BrUOG L301

IND EXEMPT 124745

BrUOG L301: Xofigo Following Frontline-Line Chemotherapy For Patients With Non-Small Cell Lung Cancer and Bone Metastases

17.0 STATISTICS

This protocol will evaluate the effect of Ra 223 on patients with NSCLC who had stable to responding disease after completion of first line chemotherapy. The primary end point is the proportion of patients who experience their first symptomatic skeletal event (including pathologic bone fracture, spinal cord compression, need for surgical intervention for a bone metastasis, and time to external beam radiotherapy) during study treatment. A second primary endpoint is to evaluate the reduction of SSEs after 4 cycles of treatment (approximately 4 months) following the first Ra 223. The control is a historic experimental arm consisting of 257 patients (the majority having advanced NSCLC) from a study by Rosen *et al* [7,8] who received zoledronic acid 4mg q 3 weeks with concomitant antineoplastic therapy. Approximately 40% patients experienced their first symptomatic skeletal event by 4 months in that study.

We hypothesize that the addition of Ra 233 to standard chemotherapy would reduce the proportion of patients with first symptomatic skeletal event at 4 months by half, i.e., to 20% compared to historic controls who received zoledronic acid. Using Fisher's exact test, we calculated a sample size of 36 patients to detect this 20% difference in the proportion of patients having their first symptomatic skeletal event at 4 months with power of 75% and two sided α error probability of 0.1.

Progression-free survival (PFS) and overall survival (OS): PFS and OS will be determined from the time of study entry.

Time to symptomatic skeletal events: Will be determined from the time of study entry.