**Table II: Main RTK inhibitors assessed in bone sarcomas**

|  |  |  |  |
| --- | --- | --- | --- |
| **RTK inhibitor** | **Molecular targets** | **Investigations, Patients, doses** | **References** |
| Imatinib mesylate (Gleevec) | PDFGR, c-KIT | Pre-clinical *in vitro* and *in vivo* assessment  Phase II, 189 sarcoma patients (13 ES, 27 OS), 100 to 300 mg/day of gleevec , orally twice a day according the body-surface area  Phase II, 7 ES, 400 mg of gleevec, orally twice daily prescribed with a cycle length of 28 days.  Phase II, 70 patients, 12 ES, 26 OS, 440 mg/m2/day of gleevec  Pre-clinical *in vitro* assessment (drug combinations) | 60, 69  71  72  73  74 |
| Dasatinib | Src (inhibition of RTK-transduced signalling pathways)  c-KIT, EPHA2, PDGF-β | Pre-clinical *in vitro* assessment  Pre-clinical *in vivo* assessment  Phase I, 39 patients (2 ES, 1 OS) of 50, 65, 85, and 110 mg/m2/dose of dasatinib, administered orally twice daily for 28 days | 75  76  77 |
| Sunitinib | FLT3, PDGFR, VEGFR, cFMS | Pre-clinical *in vitro* and *in vivo* assessment  Phase I, 33 patients (2 ES, 2 OS), from 15 and 20 mg/m2/days of sunitinib with dose escalation | 78  79 |
| Pazotinib | VEGFR, PDGFR, c-KIT | Pre-clinical *in vitro* and *in vivo* assessment  Phase I, 51 patients (3 ES, 4OS) (tablet formulation), pazotinib administered once daily in 28-day cycles at four dose levels (275 to 600 mg/m2) ; powder suspension initiated at 50% of the maximum-tolerated dose for the intact tablet  Pre-clinical *in vitro* and *in vivo* assessment (combination with Topotecan) | 80  81  82 |
| Sorafenib | RET, VEGFR | Pre-clinical *in vitro* and *in vivo* assessment  Phase I, 11 patients (2 OS), from 90 mg/m2 to 110 mg/m2 ofsorafenib twice daily  Phase II, 35 OS, 400 mg of sorafenib twice daily until progression or unacceptable toxicity | 83  84  85 |

OS: osteosarcoma; ES: Ewing’s sarcoma