Summary table of included studies in review

Author, year	Country	Study design	N patients, type	Outcomes
Chang 1998 (1)	United States	Cohort	1074, MM	Site, MM; head and neck=55.4%, female genital=18.0%, anorectal=23.8%; urinary tract=2.8%
			595, MMHN (84836 melanoma cases total)	Age, MM; 70-79=28.5%, ⩾80=20.5%, mean =67.0
				Ethnicity, MM; African-American or Hispanic=8.8%, white non-Hispanic=85.5%
				Sex, MM; male=36.4%, female MM=63.5% (due to female genital MM)
Cui 2022 (2)	China	Cohort	1814, MM	Proposed a novel TNM staging system for mucosal melanoma inclusive of all anatomical sites. The proposed staging system significantly correlated with OS (P<0.001). No comparative analysis was performed with MMHN staged via the AJCC7 or AJCC8 staging system.
Mallone 2012 (3)	Europeb	Cohort	2091, MM	Crude incidence=2.6 per million
				1-yr OS=71.0%, 5-yr OS=32.1%
				Site, MM; head and neck=40.6%, female genital tract=36.3%, anorectal=18.5%
				Age, MM, rate per million; 15-24=0.07, 25-64=1.43, ⩾65=11.59
Jethanamest 2011 (4)	United States	Cohort	815, MMHN	Site; nasal cavity=49.1%, paranasal sinuses=23.1%, oral cavity=18.8%, nasopharynx=5.5%
				Ethnicity; White=87.9%, Asian or Pacific Islander=7.7%, Black=4.3%, American Indian/Alaska Native=0.2%
				Sex; male=46.1% men, female=53.9%
				3-yr OS=37.2%, 5-yr OS=25.2%, 10-yr OS=12.2%, mean OS=58.3 mo
				3-yr DSS=44.4%, 5-yr DSS=34.4%, 10-yr DSS=19.3%, mean DSS=87.9 mo
				Prognostic factors for MMHN=age >70 (OS: HR 2.65, 95% CI 2.37–2.98; DSS: HR 1.57, 95% CI 1.44–1.75); tumour size 2-4cm (OS: HR 1.43, 95%CI 1.13–1.82; DSS: HR 1.56, 95%CI 1.48–1.64); tumour size >4cm (OS: HR 1.49, 95%CI 1.14–1.75; DSS: 1.59, 95%CI 1.15–2.17); N1 at presentation (OS: HR 1.59, 95% CI 1.22–2.08; DSS: HR 1.59, 95% CI 1.16–2.13); and M1 at presentation (OS: HR 1.75, 95% CI 1.33–2.27; DSS: HR 1.92, 95% CI 1.43–2.63).
Schmidt 2017 (6)	United States	Cohort	1368, MMHN	Clinical tumour stage cT4b (P<0.001) and clinical nodal stage cN1 (P<0.001) and cNX (P=0.004) are independent predictors of worse OS on multivariate analysis.
Heppt 2017 (7)	Germany	Cohort	444, MM	Site; head and neck=37.2%, female genital tract=30.4%, anorectal region=21.8%
				Local relapse=32.4%, most commonly in MMHN group (P=0.016)

				Prognostic factors or disease progression=male gender (P=0.047), advanced tumour stage (P=0.001), nodal disease (P=0.001) and incomplete resection status (P=0.001)
Chan 2012 (10)	China	Cohort	35, MMHN	Age; median=66, range 27-89
				Sex; male:female=1.5:1
				Nodal involvement at presentation; oral cavity MM vs MMSN, 50% vs 10%, P=0.038
				1-yr OS=65.7%, 5-yr OS=22.9%, mean OS=50 mo, median OS=26 mo
				Median OS: stage I=39 mo, stage II=10 mo, stage III=16 mo
Lian 2017 (13)	China	Cohort	706, MM	Site; lower GI tract=26.5%, nasal cavity and paranasal sinuses=23.0%, gynaecological sites=22.5%, oral cavity=15.0%, urological=5.0%, upper GI tract=5%, other=3.0%
				Age; median=55, range 17-86
				Sex; male=37%, female=63%
				Metastasis on first presentation; regional lymph nodes=21.5%, liver=18.5%, lung=21.0%, distant nodes=9.0%
				Oral cavity MM had higher incidence of regional node metastasis (31.7% versus 19.8%, P=0.009) and lung metastasis (32.5% versus 18.5%, P=0.007) as compared to other primary MM.
Temmermand 2022 (14)	United States, Europe (20 countries)	Cohort	1294, MMSN; 359 (United States), 1294 (Europe)	5-yr OS, Europe=25.4%, United States=29.7%
				Europe: Sex; male=44%, female=56%. Age ⩾65=70%
				United States: Sex; male=45%;, female=55%. Age ⩾65=71%
				Most common subsite=nasal cavity (Europe, 83.4%; United States, 65.2%) and maxillary sinus (Europe, 7.3%; United States, 15.9%)
McLaughlin 2005 (15)	United States	Cross-sectional	1806, MM	MM=1.4% of all melanoma
			559, MMHN	Site, MM; nasal cavity=14.11%, accessory sinuses=7.8%, oral cavity=9.1%, anorectal=16.6%, genital tract=43.0%
				Age-adjusted incidence, MM, rate per million; nasal cavity=0.4 male, 0.3 female, accessory sinuses=0.2 male, 0.2 female, oral cavity=0.3 male, 0.2 female
				White/black incidence rate ratio; cutaneous melanoma=16.5 male, 16.0 female, MM=2.3 male, 1.9 female

