Lung cancer I
Monday 21 September 2009, 11:00–13:00

20LBA LATE BREAKING ABSTRACT

A double-blind, randomized study of denosumab versus zoledronic acid for the treatment of bone metastases in patients with advanced cancer (excluding breast and prostate cancer) or multiple myeloma

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Bone metastases (BM) lead to frequent debilitating complications in advanced cancer, resulting in bone destruction and skeletal-related events (SRE). The osteoclastic component of BM is a primary cause for the development of SREs. Inhibition of RANKL, a central mediator of osteoclast activation and differentiation, may delay or prevent SREs. We assessed the efficacy and safety of denosumab, an investigative fully human monoclonal antibody against RANKL, for the treatment of BM in patients with solid tumors (excluding breast and prostate) or multiple myeloma (MM) in a phase 3 study. A total of 1776 eligible adult patients who were naïve to intravenous bisphosphonates were randomized 1:1 in a double-blind, double-dummy design to receive subcutaneous denosumab 120 mg or intravenous zoledronic acid (ZA) 4 mg or adjusted for creatinine clearance every 4 weeks. Patients were stratified by tumor type (non-small cell lung cancer, MM, or other), among other variables. All patients were strongly recommended to take daily supplemental calcium ($\geqslant$500 mg) and vitamin D ($\geqslant$400 IU). This study is sponsored by Amgen Inc. (ClinicalTrials.gov NCT00330759). Treatment groups were generally balanced for baseline characteristics, except for gender, age category, and visceral metastases (lung). Denosumab delayed the time to first on-study SRE (pathologic fracture, radiation therapy or surgery to bone, or spinal cord compression) and was noninferior to ZA (hazard ratio [HR]: 0.84; 95% CI: 0.71−0.98; P = 0.0007). The median time to first on-study SRE was 20.6 months for denosumab and 16.3 months for ZA. Although numerically greater, the delay in time to first on-study SRE with denosumab was not superior to ZA based upon the statistical testing strategy (adjusted P = 0.06). Time to first-and-subsequent SRE was also numerically greater but not statistically superior for denosumab compared with ZA (HR: 0.90; 95% CI: 0.77−1.04; P = 0.14). Adverse events (96% denosumab, 96% ZA) and serious AEs (63% denosumab, 66% ZA) were consistent with what has previously been reported for these two agents. Overall survival was balanced between the groups (HR: 0.95; 95% CI: 0.83−1.08; P = 0.43). Osteonecrosis of the jaw was seen in 10 patients (1.1%) on denosumab and 11 patients (1.3%) on ZA (P = 1.0). In conclusion, denosumab was noninferior to ZA in delaying the time to first on-study SRE in patients with advanced solid tumors and MM. This study continues as an open-label study with denosumab.

Lung cancer II
Tuesday 22 September 2009, 09:00–11:30

21LBA LATE BREAKING ABSTRACT

Assessing the value of preoperative chemotherapy in early-stage non-small cell lung cancer: mature data and prognostic factors analysis of a Phase III randomized trial of surgery alone vs preoperative Paclitaxel/Carboplatin (PC) vs postoperative PC. Final NATCH data. A Spanish Lung Cancer Group Trial

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Background: 5-year survival of NSCLC patients (p) is poor even in early stages I and II with R0 surgery. Addition of chemotherapy (CT) to surgery could improve outcomes. Postoperative CT is considered standard of care for resected stages II and III and remains controversial in stage I. Preoperative CT is feasible with a better compliance and a trend to improve outcomes compared to surgery alone.
Methods and Study objectives: Phase III multicenter open prospective trial to assess if 3 cycles of preo or postoperative CT improves 5-year disease-free survival (DFS) compared to surgery alone in early stage NSCLC clinically staged. Secondary objectives: toxicity profile, CT compliance, overall survival and prognostic and predictive value of molecular markers. P with clinical stage IA (>2 cm), IB, II and T3N1M0 stratified by tumor size and age were randomly assigned to Surgery alone (S), Preop CT followed by S (PreCT) or S followed by CT (PostCT). CT: 3 cycles Carboplatin AUC 6 + Paclitaxel 200 mg/m2 q3wk. Statistical design to demonstrate 15% increase in 5-y-DFS with 0.05 significance (log-rank).
Results: From April 2000 to March 2007 624 p were included in 42 european centers. 212 allocated to S, 211 allocated to PostCT and 201 allocated to PreCT. 374 events for DFS has been registered for the final analysis. Patient's characteristics well balanced between arms. Thoracothomy performed in 200 p (95%) in S; 201 p (96%) in PostCT and 181 p (91%) in PreCT. Radiologic response (PreCT group) 53% (CR 9%), 32% SD, 5% PD. Pathologic CR was found in 19 p (9.5%). CT compliance: 97% in PreCT vs 66% in PostCT (p < 0.0001 Fisher's exact test). Toxicity was mild without differences in G3−4 for PreCT or PostCT (1 toxic death in each CT arm, <1%). Median 5-y-DFS: 25.1 m in S arm, 26 m in PostCT and 31.5 m in PreCT. Referenced to S arm HR for PostCT 0.96 (0.75–1.22) and 0.92 for PreCT (0.81–1.04). In PreCT group a trend for better DFS in older (>65 y), Stage II-T3N1 and non-pneumonectomy procedure. For T3N1M0 subgroup 5-y-DFS 36.6% with PreCT vs 25% with S alone (HR 0.81; p = 0.07). No differences for overall survival were observed.
Conclusions: In clinical early stage NSCLC p, PreCT showed a trend towards improvement for 5-y-DFS (4.2% absolute increase, p = 0.07). Significant improvement for compliance of PreCT vs Post-CT (97% vs 66%). Improved PreCT effect in clinical stage II-T3N1 subgroup. No significant differences in secondary effects, surgical procedures and post-operative mortality. Analysis of molecular markers are ongoing and could help to better selection of p for PreCT approach.