**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 ≥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 ΙΙ 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 metastatic | Phase I/II | 14 | nr | yes | yes | yes | yes | yes | na | na | no |
| vandetanib | Chougnet 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 | Οpen label single arm | 19 | 19 | yes | yes | yes | na | yes (none) | na | no | no |
| vandetanib | Wells, 2010 [20] | Locally advanced or metastatic | Οpen 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