Jangard 2013 (17)	Sweden	Cohort	186, MMSN	Age; median=72, range=31-93
				DSS; median=21 mo, 5-yr DSS=20.4%
				AJCC7 T stage; T3=62.4%, T4a=26.3%, T4b=1.6%, unknown=9.7%
				AJCC7 prognostic stage; stage I=83.9%, stage II=2.2%, stage III=4.3%, unknown=9.7%
				Sex; male=45%; female=55%
				DSS; median=21 mo (male=16.8 mo, female=30.5 mo)
				Increase in age-standardised incidence of MMSN per million from 1960-1964 to 1995=200; female=0.54 to 1.08, male=0.25 to 0.67
Youssef 2017 (18)	Australia	Cross-sectional	353, MMHN	Sex, male=45.3%, female=54.7%
				Site; nasal cavity=60.3%, paranasal sinuses=17.8%, nasopharynx=3.4%, oral cavity=15.0%, oropharynx=3.4%
				Total percentage change in age-standardised incidence rates: sinonasal=29.4%, non-sinonasal=24.8%; male=35.8%; female-24.5%
Holmstrom 1991 (19)	United Kingdom	Case report	3, MMSN	Three cases of malignant melanoma of the nasal cavity described, as well as the patients' history of exposure to formaldehyde (including duration and frequency of exposure, protection used, exposure other carcinogens).
Aguas 2009 (20)	Argentina (international for literature review)	Cohort and literature review	10 + 177 (literature review), oral MM	Cohort study: Sex; male:female =1:1
				Age; mean=67.5 yrs, range=30-88 yrs
				Micro-trauma by dentures found in 60% of patients
				No relationship with tobacco use
				Literature review: Sex; female=46.9%, male=53.1%
				Age; mean=59.2 yrs, range=16-91 yrs
Marcus 2012 (21)	United States	Cross-sectional	45, MMHN	Sex, male=47.6%, female=52.4%
				Site, nasal cavity=52.4%, paranasal sinuses=19.7%, oral cavity=17.3%, oropharynx=2.9%, nasopharynx=4.4%, parotid gland=2.9%

				Increased incidence of MMHN in the United States from 1987 to 2009; APC 2.4%, P<0.01. While non-nasal cavity MM remained stable, nasal cavity MM saw a substantial increase in incidence (APC 2.7%, P<0.01)
				Highest rate of increase observed in white females aged 55-84 (APC 5.11%, P=0.01)
Altieri 2017 (22)	United States	Cross-sectional	1,919, MM (13,289 melanoma cases in total)	MM=1.3% of all melanomas
				MM of all melanomas in non-Hispanic whites=1.1%, non-Hispanic blacks=9.4%, Hispanics=4.0%, Asian/Pacific Islander=14.8%, other=0.3%
				Site, MM; genitourinary=39.1%, sinonasal=23.8%, anorectal=18.2%, oral cavity=9.5%, other=9.3%.
				MM at presentation; localised=45.6%, regional=25.9%, remote=18.6%
				Compared to non-Hispanic whites (12.6%), a greater proportion of racial minorities presented with regional or distant melanoma (Hispanic=21.0%; non-Hispanic blacks=34.1%; Asian/Pacific Islander=28.6%; non-Hispanic American Indian/Alaska native=18.6%).
Chi 2011 (23)	China	Cohort	118, MM (522 melanoma cases in total)	MM=22.6% of all melanomas
				Median OS=3.58 yrs, 5-yr OS=26.8%
				Median DFS=17.0 mo
Qian 2021 (25)	United States	Cohort	4,592, MM (381,035 melanoma cases in total)	MM of all melanoma in non-Hispanic whites=0.9%, Hispanic=3.6%, non-Hispanic blacks=10.1%, Asian/Pacific Islander=11.2%, non-Hispanic American Indian/Alaska native=2.8%
				No significant worsening in racial disparity in DSS (Hispanic, P=0.69; non-Hispanic blacks, P=0.27; Asian/Pacific Islander, P=0.61; non-Hispanic American Indian/Alaska native, P=0.49)
				Compared to non-Hispanic whites (12.6%), a greater proportion of racial minorities presented with regional or distant melanoma (Hispanic=21.0%, non-Hispanic blacks=34.1%, Asian/Pacific Islander=28.6%, non-Hispanic American Indian/Alaska native=18.6%)
Moya-Plana 2019 (31)	France	Cohort	314, MMHN; prognostic analysis only conducted on surgery/M0 group (n=199)	Tumour stage (P=0.0145; P=0.0095) and AJCC7 prognostic stage (P=0.005; P=0.0053) were associated with OS and PFS respectively in univariate analyses. Only the AJCC7 prognostic stage (P=0.0047; P=0.00126) was linked to OS and PFS respectively in multivariate analysis
				Nodal stage was not associated with OS and PFS in univariate or multivariate analysis
Moya-Plana 2019 (32)	France	Cohort	96, MMHN	Both the AJCC7 and AJCC 7th edition staging system for nasal cavity, paranasal sinuses, and oral cavity malignancies correlated with OS, PFS, and DMFS. Defining new stages (mmT3A and mmT3B) by combining both TNM staging systems enabled more accurate risk stratification (P<0.001)

