

Supplementary Online Content

McQuade JL, Hammers H, Furberg H, et al. Association of body mass index with the safety profile of nivolumab with or without ipilimumab. *JAMA Oncol*. Published online December 8, 2022. doi:10.1001/jamaoncol.2022.5409

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eReferences.

This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1. Included clinical trials

Trial	Tumor type	Immunotherapy dosing schedule ^a	Patients, no. (immunotherapy)	Comparator arm dosing schedule	Patients, no. (comparator)	
NIVO3						
CheckMate 142¹	MSI-H/dMMR mCRC	NIVO3 Q2W	74	NA	NA	
CheckMate 040²	HCC		214	NA	NA	
CheckMate 039³	Hodgkin lymphoma	NIVO3 W1 and W4 then Q2W	99	NA	NA	
CheckMate 205⁴	Hodgkin lymphoma	NIVO3 Q2W	243	NA	NA	
CheckMate 066⁵	Metastatic melanoma		206	Dacarbazine 1000 mg/m ² Q2W	205	
CheckMate 067⁶	Metastatic melanoma		313	NIVO1 + IPI3 Q3W for 4 cycles, then NIVO3 Q2W		313
				IPI3 Q3W for 4 cycles		311
CheckMate 017⁷	NSCLC		131	Docetaxel 75 mg/m ² Q3W	129	
CheckMate 057⁸	NSCLC		287	Docetaxel 75 mg/m ² Q3W	268	
CheckMate 026⁹	NSCLC		267	Platinum-based chemotherapy Q3W for 6 cycles	263	
CheckMate 025¹⁰	RCC		406	Everolimus 10 mg QD	397	

Trial	Tumor type	Immunotherapy dosing schedule^a	Patients, no. (immunotherapy)	Comparator arm dosing schedule	Patients, no. (comparator)
CheckMate 141¹¹	SCCHN	NIVO3 Q2W	236	Methotrexate 40–60 mg/m ² or: Docetaxel 30–40 mg/m ² or: Cetuximab 250 mg/m ² after 400 mg/m ² loading dose	111
CheckMate 275¹²	mUC		270	NA	NA
NIVO3 + IPI1					
CheckMate 142¹³	MSI-H/dMMR mCRC	NIVO3 + IPI1 Q3W for 4 cycles, then NIVO3 Q2W	119	NA	NA
CheckMate 016¹⁴	RCC		47	NIVO1 + IPI3 Q3W for 4 cycles, then NIVO3 Q2W	47
				NIVO3 + IPI3 Q3W for 4 cycles, then NIVO3 Q2W	6
CheckMate 214¹⁵	RCC		547	Sunitinib 50 mg QD for 4 weeks (6-week cycle)	535
NIVO1 + IPI3					
CheckMate 067⁶	Metastatic melanoma	NIVO1 + IPI3 Q3W for 4 cycles, then NIVO3 Q2W	313	NIVO3 Q2W	313
				IPI3 Q3W for 4 cycles	311

^a Where applicable, comparator arms are described in the primary publications of each study. dMMR, mismatch repair deficient; HCC, hepatocellular carcinoma; IPI1, ipilimumab 1 mg/kg; IPI3, ipilimumab 3 mg/kg; mCRC, metastatic colorectal cancer; MSI-H, microsatellite instability-high; NIVO1, nivolumab 1 mg/kg; NIVO3, nivolumab 3 mg/kg; mUC, metastatic urothelial carcinoma; n/a, not applicable; NSCLC, non-small cell lung cancer; QD, once a day; QxW, every x weeks; RCC, renal cell carcinoma; SCCHN, squamous cell carcinoma of the head and neck.

eTable 2. Cumulative dose of nivolumab by BMI

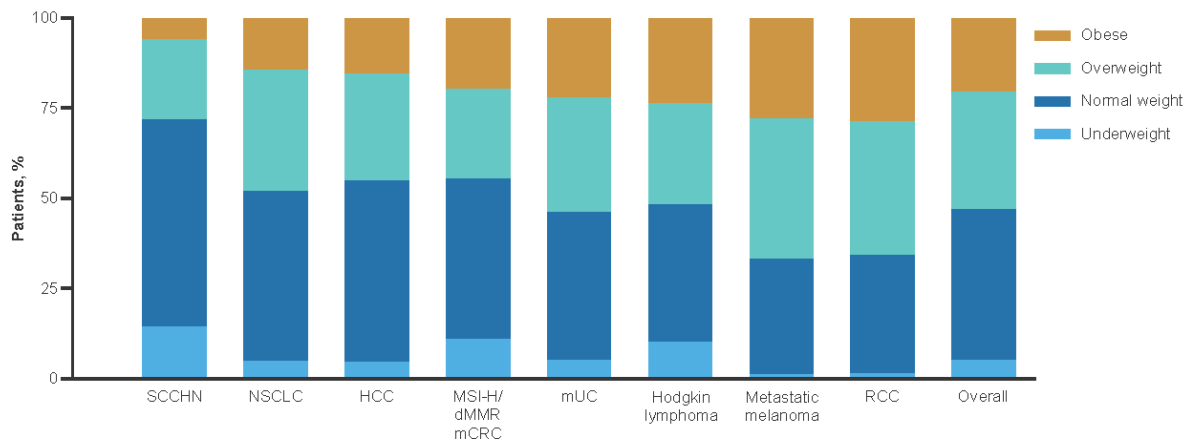
Cumulative dose				
NIVO3	All patients	BMI <25 kg/m²	BMI ≥25 to <30 kg/m²	BMI ≥30 kg/m²
No.	2746	1266	881	543
Cumulative nivolumab dose, median mg/kg (range)	30.0 (0.5–447.0)	26.9 (2.9–426.0)	33.7 (0.5–447.0)	36.0 (3.0–435.0)
Number of nivolumab doses, median (range)	10.0 (1–149)	9.0 (1–142)	11.0 (1–149)	12.0 (1–145)
NIVO3 + IPI1				
No.	713	232	277	200
Cumulative nivolumab dose, median mg/kg (range)	46.9 (2.9–393.1)	47.2 (3.0–317.4)	46.9 (2.9–350.3)	46.8 (2.9–393.1)
Number of nivolumab doses, median (range)	16.0 (1–131)	16.0 (1–105)	15.0 (1–116)	15.5 (1–131)
Cumulative ipilimumab dose, median mg/kg (range)	4.0 (1.0–6.0)	4.0 (1.0–6.0)	4.0 (1.0–5.2)	4.0 (1.0–4.3)
Number of ipilimumab doses, median (range)	4.0 (1–4)	4.0 (1–4)	4.0 (1–4)	4.0 (1–4)
NIVO1 + IPI3				
No.	313	94	108	104
Cumulative nivolumab dose, median mg/kg (range)	4.0 (1.0–403.0)	4.0 (1.0–403.0)	5.5 (1.0–400.0)	4.0 (1.0–394.0)
Number of nivolumab doses, median (min–max)	4.0 (1–137)	4.0 (1–137)	4.5 (1–136)	4.0 (1–134)
Cumulative ipilimumab dose, median mg/kg (range)	12.0 (2.9–15.7)	12.0 (3.0–15.7)	12.0 (3.0–12.0)	12.0 (2.9–12.0)
Number of ipilimumab doses, median (min–max)	4.0 (1–4)	4.0 (1–4)	4.0 (1–4)	4.0 (1–4)

