**Table III: Main RTK inhibitors assessed in carcinoma and associated-bone metastases**

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| --- | --- | --- | --- |
| **RTK inhibitor** | **Molecular targets** | **Investigations, Patients, doses** | **References** |
| Imatinib mesylate (Gleevec) | PDFGR, c-KIT | Pre-clinical *in vivo* assessment  Phase I, 28 patients (MeCRPC) 400 mg/day of gleevec, combination with zoledronic acid  Phase I, 21 patients (MeCRPC) 600 mg/day of gleevec, combination with docetaxel  Phase II, 144 patients (MeCRPC) docetaxel combined with 600 mg/kg/day of gleevec or placebo | 103, 104  105  106  107 |
| Dasatinib | Src (inhibition of RTK-transduced signalling pathways)  c-KIT, EPHA2, PDGFR-β | Pre-clinical *in vivo* assessment  Phase I, 16 patients with solid tumours, 100 mg of dasatinib, increased by increments of 50 mg up to a maximum dose of 250 mg for 4 weeks  Phase II, 47 patients (MeCRPC), 700 or 70 mg/day  Phase III, 1522 patients (MeCRPC), 100 mg/day of dasatinib combined with docetaxel | 108-109  110  111, 112  113 |
| Sunitinib | FLT3, PDGFR, VEGFR, cFMS | Pre-clinical *in vivo* assessment  Phase II, 36 patients (MeCRPC), 50 mg/day of sunitinib 4-weeks on followed by 2-weeks off per cycle up to a maximum of eight cycles prior docetaxel  Phase III, 873 patients (docetaxel-refractory MeCPRC), 37.5 mg/day of sunitinib with or without prednisolone  Phase II, 60 patients (Her-2+ advanced breast carcinoma) 37.5 mg/day of sunitinib combined with trastuzumab  223 patients (clear-cell renal cell carcinoma with bone metastases), 50 mg/day, 4 weeks on, 2 weeks off  209 patients (renal clear carcinoma, 76 with bone metastases) 50 mg/day, in 6-week cycles (4 weeks on, 2 weeks off) combined with bisphosphonates | 114  115  116  117  118  119 |
| Sorafenib | RET, VEGFR | Pre-clinical *in vivo* assessment  Phase II, 22 patients (MeAIPC), 400 mg/day of sorafenib in 28-day cycles  Case report, bone metastases bilateral carcinoma, 400 mg/day of sorafenib | 120  121, 122  123 |
| Cabozantinib | c-MET, VEGFR2 | Pre-clinical *in vitro* assessment  Pre-clinical *in vivo* assessment  Phase I, 11 patients (MeCRPC), 60, 40 or 20 mg of cabozantinib  Phase II, 144 patients (MeCRPC), 40 or 100 mg/day of sorafenib until disease progression or unacceptable toxicity  Phase II, 171 patients (CRPC), 100 mg/day of cabozantinib vs placebo  Phase II, 65 patients (MeCRPC) 100 mg/day or 40 mg/day of cabozantinib. | 124-128  129-131  132  133  134  135 |
| Tivantinib | c-MET | Pre-clinical *in vivo* assessment | 136, 137 |
| Cediranib | VEGFR | Pre-clinical *in vivo* assessment  Phase I, 26 patients (hormone refractory prostate cancer), escalating doses of 1 to 30 mg/day of cediranib | 138  139 |
| Vatalanib | VEGFR | Pre-clinical *in vivo* assessment | 140 |
| Erlotinib | EGFR | Pre-clinical *in vivo* assessment  Phase I, 29 patients (MeCRPC), 150 mg of erlotinib daily until disease progression  Phase II, 22 patients (AIPC), docetaxel 60 mg/m2 IV on day 1 and erlotinib 150 mg/day (days 1-21) | 141  142  143 |
| Gefinilib | EGFR | Pre-clinical *in vivo* assessment  Phase II, 38 patients (MeCRPC), 500 mg/day of gefitinib  Phase II, 82 patients (hormone-refractory prostate cancer)  Phase II, 37 patients, 250 mg/day of gefitinib combined with docetaxel  Phase I/II, 31 patients (stage IV HER-2+ metastatic breast cancer), 250 mg/day of gefitinib on days 2–14 combined with trastuzumab and docetaxel  Phase II, 148 patients (hormone-positive metastatic breast cancer), 500 mg/day of gefitinib with either anastrozole or fulvestrant  Phase II, more than 200 patients (hormone receptor-positive metastatic breast cancer), 250mg/day of gefitinib with or without tamoxifen  Phase II, 174 patients (hormone receptor-positive metastatic breast cancer), anastrozole combined with 250 mg/day of gefinitib or placebo | 144-146  147  148  149  150  151  152  153 |
| Lapatinib | EGFR, HER-2 | Phase II, 29 patients (CRPC), 1,500 mg/day of lapatinib  Phase II, 24 patients (Advanced HER2-positive Breast Cancer), 1,250 mg/day of lapatinib and pegylated liposomal doxorubicin  Phase II, 23 patients (hormonally untreated advanced prostate cancer), 1,500 mg/day of lapatinib | 154  155  156 |
| Vandetanib | EGFR, VEGFR, RET | Phase II, 39 patients (CPRC), 300 mg/day of vandetanib combined with bicalutamide vs bicalutamide  Phase II, 61 patients (hormone-receptor-positive metastatic breast cancer), fulvestran with either 100 mg/day of vandetanib or placebo | 157  158 |
| Dovotinib | FGFR, VEGFR | Pre-clinical *in vitro and in vivo* assessment | 159, 160 |

(The list of references and clinical trials of this table is not exhaustive). MeCPRC: metastastic castration-resistant prostate cancer including bone metastasis; MeAIPC: androgen-independent prostate cancer with bone metastases