Flukes 2020 (33)	United States	Cohort	61, MMSN	The AJCC7 prognostic stage (P<0.001) and tumour stage (P=0.004) were both predictive of DMFS
				However, the AJCC7 prognostic stage groupings were not predictive of LPFS (P=0.011), OS (P=0.09), or DSS (P=0.21). Tumour stage was also not predictive of LPFS (P=0.38), OS (P=0.07), or DSS (P=0.17)
				Meanwhile, mean tumour volume was predictive of LPFS (P=0.03), DMFS (P=0.002), and OS (P=0.02), and was a better predictor than AJCC7 and tumour stage
Gal 2011 (34)	United States	Cohort	304, MMSN	Prognostic stage groups using either the 6th or the 7th edition of the AJCC staging system for sinonasal melanoma was significantly associated with survival (P<0.0001)
				As compared to the AJCC 6th edition site-specific staging, the AJCC7 provides improved delineation of stage IV disease (P<0.0001)
Koivunen 2012 (35)	Finland	Cohort	50, MMSN	The AJCC7 was significantly correlated with OS according to tumour stage (P=0.028) and prognostic stage (P=0.02)
				Tumour extension to the sphenoid sinus had a significant negative impact on survival (P=0.03), and retained significance after multivariate analysis considering tumour stage (P=0.01)
Michel 2014 (36)	France	Cohort	35, MMSN	AJCC7 prognostic stages IVb (P=0.000) and IVc (P=0.012) were significantly associated with decreased OS, but the classification did not seem to be significantly correlated with RFS
				The AJCC classification for carcinoma of the nasal cavity and sinuses demonstrated significantly worse OS (P=0.012) and DFS (P=0.041) for MMSN classified as T1/T2 versus T3/T4
Prinzen 2019 (37)	Germany	Cohort	50, MMHN	DSS (P=0.081, P=0.098), DMFS (P=0.212, P=0.214), and DFS (P=0.132, P=0.109) were not significantly associated with AJCC7 prognostic stage (III versus IVa) or tumour stage (T3 versus T4a) respectively
Houette 2016 (38)	France	Cohort	18, MMSN	AJCC7 prognostic stage groupings was not significantly correlated with OS (P=0.108).
				The AJCC 6th edition for nasal cavity and paranasal sinuses demonstrated significant correlation with OS (P=0.0476)
Xu 2021 (39)	China	Cohort	262, MMHN	The AJCC8 tumour stage was significantly correlated with OS in multivariate analysis (P<0.001). The AJCC8 tumour stage and nodal stage were independent prognostic factors for DMFS (tumour stage, P<0.001; nodal stage, P=0.037), DFS (tumour stage, P=0.001; nodal stage, P=0.003), and local regional relapse free survival (tumour stage, P=0.015; nodal stage, P=0.022).
Lechner 2022 (41)	United States; Italy; Spain; Czech Republic; United	Cohort	505, MMSN	AJCC8 tumour stage (P=0.007) and metastasis stage (P=0.031) was significantly correlated with OS on univariate analysis, but lost significance on multivariable analysis (tumour stage, P=0.923; metastasis stage, P=0.086). AJCC8 nodal stage was not significantly associated with OS in univariate analysis (P=0.224).