BMI, body mass index; IPI1, ipilimumab 1 mg/kg; IPI3, ipilimumab 3 mg/kg; NIVO1, nivolumab 1 mg/kg; NIVO3, nivolumab 3 mg/kg.

eFigure 1. Distribution of patients into BMI categories by tumor type in the NIVO3 cohort

BMI, body mass index; dMMR, mismatch repair deficient; HCC, hepatocellular carcinoma; mCRC, metastatic colorectal cancer; MSI-H, microsatellite instability-high; NIVO3, nivolumab 3 mg/kg; mUC, metastatic urothelial carcinoma; NSCLC, non-small cell lung cancer; RCC, renal cell carcinoma; SCCHN, squamous cell carcinoma of the head and neck.

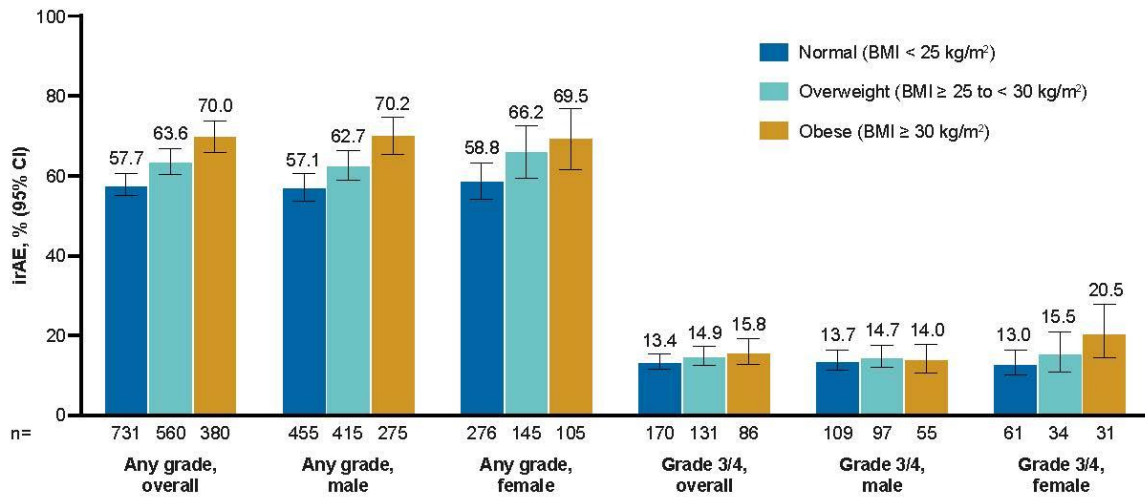
^a BMI was not available for 56 patients.



Patients, n	SCCHN	NSCLC	HCC	MSI-H/ dMMR mCRC	mUC	Hodgkin lymphoma	Metastatic melanoma	RCC	Overall
Underweight	34	33	10	8	14	35	6	6	146
Normal BMI	134	318	106	32	109	129	163	129	1120
Overweight	52	224	63	18	85	95	199	145	881
Obese	13	96	32	14	58	79	140	111	543
Total	233	671	211	72	266	338	508	391	2690*

eFigure 2. Incidence of irAEs by sex and BMI in the NIVO3 cohort

BMI, body mass index; irAE, immune-related adverse event; NIVO3, nivolumab 3 mg/kg.

