

Supplementary Table 1. Summary of Grade 3 or 4 AE

Study (Publication Year)	All (%)	CNS-Related (%)	Details of Non-CNS-Related AEs	Details of CNS-Related AEs
ICI monotherapy				
Weber et al. (2011) (5)	-	2/12 (16.7)	-	-
Margolin et al. (2012) (6)	-	2/72 (2.8)	-	-
Queirolo et al. (2014)* (1)	15/145 (10.3)	5/145 (3.4)	Liver toxicity (n = 4), diarrhea (n = 2), nausea (n = 1), vomiting (n = 1), asthenia (n = 1)	Headache (n = 1), confusion (n = 1)
Long et al. (2018) (2)	6/41 (14.6)	2/41 (4.9)	Hepatitis (n = 2), increased amylase (n = 1), increased ALP or γ -GT (n = 1)	Headache (n = 1), radionecrosis (n = 1)
Kluger et al. (2019) [†] (7)	-	1/23 (4.3)	-	Cognitive dysfunction (n = 1)
ICI combined with radiotherapy				
Anderson et al. (2017) (8)	1/21 (4.8)	1/21 (4.8)	None	Perilesional edema (n = 1)
Nardin et al. (2018) (9)	-	3/25 (12.0)	-	Radionecrosis (n = 3)
Trommer-Nestler et al. (2018) (3)	0/13 (0)	0/13 (0)	None	None
ICI combination therapy				
Long et al. (2018) (2)	22/35 (62.9)	2/35 (5.7)	Diarrhea or colitis (n = 7), hepatitis (n = 7), rash (n = 4), increased ALT or AST (n = 2), increased lipase (n = 2), hypophysitis or hypopituitarism (n = 2), nausea or vomiting (n = 1), increased amylase (n = 1), increased ALP or γ -GT (n = 1), fatigue (n = 1), pneumonitis (n = 1), pulmonary edema (n = 1), nephritis (n = 1), increased creatinine phosphokinase (n = 1), decreased neutrophil (n = 1)	Headache (n = 1), radionecrosis (n = 1)
Tawbi et al. (2018) (4)	56/94 (59.6)	7/94 (7.4)	Increased ALT level (n = 15), increased AST level (n = 14), increased lipase level (n = 8), maculopapular rash (n = 7), colitis (n = 7), diarrhea (n = 6), increased amylase level (n = 6), hypophysitis (n = 5), fatigue (n = 4), headache (n = 3), hyperthyroidism (n = 3), nausea (n = 2), vomiting (n = 2), pneumonitis (n = 2), rash (n = 2), hypothyroidism (n = 1), decreased appetite (n = 1), anemia (n = 1), abdominal pain (n = 1), adrenal insufficiency (n = 1), increased blood bilirubin level (n = 1), hyponatremia (n = 1)	Headache (n = 3), brain edema (n = 2), intracranial hemorrhage (n = 1), peripheral neuropathy (n = 1), syncope (n = 1)
Tawbi et al. (2019) (10)	10/18 (55.6)	3/18 (16.7)	-	-

*Only details of treatment-related AEs were reported, [†]Per-patient incidence rate of grade 3 or 4 AEs was not available because only number of cases of each grade 3 or 4 AEs were reported. AE = adverse event, ALP = alkaline phosphatase, ALT = alanine transaminase, AST = aspartate transaminase, CNS = central nervous system, GT = glutamyl transferase, ICI = immune checkpoint inhibitor