	Kingdom; Ireland			
				AJCC8 tumour stage (P=0.468), nodal stage (P=0.122), and metastasis stage (P=0.674) were not significantly correlated with DFS.
				A modified tumour staging system, where T3 with sinus involvement has been combined with T4a, had a strong prognostic value (P<0.001).
Torabi 2019 (42)	United States	Cohort	432, T3-4a N0M0 MMHN (MMSN =353, non-MMSN =79)	The AJCC8 tumour stage (T3 versus T4a) significantly correlated with OS for MMSN (P=0.004), but did not demonstrate significant correlation with OS for non-MMSN (P=0.313). 3-yr OS was comparable between the T3 (53.6%) and T4a (42.7%) cohort in the non-MMSN group.
Dimitriou 2022 (46)	International (Australia, Europe, United States, Asia)	Cohort (comparative, cc)	545, MM	Treatments: IMT(aPD-1)± Surgery±RT, n=348; IMT(aPD-1±aCTLA4)±Surgery ±RT, n=197
				Response rate, IMT(aPD-1)±Surgery±RT; 29%, IMT(aPD-1±aCTLA4)±Surgery ±RT; 31%
				Median PFS; IMT(aPD-1)±Surgery±RT; 5 mo, IMT(aPD-1±aCTLA4)±Surgery ±RT; 4 mo
				Median survival; IMT(aPD-1)±Surgery±RT; 19 mo, IMT(aPD-1±aCTLA4)±Surgery ±RT; 21 mo
				3-yr survival; IMT(aPD-1)±Surgery±RT;33%, IMT(aPD-1±aCTLA4)±Surgery ±RT; 30%
Lu 2022 (52)	United States	Cohort	288, MMHN	Proposed a novel nomogram prediction model with five independent risk predictors (age, location, AJCC7 tumour stage, nodal stage, and surgery) for MMHN. This nomogram demonstrated superior predictive performance over the AJCC7 staging system in both internal (C-index OS, 0.764 versus 0.683; DSS, 0.783 versus 0.705) and external (C-index OS, 0.808 versus 0.644; DSS, 0.823 versus 0.648) validation cohorts for OS and DSS.
Farber 2019 (54)	United States	Cohort (comparative, cc)	686, MMSN	Treatments: Open surgery, n=240, matched; Endoscopic Surgery, n=240, matched
				1-yr survival, Open; 77.41%, Endoscopic; 78.1%
				3-yr survival, Open;43.6%, Endoscopic; 50.5%
				5-yr survival, Open; 34.7%, Endoscopic; 38.0%
				Length of stay; Open; 3.0 days, Endoscopic; 1.4 days
				30-day readmission Open; 0.0%, Endoscopic; 4.8%
				30-day mortality, Open; 1.3%, Endoscopic; 0.0%
				90-day mortality, Open; 3.2%, Endoscopic; 0.7%

Swegal 2014 (55)	United States	Cohort (comparative, cc)	25, MMSN	Treatments: Open surgery, n=13; Endoscopic surgery, n=12
				Median survival; Open; 1.9 yrs, Endoscopic; 1.2 yrs
				Disease-free survival; Open; 1.9 yrs, Endoscopic; 1.2 yrs
				2-yr survival, Open; 63%, Endoscopic; 44%
				Length of stay; Open; 3.6 days, Endoscopic; 3.8 days
				Intraoperative bleed, Open; 1 pt (8%), Endoscopic; 2 patients (17%)
				CSF leak, Open; 2 patients (15%), Endoscopic; 3 patients (35%)
				Operative deaths, Open; 0, Endoscopic; 0
				Local recurrence, Open; 3 patients (23%), Endoscopic; 1 pt (8%)
				Distant metastasis, Open; 2 pt (15%), End; 3 patients (25%)
				Multi site recurrences, Open; 2 patients (15%), Endoscopic; 3 patients (25%)
Lombardi 2016 (56)	Italy	Cohort (comparative, cc)	58, MMSN	Treatments: Endoscopic (n=29)+RT (n=7)
				Endoscopic+Transnasal craniectomy (n=6)+RT (n=4)
				Cranioendoscopic ±RT, n=4
				External±RT, n=7
				5-yr survival, Endoscopic; 84.6%, Endoscopic+Transnasal; 66.7%, Cranioendoscopic/External; 54.6%
				3-yr survival, Endoscopic; 59.9%, Endoscopic+Transnasal; NR, Cranioendoscopic/External; 13.6%
				5-yr survival, Endoscopic; 38.0%, Endoscopic+Transnasal; NR, Cranioendoscopic/External; 13.6%
				Relapse, Endoscopic; 65%, Endoscopic+Transnasal; 50%, Cranioendoscopic/External;91%
				HR (Death), MVA, Endoscopic+Transnasal vs Endoscopic; 2.6, Endoscopic+Transnasal/Cranioendoscopic/External vs Endoscopic; 2.1, Cranioendoscopic/External vs Endoscopic; 1.9
				HR(Further disease), MVA, Endoscopic+Transnasal vs Endoscopic; 1.4, Endoscopic+Transnasal/Cranioendoscopic/External vs Endoscopic; 1.6, Cranioendoscopic/External vs Endo;1.5
Hur 2019 (57)	United States	Systematic review with meta-analysis of non-randomised	510, MMSN	Treatments: Open Surgery, n=253; Endoscopic Surgery, n=232; Combined approach, n=25

