Supplementary Figure S1: c-Met dependency of the used cell lines.
A, Cell lysates were electrophoresed and immunoblotted with the indicated antibodies.
B, Cells were infected with the scramble shRNA (scRNA) or MET shRNAs (MET KD 345 and MET KD 4571). After infection for 24 hr, media was changed. Then, cells were further incubated for 72 hr. Viable cells were assessed by CellTiter-Glo assay and were graphed relative to untreated cells. Experiments were carried out in triplicate. The average values and SDs are shown. C, 48 hr after shRNA infection, cells were collected and cell lysates were analyzed with the indicated antibodies. “sc” in shRNA indicates scramble shRNA, and “345” or “4571” indicates MET shRNA.
Supplementary Figure S2: Antitumor activity of tivantinib on c-Met-non-addicted tumor cells.

A-C, The Met amplified SNU-5 and HER2 amplified SKBR3 and BT-474 cells were treated with the increasing concentrations of tivantinib (A), PHA-665752 (B) or crizotinib (C) for 72 hr. Viable cells were assessed by CellTiter-Glo assay and were graphed relative to untreated cells. Experiments were carried out in sextuplet. The average values and SDs are shown.
Supplementary Figure S3:
Change in c-Met signaling after exposure to Tivantinib or Crizotinib for 24 h.
MKN45, EBC1, A549 and SNU638 cells were treated with the indicated concentrations of tivantinib or crizotinib for 24 hr. Cell lysates were electrophoresed and immunoblotted with the indicated antibodies. Repeated experiments gave similar results.
**Supplementary Figure S4:**

Tivantinib did not inhibit c-MET activation in A549 cells. A549 cells were treated with the indicated concentrations of tivantinib or crizotinib for 1 or 24 hr. 10 minutes before collecting cells, 100 ng/mL of recombinant human HGF (rhHGF) were treated for 10 min. Cell lysates were electrophoresed and immunoblottedted with the indicated antibodies.
Supplementary Figure S5:
Apoptosis induction by Tivantinib long time treatment in EBC-1 and MKN45 cells.
A, EBC-1 cells were treated with vehicle control, Tivantinib (1 μM or 3 μM), Vincristine (1 μM) or crizotinib (1 μM). After 72 hr, cells were stained with FITC labeled Annexin-V and PI, and analyzed by flow cytometer. B, The percentage of cells undergoing apoptosis is shown as bar graph for each treatment condition. C, MKN45 cells were treated with vehicle control, Tivantinib (1 μM or 3 μM), Vincristine (1 μM) or crizotinib (1 μM). After 48 hr, cells were stained with FITC-labeled Annexin-V and PI, and analyzed by flow cytometry. The percentage of cells undergoing apoptosis is shown as bar graph for each treatment condition.
Supplementary Figure S6: Tivantinib induces G2/M arrest as similar as tubulin inhibitor vincristine. A, B, H460 or A549 cells were treated with indicated concentration of tivantinib, vincristine, PHA-665752 or crizotinib for 24 hr. Cells were trypsinized, fixed and stained with propidium iodide, and the cell cycle was analyzed by flow cytometry. The histogram shows cell distribution versus DNA content.
**Supplementary Figure S7:**

**Growth inhibition against a panel of 39 human cancer cell lines by vincristine.**

The mean graph was produced by computer processing of the 50% growth inhibition (GI50) values as described under “Materials and Methods”. The x-axis represents the logarithm of difference between the mean of GI50 values for 39 cell lines and the GI50 value for each cell line. MG-MID, the mean of log GI50 values for 39 cell lines; Delta, the logarithm of difference between the MG-MID and the log GI50 of the most sensitive cell line; Range, the logarithm of difference between the log GI50 of the most resistant cell line and the log GI50 of the most sensitive cell line. Quantification of the GI50 value was represented as the mean of four different experiments. Br, breast; CNS, central nervous system; Co, colon; Lu, lung; Me, melanoma; Ov, ovarian; Re, renal; St, stomach; xPg, prostate.
Supplementary Figure S8:
Tivantinib treatment led to a loss of microtubules in EBC1 cells.
Tivantinib (10 μM, 16 hr) or Vincristine (100 nM, 16 hr) treated EBC1 cells were fixed and stained with Alexa488 labeled anti α-tubulin antibody, Alexa 568 conjugated phalloidin (F-actin) or Hoechst33342. White scale bar indicate 20 μm.
Supplementary Figure S9:
Tivantinib short time treatment led to a loss of microtubules in A549 and EBC-1 cells. Tivantinib (1 µM, 2 hr) or Vincristine (100 nM, 2 hr) treated A549 (A) or EBC-1 (B) cells were fixed and stained with Alexa488 labeled anti α-tubulin antibody, Alexa 568 conjugated phalloidin (F-actin) or Hoechst33342. White scale bar indicate 20 µm.
Supplementary Figure S10: Tivantinib inhibits tubulin polymerization in a dose dependent manner. Tubulin polymerization assay were performed with or without indicated concentration of tivantinib or vincristine. Experiments were carried out in triplicate. The average values and SEMs are shown.