Title of the Article:
Prospective randomized double-blind multicentre phase II study comparing gemcitabine and cisplatin plus sorafenib chemotherapy with gemcitabine and cisplatin plus placebo in locally advanced and/or metastasized urothelial cancer: SUSE (AUO-AB 31/05).

Abstract:
To evaluate the efficacy and safety of gemcitabine and cisplatin in combination with sorafenib, a tyrosine-kinase inhibitor, compared with chemotherapy alone as first-line treatment in advanced urothelial cancer. The study was a randomized phase II trial. Its primary aim was to show an improvement in progression-free survival (PFS) of 4.5 months by adding sorafenib to conventional chemotherapy. Secondary objectives were objective response rate (ORR), overall survival (OS) and toxicity. The patients included in the trial had histologically confirmed locally advanced and/or metastatic urothelial cancer of the bladder or upper urinary tract. Chemotherapy with gemcitabine (1250 mg/qm on days 1 and 8) and cisplatin (70 mg/qm on day 1) repeated every 21 days, was administered to all patients in a double-blind randomization of additional sorafenib (400 mg twice daily) vs placebo (two tablets twice daily) on days 3-21. Treatment continued until progression or unacceptable toxicity, the maximum
number of cycles was limited to eight. The response assessment was repeated after every two cycles. Between October 2006 and October 2010, 98 of 132 planned patients were recruited. Nine patients were ineligible. The final analysis included 40 patients in the sorafenib and 49 patients in the placebo arm. There were no significant differences between the two arms concerning ORR (sorafenib: complete response [CR] 12.5%, partial response [PR] 40%; placebo: CR 12%, PR 35%), median PFS (sorafenib: 6.3 months, placebo: 6.1 months) or OS (sorafenib: 11.3 months, placebo: 10.6 months). Toxicity was moderately higher in the sorafenib arm. Diarrhoea occurred significantly more often in the sorafenib arm and hand-foot syndrome occurred only in the sorafenib arm. The study was closed prematurely because of slow recruitment. Although the addition of sorafenib to standard chemotherapy showed acceptable toxicity, the trial failed to show a 4.5 months improvement in PFS.