		comparative studies		
				HR(death), Endoscopic vs Open; 0.68 (95%CI 0.49, 0.95)
				HR(Further disease), Endoscopic vs Open; 0.59 (95%CI 0.28, 1.25)
Penel 2006 (59)	France	Cohort (non-comparative)	20, MMHN	Treatments: Surgery alone, n=14; Surgery+RT, n=4; Debulk Surgery+RT+Chemotherapy, n=1; No curative intended treatment, n=1
				Median survival; 23 mo
				2-yr survival; 68%
				5-yr survival; 43%
				Local recurrence; 5 patients (20%)
				Nodal recurrence; 7 patients (35%)
				Distant metastases; 6 patients (30%)
				Metachronous cancers; 3 patients (15%)
				Deaths; 9 patients (45%)
Lee 1994 (60)	United States	Cohort (comparative, cc for local control)	35, MMHN	Treatments: Radical surgery alone, n=9; Radical surgery+RT, n=4; Radical surgery+Chemotherapy, n=2; Local surgery alone, n=6; Local surgery+RT, n=1; Local surgery+Chemotherapy, n=4; RT alone, n=10; RT+Chemotherapy, n=1; Chemotherapy alone, n=2
				Median survival; 54 mo
				5-yr survival; 45%
				Local control; 7 patients (Radical surgery;3/9 patients, Radical surgery+RT 1/4 patients, Radical surgery+Chemotherapy 2/2 patients, Local surgery 1/6 patients)
				Distant metastasis; 20 patients
				Median DFS duration; 54 mo
Manolidis 1997 (64)	Canada	Cohort (comparative) + literature summary	14 + 484 (literature review; 14 studies) MMHN	Treatments: Surgery (total), n=9; Surgery (subtotal), n=1; Surgery+RT, n=2; RT alone, n=1; No treatment, n=1
				Median survival; All 17.5 mo. SurgeryT; med 30 mo, SurgeryST;;4mo. Surgery+RT; 19, 42 mo, RT; 4 mo, No treatment; 10 mo
				Recurrences; All; 6/14 patients. SurgeryT; 4/9 patients, Surgery+RT; 2/2 pt
				Local recurrence; 42% (6/14 patients)

				Regional metastasis; 7% (1/14 patients)
				Dead of disease; All; 7/14 patients. Surgery (total); 4/9 patients, Surgery (subtotal); 1/1 patients, RT; 1/1 patients, No treatment; 1/1 patients
				Alive without disease; All; 3/14 patients. Surgery (total); 1/9 patients, Surgery+RT; 2/2 patients
				5-yr survival; All; 14% (2/14 patients)
				Literature summary; Local recurrences; 53% (258/484 patients)
				Salvage therapy-Local control; 25% (49/196 patients)
				Local recurrence+distant metastases; 73% (90/123 patients)
Wu 2014 (67)	China	Cohort (comparative, cc)	254, oral MM	Treatments: Radical surgery+Chemotherapy, n=38; Radical surgery+Chemotherapy+ND, n= 216)
				5-yr survival; 30.5%. Radical surgery+Chemotherapy; 48%, Radical surgery+Chemotherapy+ND; 21%
Starek 2006 (68)	Czech Republic	Case report	2, oral MM	Treatments: Surgery+SNB+ND, n=1
				Surgery+SNB+ND+Chemotherapy, n=1
				Disease free at follow-up; Surgeryery+SNB+Nd(-ve); 1pt at 19 mo
				Further disease; Surgeryery+SNB+ ND(+ve); 1 pt at 3 mo (+chemotherapy)
Baptista 2008 (69)	Italy	Case report	1, MMSN	Treatment: SNB+Radioguided surgery+ND
				Disease free at 1-yr; SNB+Surgery+ND(-ve); 1/1 pt
Grant-Freemantle 2021 (71)	Ireland	Systematic review and meta-analysis of non-randomised comparative studies	2,489, MMHN (22 studies)	Treatments: Surgery alone, n=1039; Surgery+RT, n=1276; RT alone, n=174
				HR(Death by 5-yrs), All;, Surgery+RT vs Surgery alone; 0.93(95%Ci 0.87, 0.98)
				Sinonasal; Surgery+RT vs Surgery alone; 0.93 (95%CI 0.78, 1.10)
				All; RT alone vs Surgery alone; 1.2 (95%CI 1.03, 1.33)
				HR(Local recurrence at 5 yr); All; Surgery+RT vs Surgery alone;0.63 (95%CI 0.48, 0.82)
				Sinonasal; Surgery+RT vs Surgery; 0.80 (95%CI 0.48, 1.33)
				HR(Distant metastasis at 5 yrs); All; Surgery+RT vs Surgery alone; 0.95 (95%CI 0.76, 1.17)