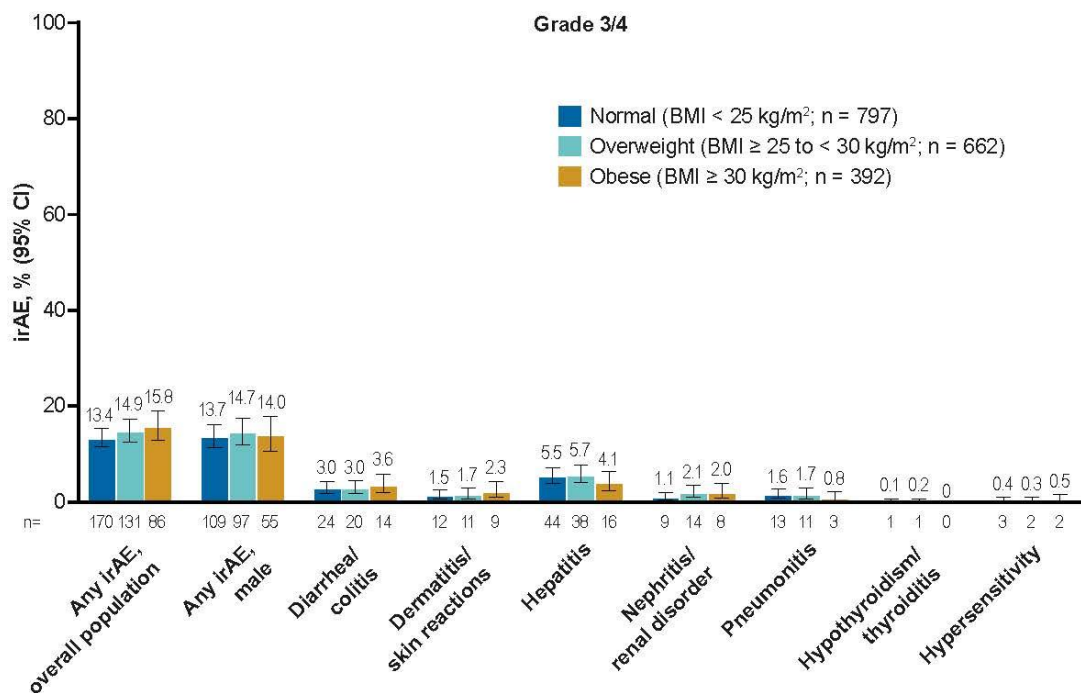
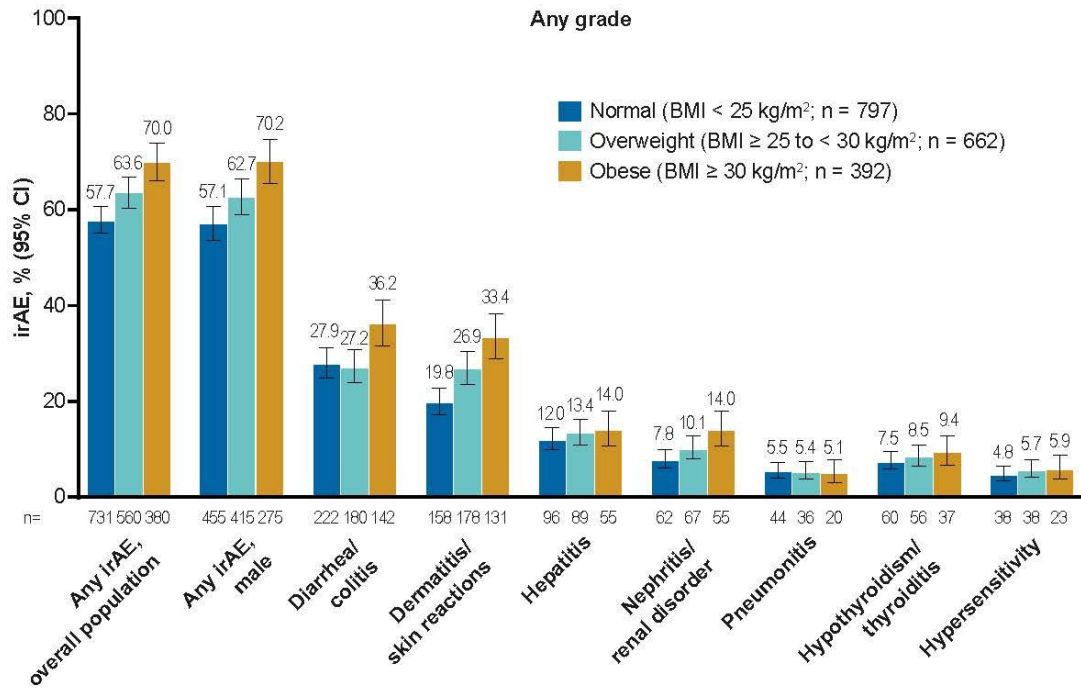


Patients, n	Normal (BMI < 25 kg/m ²)	Overweight (BMI ≥ 25 to < 30 kg/m ²)	Obese (BMI ≥ 30 kg/m ²)
Overall	1266	881	543
Male	797	662	392
Female	469	219	151

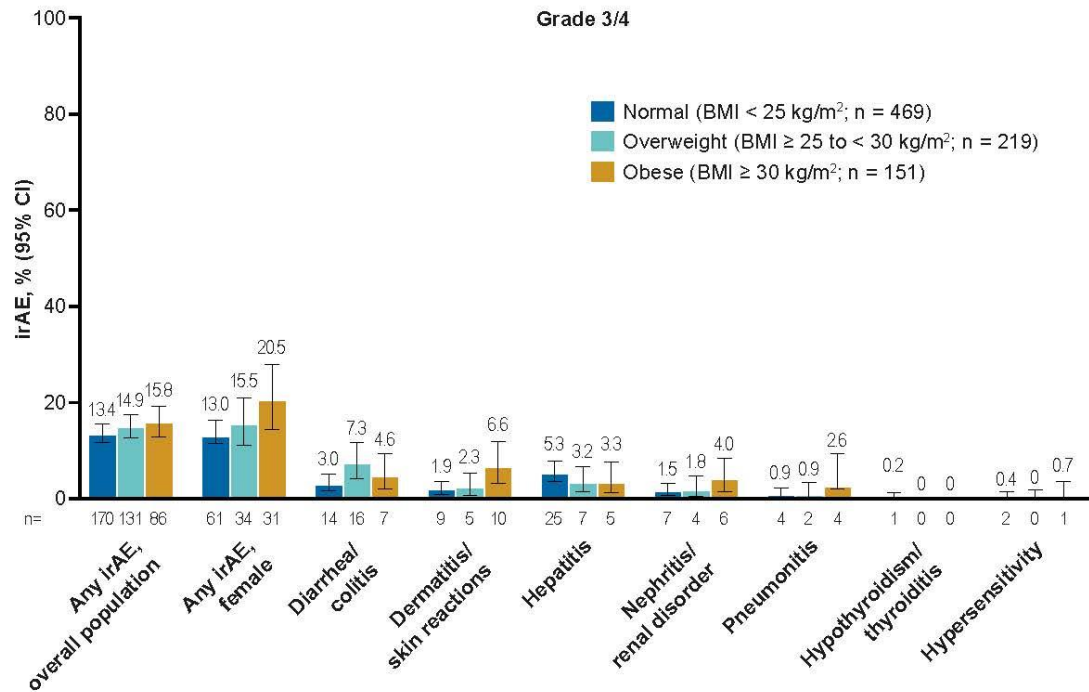
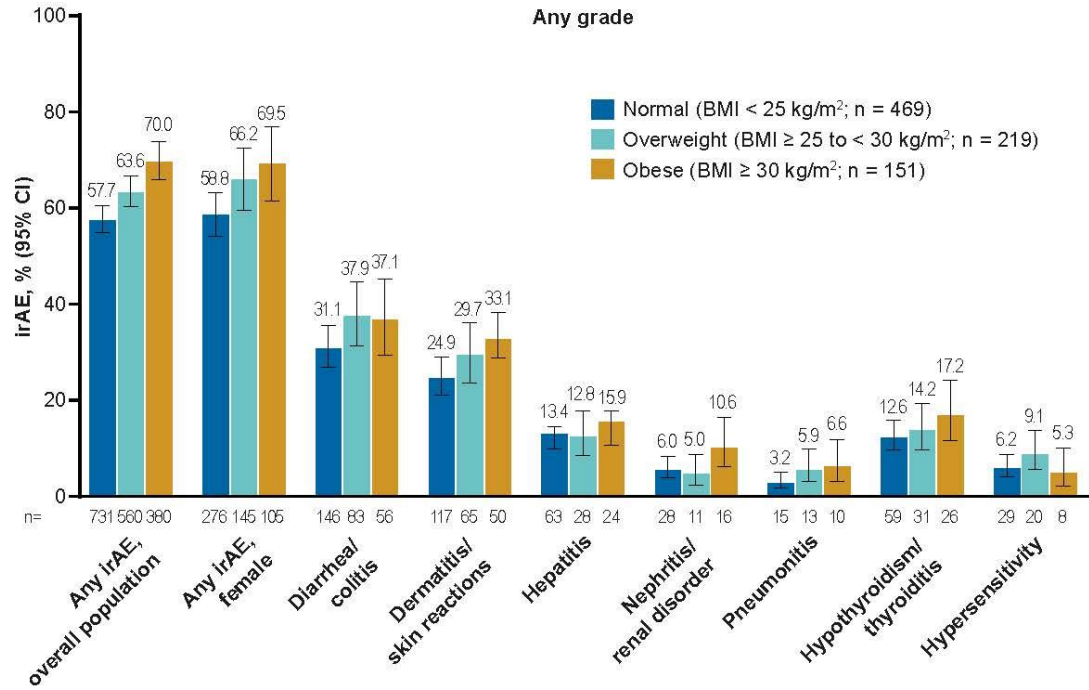
eFigure 3. Incidence of Any-Grade (Top) and Grade 3 or 4 (Bottom) irAEs in (A) Male and (B) Female Patients in the NIVO3 Cohort

