

**Supplementary table 1.** Study characteristics and quality assessment

TKI studied	First author (year of publication)	Inclusion criteria	type of study	Number of patients	Number of patients with familial MTC	RECIST criteria used?	CTCAE criteria used?	Duration SD stated?	Adequate follow-up? (median $\geq 12$ mo)	< 10% lost to follow-up within 1 year	Consecutive patients or Random sample	Independent or central review of tumor response?	PD according to RECIST in previous year as inclusion criterion?
axitinib	Capdevila, 2017 [38]	Progressive disease	retrospective	13	nr	yes	yes	yes	yes	yes	na	na	no
axitinib	Locati, 2014 [28]	Locally advanced or metastatic	phase II trial	6	nr	yes	yes	yes	yes	yes	na	na	yes
axitinib	Cohen, 2008 [15]	Locally advanced or metastatic	phase II	11	nr	yes	yes	na	yes	na	na	no	no
cabozantinib	Elisei, 2013 [9]	Progressive disease	double-blind, phase III	330	45	yes	yes	no	yes	yes	na	yes	yes
cabozantinib	Kurzrock, 2011 [24]	Locally advanced or metastatic	phase I, dose-escalation study	37	3	yes	yes	yes	yes	na	na	no	no
dovitinib	Lim, 2015 [33]	Progressive disease	open label, multicenter, phase II	12	nr	yes	yes	yes	yes	na	na	na	yes
imatinib	Gross, 2006 [12]	Locally advanced or metastatic	non-randomized open label, phase II study	6	1	no	yes	no	no	yes	na	no	no
imatinib	de Groot, 2007[13]	Locally advanced or metastatic	phase II	15	4	yes	yes	yes	yes	no	na	no	no
Imatinib	Frank-Raue, 2007 [14]	Progressive disease	open-label study	9	1	yes	yes	yes	yes	yes	na	no	no
lenvatinib	Schlumberger, 2016 [36]	Progressive disease	phase II	59	nr	yes	yes	yes	yes	yes	na	na	yes
motesanib	Schlumberger, 2009 [16]	Progressive disease and/or symptomatic	phase II, open label, single arm, multicenter, prospective	91	nr	yes	yes	yes	yes	yes	na	yes (independent)	no

pazopanib	Bible, 2014 [27]	Progressive disease	Multicenter phase II trial	35	0	yes	yes	no	yes	yes	na	na	yes
sorafenib	Castroneves, 2016 [35]	Progressive disease	retrospective	13	3	yes	yes	yes	yes	yes	na	na	no
sorafenib	Ito, 2017 [39]	Locally advanced or metastatic	phase II	8	nr	yes	yes	yes	yes	yes	na	na	no
sorafenib	Benekli, 2015 [30]	Locally advanced or metastatic	retrospective	16	0	yes	yes	no	yes	na	na	na	yes
sorafenib	Frank-Raue, 2011 [22]	Progressive disease	off label	5	0	yes	yes	yes	Yes	no	na	no	no
sorafenib	Lam, 2010 [18]	Locally advanced or metastatic	phase II prospective	21	5	yes	yes	yes	yes	na	na	no	no
sorafenib	Capdevila, 2012 [25]	Progressive disease	retrospective	15	nr	yes	yes	yes	yes	na	yes	no	yes
sorafenib	Ahmed, 2011 [21]	Progressive disease	observational	15	3	yes	no	yes	yes	na	na	no	no
sorafenib n=6,	Chrisoulidou, 2015 [32] (subgroup 1)	Progressive disease	retrospective	6	nr	no	yes	no	no	yes	na	na	no
sorafenib, sunitinib	Massicotte 2014 [29] (subgroup1)	Locally advanced or metastatic	Retrospective [outside trial]	7	nr	yes	yes	yes	yes	yes	na	yes	na
sorefenib+tipifarnib	Hong, 2011 [23]	Locally advanced or metastatic	phase 1	13	1	yes	no	yes	yes	yes	na	no	no
sunitinib	Ravaud, 2017 [40]	Progressive disease	phase II	26	nr	yes	yes	yes	yes	no	na	na	yes
sunitinib	Carr, 2010 [17]	Locally advanced or metastatic	phase II prospective	7	nr	yes	yes	yes	yes	na	na	no	no
vandetanib	Werner, 2015 [34]	Locally advanced or metastatic	retrospective	21	3	yes	no	yes	yes	yes	na	na	no
vandetanib	Tiedje, 2016 [37]	Progressive disease	retrospective	10	0	no	yes	yes	yes	yes	na	na	no
vandetanib	Uchino, 2017 [41]	Locally advanced or	Phase I/II	14	nr	yes	yes	yes	yes	yes	na	na	no

		metastatic											
vandetanib	Chougnat 2015 [31]	Locally advanced or metastatic	retrospective	60	6	yes	na	yes	yes	na	na	yes	na
vandetanib	Kraft 2018 [42]	Locally advanced or metastatic	phase I/II	17	17	yes	yes	yes	yes	yes	na	na	yes
vandetanib	NCT 01496313 [11] [subgroup 1]	Progressive disease and/or symptomatic	phase IV	41	nr	yes	na	yes	yes	yes	na	na	yes
vandetanib	NCT 01496313 [11] (subgroup 2)	Progressive disease and/or symptomatic	phase IV	40	nr	yes	na	yes	yes	yes	na	na	yes
vandetanib	Robinson, 2010 [19]	Locally advanced or metastatic	Open label single arm	19	19	yes	yes	yes	na	yes (none)	na	no	no
vandetanib	Wells, 2010 [20]	Locally advanced or metastatic	Open label, phase II	30	30	yes	yes	yes	yes	yes (none)	na	yes (central)	no
vandetanib	Wells, 2012 [26]	Locally advanced or metastatic	phase III, RCT	231	23	yes	yes	no	yes	yes	yes	yes	no
vandetanib	Chrisoulidou, 2015 [32] (subgroup 2)	Locally advanced or metastatic	retrospective	4	nr	no	yes	no	no	yes	na	na	no
vandetanib	Massicotte 2014 [29] (subgroup 2)	Locally advanced or metastatic	retrospective [outside trial]	11	nr	yes	yes	yes	yes	yes	na	yes	na

nr: not reported; na: not available