Koto 2017 (72)	Japan	Cohort (comparative, cc)	260, MMHN, Stage-M0, inoperable	Treatments: RT alone, n=105; RT+Chemotherapy, n=155
				HR(Death); RT alone vs RT+Chemotherapy; 1.61 (1.07, 2.45)
				2-yr survival; All 69%. RT alone; 62%, RT+Chemotherapy; 76%
				Local recurrence; 15% (38/260 patients)
				2-yr local recurrence; 84%
				5-yr local recurrence; 72%
				Died of disease; 39% (102/260 patients)
				Distant mets as initial recurrence; 37% (96/260 patients)
				Regional recurrence as initial recurrence; 12% (32/260 patients)
				5-yr survival;45%
				2-yr PFS; 40%, 5-yr PFS; 27%
Demizu 2014 (73)	Japan	Cohort, (comparative, cc)	62, MMHN	Treatments: Proton RT alone, n=26; CaRT alone, n=23; Surgery/Chemotherapy/ProtonRT, n=8; Surgery/Chemotherapy/CarRT, n=6
				1-yr survival, All; 93%, ProtonRT± other modes; 91%, CaRT±other modes; 96%
				2-yr survival; All; 61%, ProtonRT± other modes; 58%, CaRT±other modes; 62%
				1-yr PFS, All; 63%, ProtonRT± other modes; 64%, CaRT±other modes; 63%
				2-yr PFS; All; 31%, ProtonRT± other modes; 30%, CaRT±other modes; 41%
				1-yr local control; All; 93%, ProtonRT± other modes; 92%, CaRT±other modes; 95%
				2-yr local control, All; 78%, ProtonRT± other modes; 83%,CaRT±other modes; 59%
				Local recurrence; ProtonRT± other modes; 5/34, CaRT±other modes; 3/29
				Distant metastasis; ProtonRT± other modes; 18/34, CaRT±other modes; 11/29
				⩾Grade 3 acute toxicity; All; 29%, ⩾Grade 3 late toxicity, All; 8%
				Treatment related deaths, All; 0
Zenda 2016 (74)	Japan	Cohort (non-comparative)	32, MMSN	Treatment: Proton beam therapy
				1-yr local control; 76%
				3-yr survival; 46%
				3-yr PFS; 36%
				Recurrence; 23 patients

				Local recurrence; 4 patients
				Lymph node and distant metastases; 4 patients
				Distant metastasis; 9 patients
				Grade 3 acute toxicity; 5 patients
Fuji 2014 (75)	Japan	Cohort (non-comparative)	20, MMSN	Treatment: Proton beam RT± Chemotherapy
				3-yr survival; 68%, 5-yr survival; 54%
				3-yr PFS; 60%, 5-yr PFS; 52%
				Local recurrence; 4 patients
				Distant metastases; 7 patients
				3-yr local control; 70%
				5-yr local control; 62%
				Grade 3/4 acute toxicities; 7 patients
				Grade 3/4 late toxicities; 3 patients
Benlyazid 2010 (77)	France	Cohort (comparative, cc)	160, MMHN	Treatments: Surgery, n=82; Surgery+RT, n=78
				5-yr survival; All; 38%, Surgery; 46%, Surgery+RT; 28%
				Median survival; 37.5 mo
				HR(Death); Surgery+RT vs Surgery; 1.08 (95%CI 0.62, 1.84) MVA
				HR(Relapse) Surgery+RT vs Surgery; 0.85 (95%CI 0.51, 1.40) MVA
				Relapse; 104 patients (65%)
				Local recurrence; 53 patients (33%)
				Regional metastases; 11 patients (7%)
				Distant metastases; 40 patients (25%)
				5-yr distant metastases rate; Surgery; 18%, Surgery+RT; 41%
				HR(Distant metastases as 1st event) Surgery+RT vs Surgery; 4.17 (95% CI 1.5, 11.6)
				Median RFS; 16.6 mo
				5-yr RFS, All; 28%, Surgery; 27%, Surgery+RT; 29%
Kelly 2011 (78)	United States	Cohort (non-comparative)	54, anorectal MM	Treatment: Surgery+RT

