPY2 Trial 2020	7	69	0	181	0.2%	43.56 [2.45, 773.75]
IMpassion031 2020	11	164	2	167	0.6%	5.93 [1.29, 27.19]
KEYNOTE-522 2020	107	781	13	389	2.2%	4.59 [2.55, 8.28]
NeoTRIPaPDL1 2020	8	138	2	142	0.5%	4.31 [0.90, 20.66]
Subtotal (95% CI)		**1152**		**879**	**3.5%**	**5.04 [3.02, 8.39]**
Total events	133		17			
Heterogeneity: Tau² = 0.00; Chi² = 2.35, df = 3 (P = 0.50); I² = 0%						
Test for overall effect: Z = 6.21 (P < 0.00001)						
1.10.13 Severe skin reaction						
GeparNuevo study 2019	45	92	39	82	2.2%	1.06 [0.58, 1.92]
KEYNOTE-522 2020	34	781	4	389	1.1%	4.38 [1.54, 12.44]
Subtotal (95% CI)		**873**		**471**	**3.3%**	**2.02 [0.49, 8.34]**
Total events	79		43			
Heterogeneity: Tau² = 0.87; Chi² = 5.63, df = 1 (P = 0.02); I² = 82%						
Test for overall effect: Z = 0.97 (P = 0.33)						
Total (95% CI)		**13731**		**9471**	**100.0%**	**1.19 [1.05, 1.34]**
Total events	4642		3050			
Heterogeneity: Tau² = 0.08; Chi² = 108.41, df = 43 (P < 0.00001); I² = 60%						
Test for overall effect: Z = 2.80 (P = 0.005)						
Test for subgroup differences: Chi² = 53.00, df = 12 (P < 0.00001), I² = 77.4%						



eFigure 1.