BMI, body mass index; CI, confidence interval; irAE, immune-related adverse event; NIVO3, nivolumab 3 mg/kg.

A

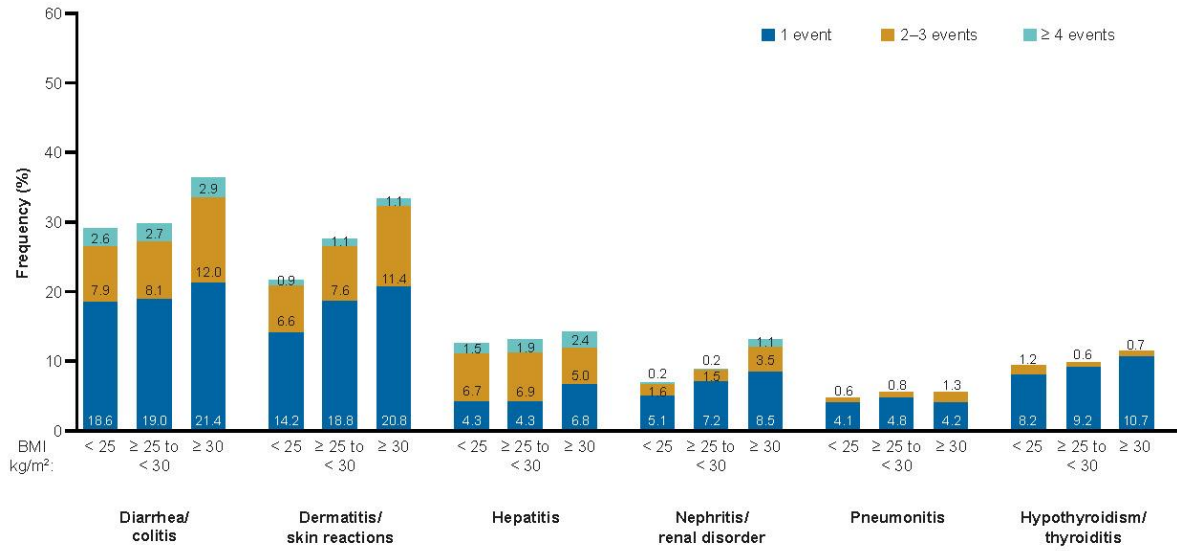


B



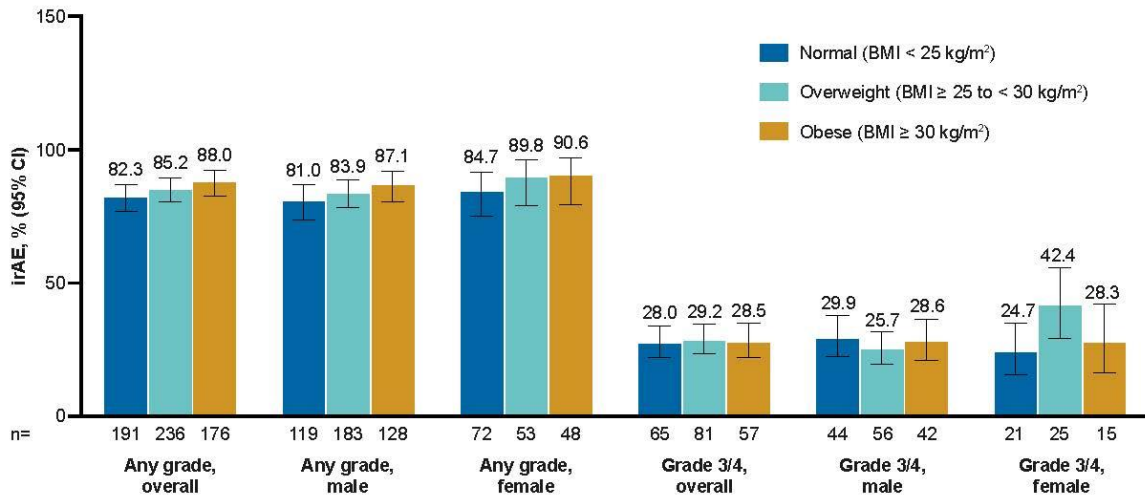
eFigure 4. Frequency of Individual irAEs of Any Grade by BMI in the Overall NIVO3 Cohort

BMI, body mass index; IR, immune-related; irAE, immune-related adverse event; NIVO3, nivolumab 3 mg/kg.



eFigure 5. Incidence of irAEs by Sex and BMI in the NIVO3 + IPI1 Cohort

BMI, body mass index; irAE, immune-related adverse event; IPI1, ipilimumab 1 mg/kg; NIVO3, nivolumab 3 mg/kg.