				5-yr survival; 30%, 2 yr-survival; 59%
				5-yr local control; 82%
				Disease relapse; 72%
				Melanoma death; 69%
				Distant metastases by 2 yrs; 59%, by 5 yrs; 72%
Tchelebi 2016 (79)	United States	Cohort (comparative, cc)	63, rectal MM	Treatments: Surgery alone, n=45; Surgery+RT, n=18
				Disease free survival; Surgery; 27 mo, Surgery+RT; 28 mo
				Median survival, All;22 mo
Plavc 2016 (80)	Slovenia	Cohort (comparative, cc)	61, MMHN	Treatments: Open Surgery ±RT±Chemotherapy, n=24; Endo Surgery±RT±Chemotherapy, n=15; No Surgery±RT±Chemotherapy, n=22
				2-yr survival, All; 43%
				5-yr survival, All; 18%
				Any further disease; All 50%
				2-yr locoregional control; Any Surgery+RT; 84%, Any Surgery, no RT; 43%
				5-yr locoregional control, Any Surgery+RT; 67%, Any Surgery, no RT; 18%
Li 2015 (81)	China	Systematic review and meta-analysis (non-randomised, comparative, cc)	1,593, MMHN (12 studies)	Treaments: Surgery alone, n=356+a; Surgery+RT, n=363+a
				HR(Death), Surgery alone vs Surgery+RT; 1.07 (95% CI 0.95, 1.20)
				HR(Local recurrence), Surgery +RT vs Surgery; 0.55 (95%CI 0.32, 0.93)
Wada 2004 (83)	Japan	Cohort (non-comparative)	31, MMHN	Treatments: Surgery+RT±Chemotherapy±IMT, n=10; RT alone ±Chemotherapy±IMT, n=21
				Local recurrence; All; 42%
				Cervical lymph node metastasis, All; 16%
				Distant metastases, All; 36%
				Melanoma deaths, at 1 -yr, All; 27%, at 3-yrs, All; 67%
D'Angelo 2017 (47)	United States	Meta-analysis (4 RCTs, 1 non-	86, MM	Treatments: IMT(aPD-1-Nivolumab), n=86; IMT(aCTLA4-Ipilimumab+aPD-1-Nivolumab), n=35; IMT(aCTLA4-Ipilimumab), n=36

		randomised, non-comparative)		
				Median PFS, IMT(Nivolumab); 3.0 mo, IMT(Nivolumab+Ipilimumab); 5.9 mo, IMT(Ipilimumab); 2.7 mo
				Response rate, IMT(Nivolumab); 23%, IMT(Nivolumab+Ipilimumab); 37%, IMT(Ipilimumab); 8%
				Grade 3/4 treatment related adverse events, IMT(Nivolumab);8%, IMT(Nivolumab+Ipilimumab); 40%
Hodi 2021 (94)	United states	Cohort (non-comparative)	47, MM (754 melanoma patients in total)	Treatment: IMT (aPD-1-Nivo+aCTLA4-Ipi 12 wks, then Nivo alone, up to 48 wks)
				1-yr survival; 75%
				2-yr survival; 56%
				Deaths; 17/47(36%)
Namikawa 2018 (95)	Japan	Cohort (non-comparative)	12, MM (30 melanoma patients in total)	Treatment: IMT(Nivolumab+Ipilimumab for 6 wks, then Nivolumab)± Surgery±RT
				Response rate; 33% (4/12 patients)
Nakamura 2021 (96)	Japan	Cohort (comparative, cc)	329, MM	Treatments: IMT(aPD-1), n=263; IMT(aPD-1+ aCTLA4), n=66
				Response rate, IMT(aPD-1); 26%, IMT(aPD-1+aCTLA4); 29%
				Median Survival; IMT(aPD-1); 20.4 mo, IMT(aPD-1+aCTLA4); 20.1 mo
				HR(Death), IMT(aPD-1+aCTLA4) vs IMT(aPD-1); 0.89 (95%CI 0.57, 1.38) MVA
				PFS, IMT(aPD-1); 5.9 mo, IMT(aPD-1+aCTLa4); 6.0 mo
				Grade 3+ adverse events; IMT(aPD-1+aCTLA4); 53%, IMT(aPD-1); 17%
Steeb 2021 (100)	Germany	Systematic review and meta-analysis of non-randomised non-comparative studies	167, MM (601 melanoma patients in total)	Treatments: c-KITi(Imatinib), n=70; c-KITi(Nilotinib), n=55; c-KITi(Dasatinib), n=42
				Response rate, All; 14%, c-KITi(Imatinib); 24% c-KIT(Nilotinib); 18%
Lian 2013 (106)	China	RCT	189, MM	Treatments: No treatment, n=63; Interferon, n=63; Chemotherapy (Temozolomide+Cisplatin), n=63
				1-yr local recurrence, No treatment; 24%, Interferon; 15%, Chemotherapy; 5%
				2-yr local recurrence, No treatment; 25%, Interferon; 18%, Chemotherapy; 15%
				1-yr distant metastases, No treatment; 37%, Interferon; 27%, Chemotherapy; 5%