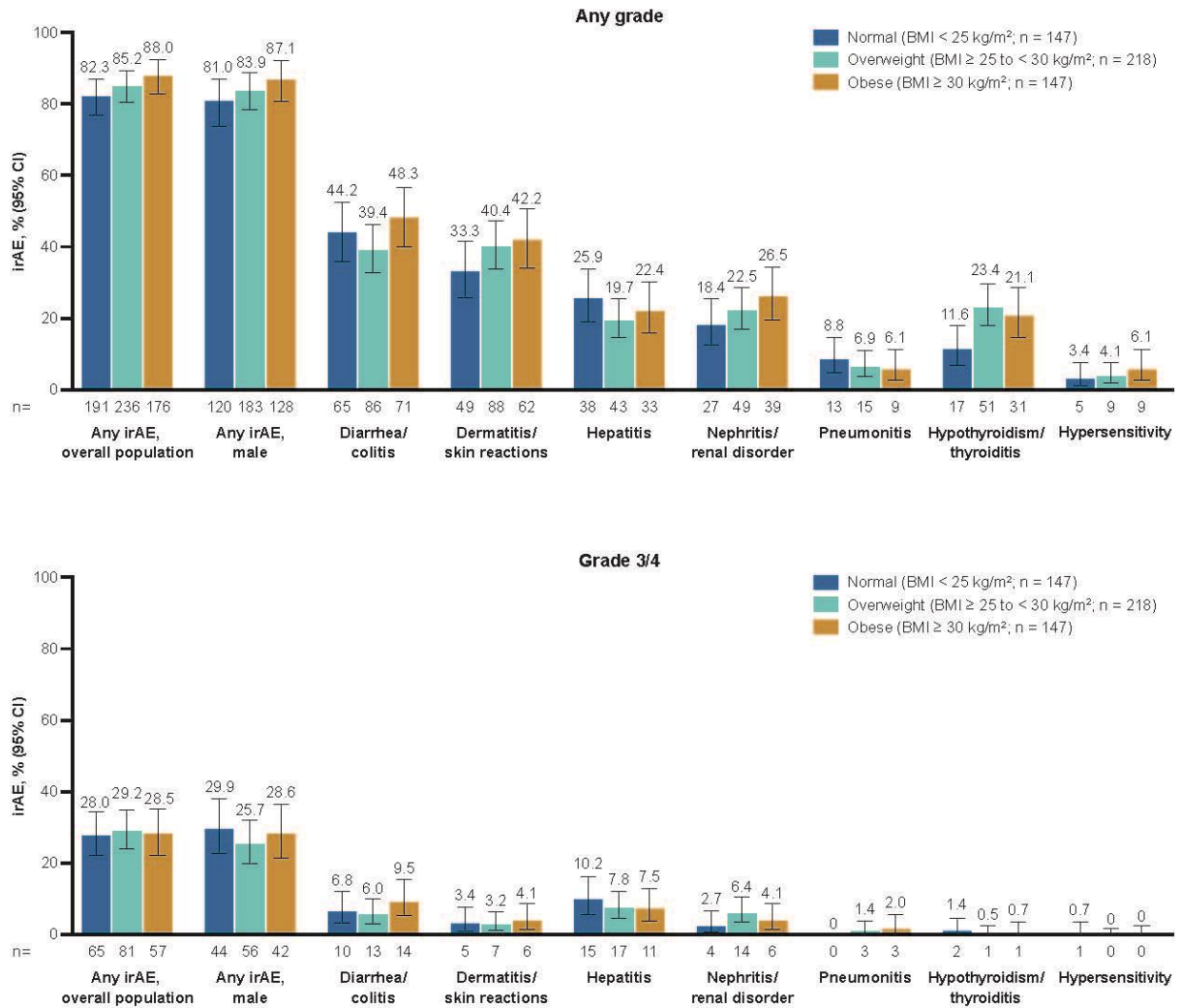


Patients, n	Normal (BMI < 25 kg/m ²)	Overweight (BMI ≥ 25 to < 30 kg/m ²)	Obese (BMI ≥ 30 kg/m ²)
Overall	232	277	200
Male	147	218	147
Female	85	59	53

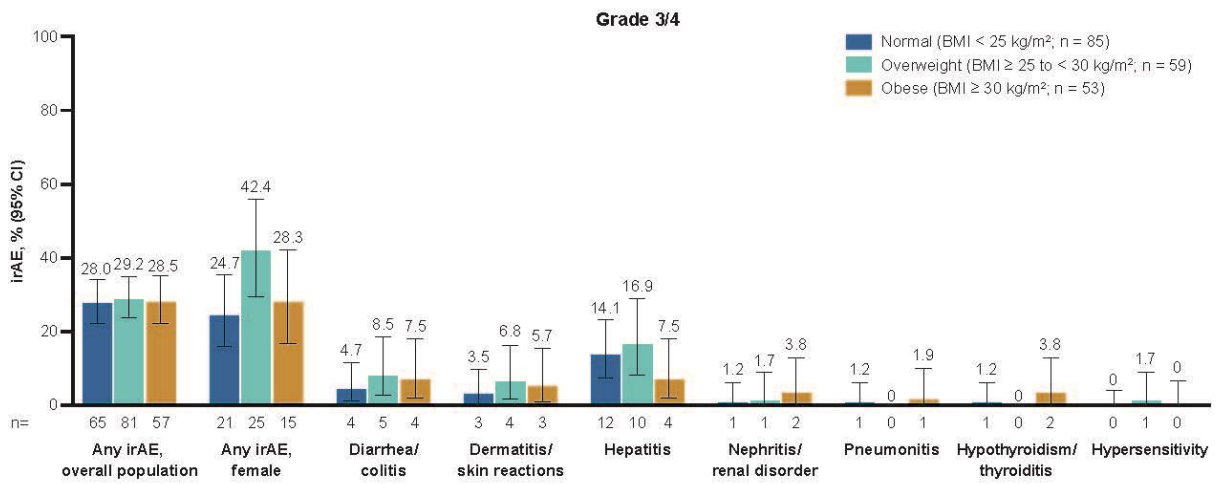
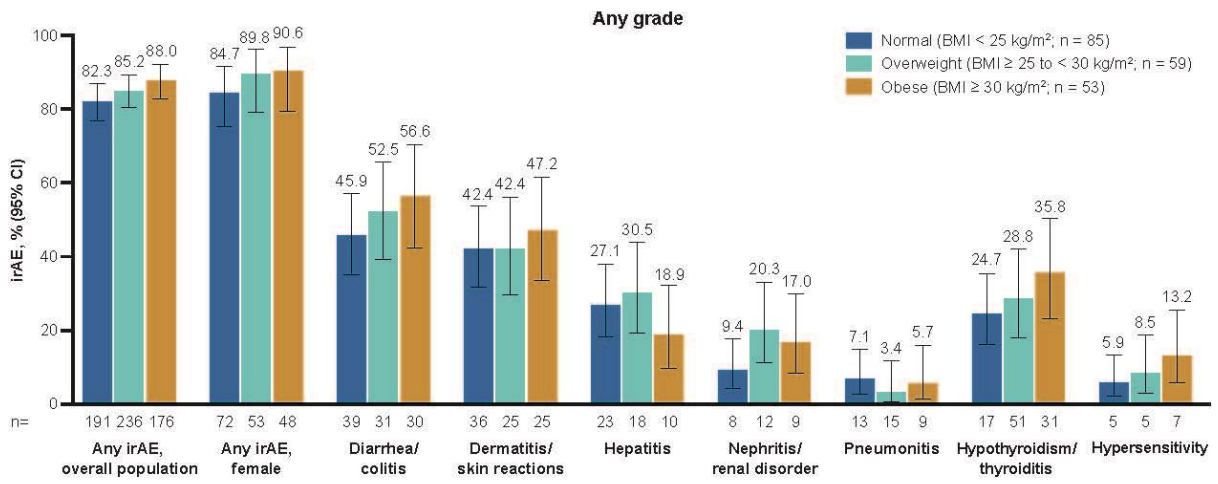
eFigure 6. Incidence of Individual Any-Grade (Top) and Grade 3 or 4 irAEs (Bottom) by BMI in (A) Male and (B) Female Patients in the NIVO3 + IPI1 Cohort

BMI, body mass index; CI, confidence interval; irAE, immune-related adverse event; IPI1, ipilimumab 1 mg/kg; NIVO3, nivolumab 3 mg/kg.

A

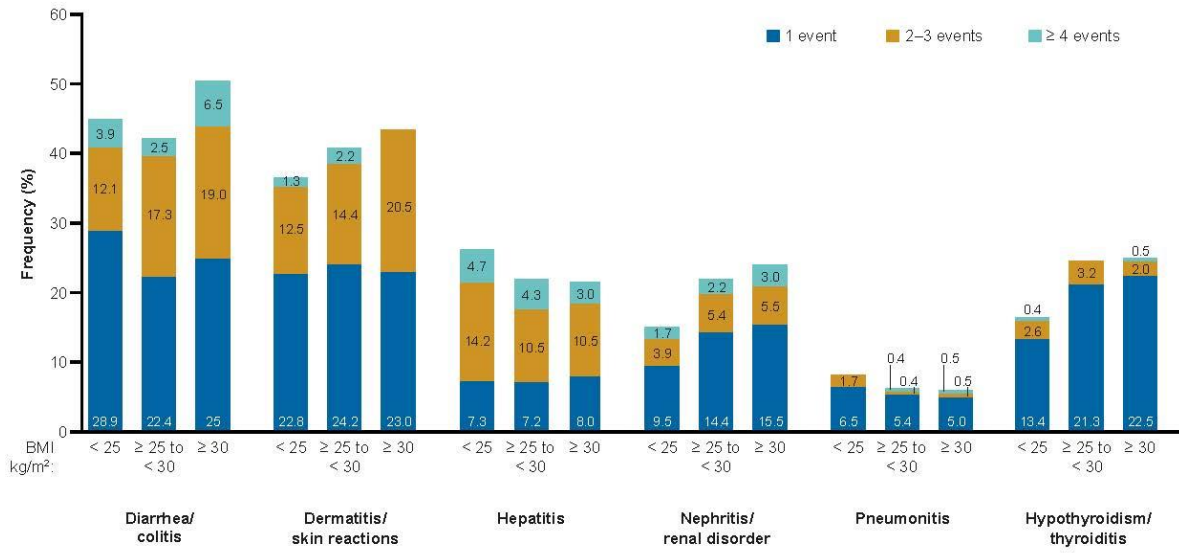


B



eFigure 7. Frequency of Individual Any-Grade irAEs by BMI in the NIVO3 + IPI1 Cohort

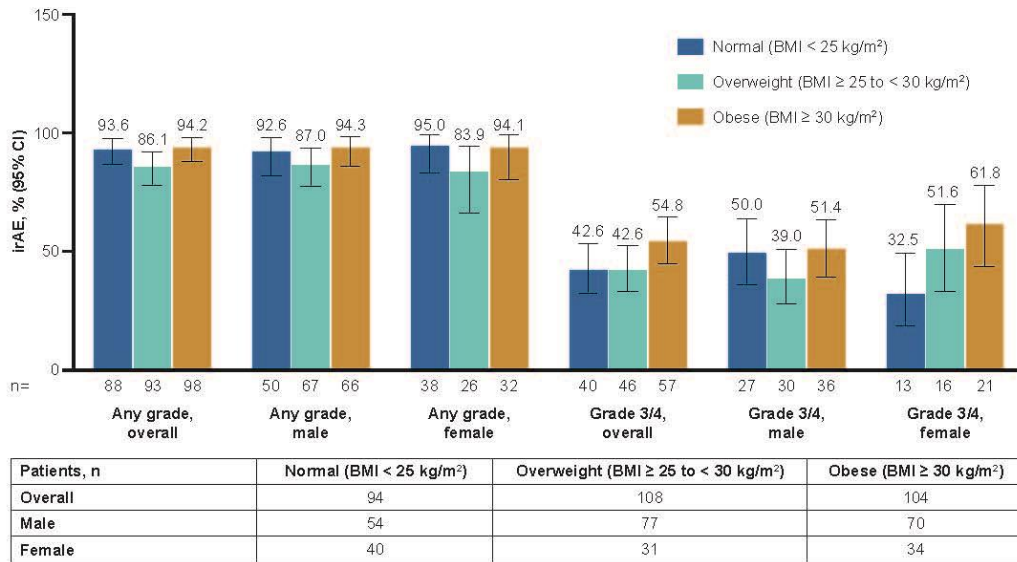
BMI, body mass index; irAE, immune-related adverse event; IPI1, ipilimumab 1 mg/kg; NIVO3, nivolumab 3 mg/kg.



eFigure 8. Incidence of irAEs by Sex and BMI in the NIVO1 + IPI3 Cohort

BMI indicates body mass index; CI, confidence interval; CRC, colorectal cancer; ECOG PS, Eastern Cooperative Oncology Group Performance Status; irAE, immune-related adverse event; IPI1, ipilimumab 1 mg/kg; NIVO3, nivolumab 3 mg/kg; OR, odds ratio; RCC, renal cell carcinoma.