				2-yr distant metastases, No treatment; 41%, Interferon; 35%, Chemotherapy; 23%
				1-yr nodal/combination site recurrences, No treatment;30%, Interferon; 25%, Chemotherapy; 7%
				2-yr nodal/combination site recurrences, No treatment;33%, Interferon; 35%, Chemotherapy; 21%
				Median survival, No treatment; 21.2 mo, Interferon; 40.4 mo, Chemotherapy; 48.7 mo
				Median RFS, No treatment; 5.4 mo, Interferon; 9.4 mo, Chemotherapy; 20.8 mo
				Grade 3/5 adverse events, No treatment; 2%, Interferon; 37%, Chemotherapy; 48%
Cui 2021 (112)	China	Cohort (non-comparative)	21, MM	Treatment: IMT(aPD-1-Toripalimab+VEGFRi-axitinib)+Surgery+IMT(aPD-1-Toripalimab)
				Grade 3/4 adverse events; 24%
				Response rate; 29%
Ho 2022 (113)	United States	Cohort (comparative, cc)	36, MM	Treatments: IMT(aCTLA4+PD-1) ± Surgery, n=28; IMT(aPD-1) ± Surgery, n=7; IMT(aCTLA4) ± Surgery, n=1
				1-yr survival, IMT(aCTLa4+aPD-1)± Surgery±RT; ~70%, IMT(aPD-1 or aCTLA4) ±Surgery±RT; ~47%
				2-yr survival, All; 64%, 3 yr survival, All; 55%
				2-yr event free survival; 36%, 3-yr event free survival; 29%
				Grade 3+ adverse events, All; 39%
				Response rate; 47%
Kim 2019 (114)	Korea	Cohort (comparative, cc)	23, MM	Treatments: RT+Surgery, n=6; RT, no surgery, n=5; RT+IMT(aPD-1)± Surgery, n=12; IMT(aPD1), no surgery, n=6; IMT(aCTLA4), no surgery, n=2
				1-yr local control, All; 90%, RT±Surgery; 57%, RT+IMT±Surgery; 94%, IMT-no Surgery; 25%
				2-yr survival, All; 56%, RT±Surgery; 43%, RT+IMT±Surgery; 86%, IMT-no Surgery; 66%
				Response rate, RT±Surgery; 53%, RT+IMT± Surgery;53%
				1-yr PFS, RT±Surgery; 7%, RT+IMT±Surgery; 0%, IMT-no Surgery; 25%
				Grade 3 or 4 adverse events; RT±Surgery; 27% (3/11), RT+IMT±Surgery; 0%
Kato 2019 (115)	Japan	Cohort (non-comparative)	7, MM (10 MM and acral melanoma patients in total)	Treatment: RT + IMT (aPD-1)
				Response rate; 57% (4/7 patients)
				Median PFS; 14 mo
Hanaoka 2020 (116)	Japan	Cohort (non-comparative)	10, MMSN	Treatments: RT+IMT (aPD-1-Nivo), n=1; RT+IMT (aPD-1-Pembro), n=9

				Median PFS; 7.5 mo
				6-mo PFS rate; 60%
				Local recurrences; 10% (1/10 patients)
				Deaths; 40% (4/10)
Sheng 2019 (117)	China	Cohort (non-comparative)	33, MM	Treatments: IMT(aPD-1-Toripalimib, + VEGFRi-Axitinib)
				Response rate; 57%
				Median PFS; 7.5 mo
				Adverse events; 39% (13/33 patients)
				Death from melanoma; 33% (11/33 patients)

aCTLA4, anti-T lymphocyte associated protein; APC, annual percentage change; aPD-1, anti-programmed cell death protein; AJCC7, American Joint Committee on Cancer 7th edition staging system for head and neck mucosal melanoma; CaRT, carbon ion radiation therapy; cc, concurrent controls; CI, confidence interval; c-KITi, c-KIT (receptor tyrosine kinase) inhibitors; CSF, cerebrospinal fluid; DFS, disease free survival; DMFS, distant metastasis-free survival; DSS, disease specific survival; HR, hazard ratio; IMT, immunotherapy; LPFS, local progression free survival; MM, mucosal melanoma; MMHN, mucosal melanoma of the head and neck; MMSN, mucosal melanoma arising from the sinonasal region; mo, months; MVA, multivariable analyses; ND, node dissection; NR, not reached; OS, overall survival; PFS, progression free survival; VEGFRi, vascular epithelial growth factor receptor inhibitor; RFS, recurrence free survival; RCT, randomised controlled trial; RT, radiation therapy; SNB, sentinel node biopsy; wks, weeks; yr, years.

[a]Studies did not report exact number of patients in treatment groups. Number depicted equates to the least possible number in the group (+ indicating unknown extra patients).