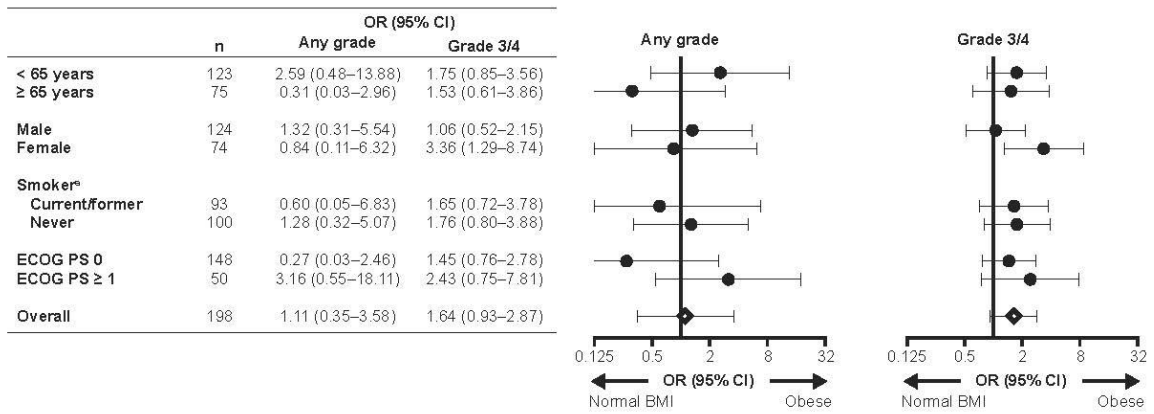
^aSmoking status was unknown for 5 patients.



eFigure 9. ORs for irAE Occurrence in Obese vs Normal or Underweight Patients in Subgroups Based on Patient Characteristics in the NIVO1 + IPI3 Cohort

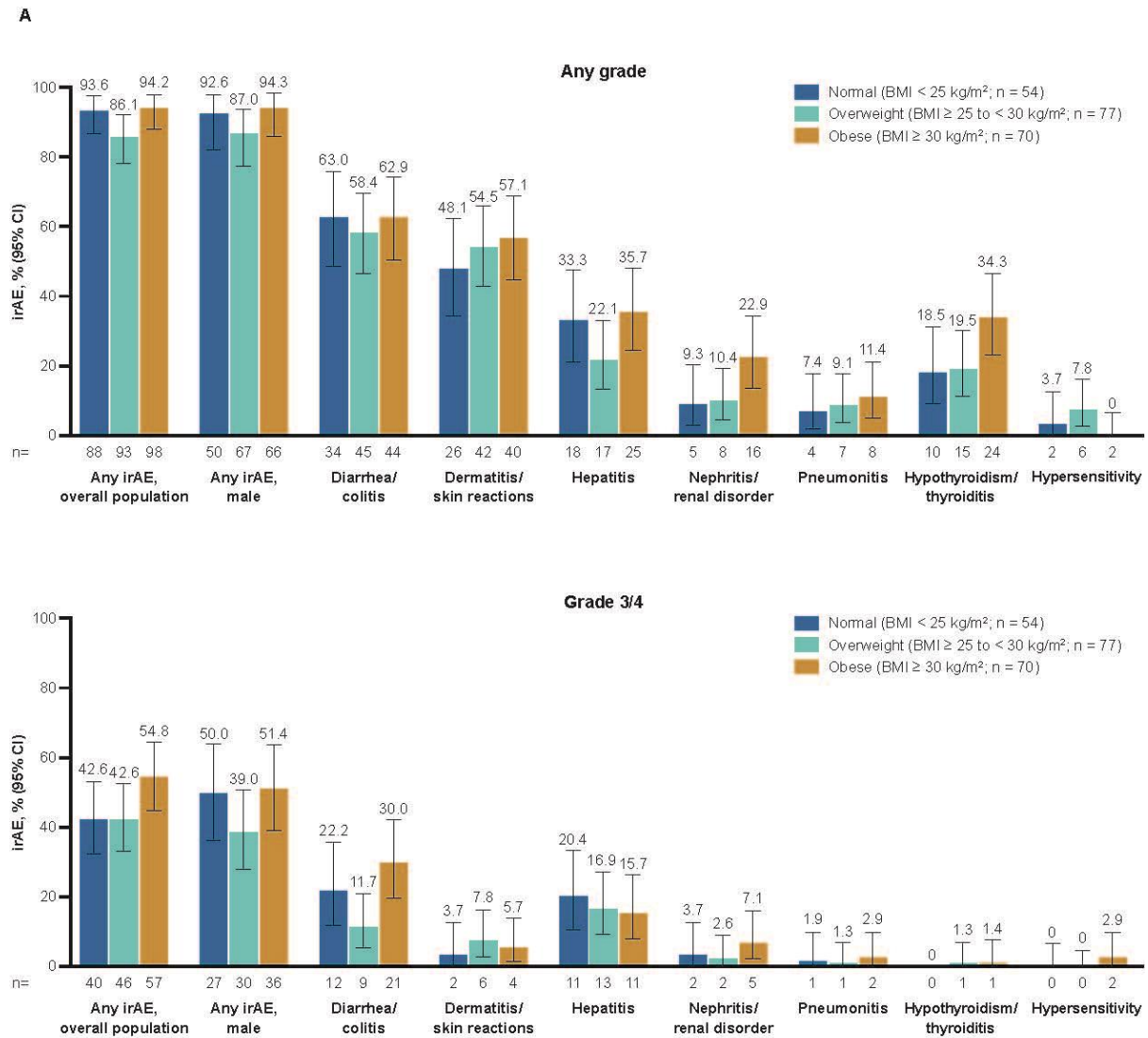
BMI indicates body mass index; CI, confidence interval; ECOG PS, Eastern Cooperative Oncology Group Performance Status; irAE, immune-related adverse event; IPI3, ipilimumab 3 mg/kg; NIVO1, nivolumab 1 mg/kg; OR, odds ratio.

^a Smoking status was unknown for 5 patients.

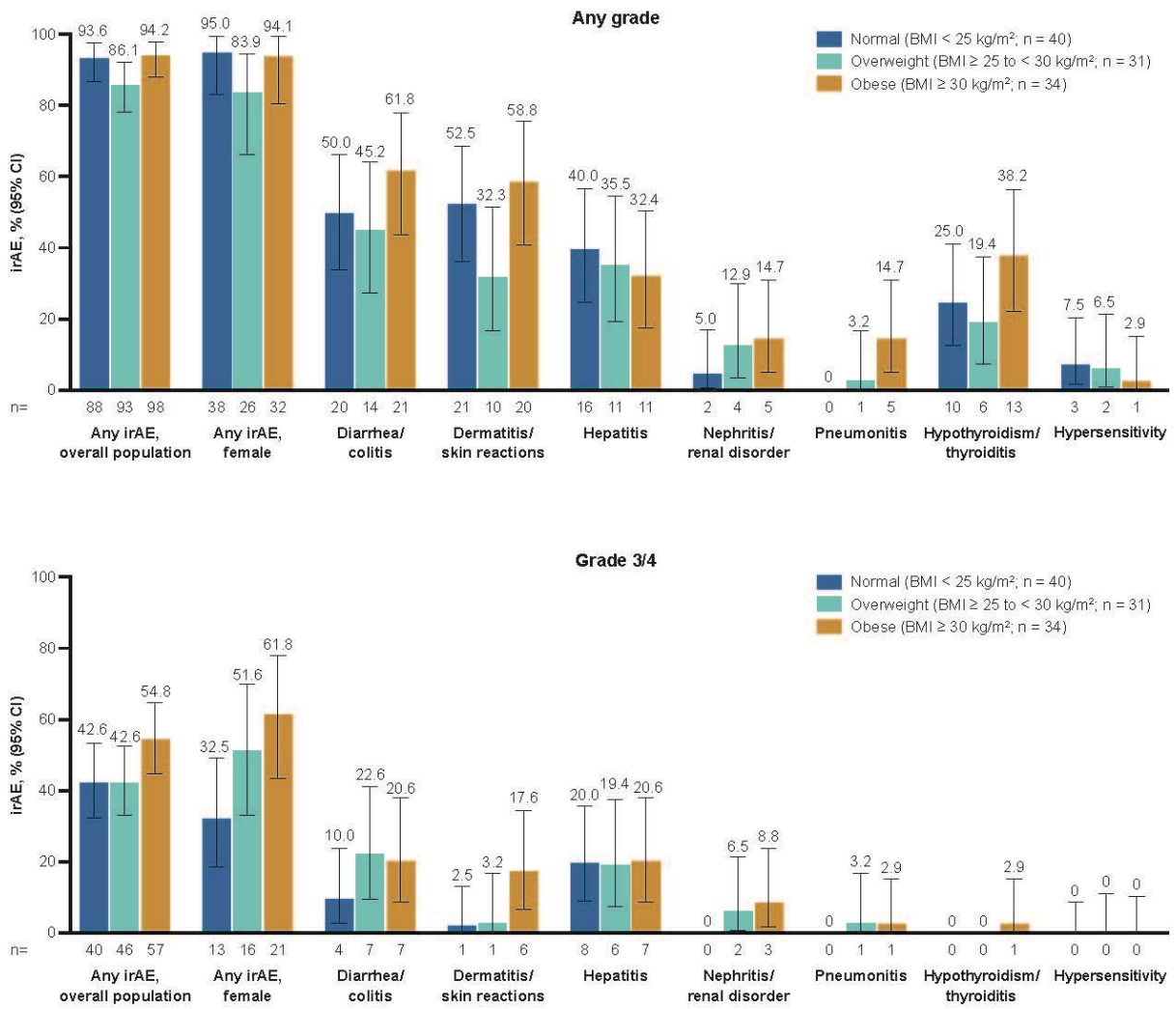


eFigure 10. Incidence of Individual Any-Grade (Top) and Grade 3 or 4 irAEs (Bottom) by BMI in (A) Male and (B) Female Patients in the NIVO1 + IPI3 Cohort

BMI, body mass index; CI, confidence interval; irAE, immune-related adverse event; IPI3, ipilimumab 3 mg/kg; NIVO1, nivolumab 1 mg/kg.

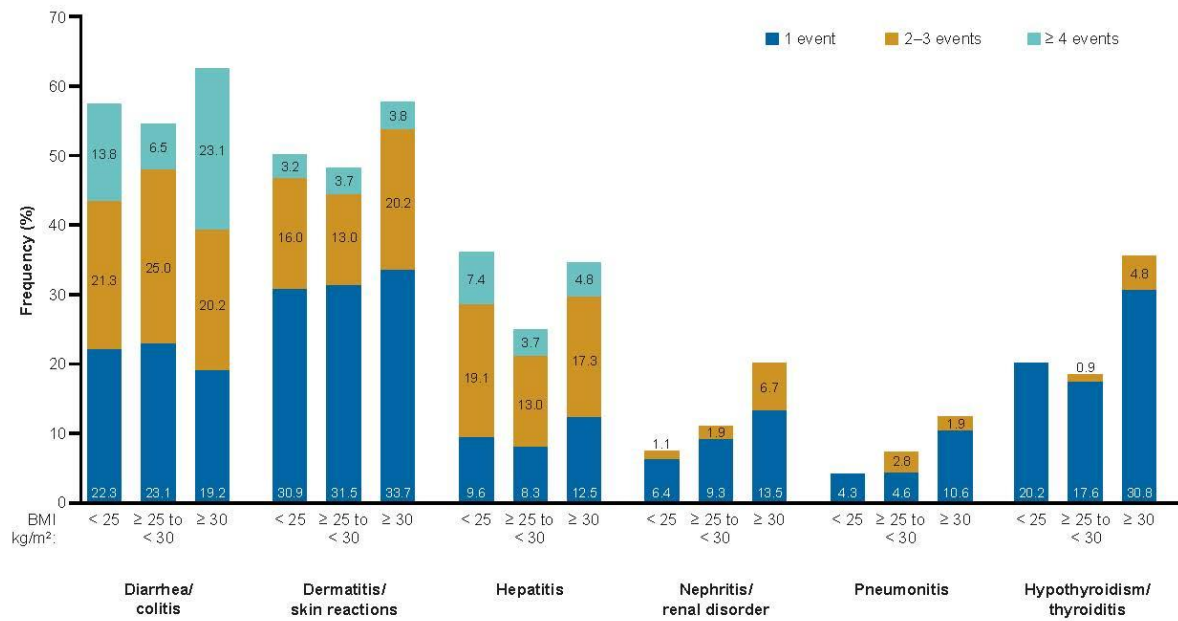


B



eFigure 11. Frequency of Individual Any-Grade irAEs by BMI in the NIVO1 + IPI3 Cohort

BMI, body mass index; irAE, immune-related adverse event; IPI3, ipilimumab 3 mg/kg; NIVO1, nivolumab 1 mg/kg.



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