



MONDAY JULY 4<sup>TH</sup>, 2011

HI FROM AMSTERDAM!

The 14<sup>th</sup> World Lung Cancer Conference kicked off today with some terrific sessions. In addition to improved efficacy, there was a general focus on assessing and improving quality of life. A pivotal trial presented today was the BTOG2 Phase III trial. This trial randomized Stage IV patients to either gemcitabine/cisplatin (80mg/m<sup>2</sup>) vs. gemcitabine/cisplatin (50mg/m<sup>2</sup>) vs. gemcitabine/carboplatin (AUC6 – Wright Method) q3 weekly for 4 cycles (Figure 1). Patients on GC80 and GCb had more grade 3/4 adverse events as compared with GC50. Response rates were significantly different between the two cisplatin containing arms; GC50 23% and GC80 33% (p=0.01; Figure 2). There was no difference between the carboplatin vs. cisplatin arms. Median survival also was similar in GC80 (9.5m) and GCb (10m). The GC50 arm (7.8m) had inferior efficacy. Despite previous meta-analysis (CISCO) suggesting improvements with cisplatin compared to carboplatin when given in third generation combination, this large well conducted RCT clearly shows that carboplatin when given with adequate dosing (AUC=6) provides similar efficacy. In this study there was no significant difference in quality of life between the three arms.

Continuing on QOL theme, the QOL data were presented from PARAMOUNT study. Maintenance pemetrexed significantly improved PFS. Safety analysis showed that long term use of pemetrexed maintenance until disease progression was well tolerated. Resource use corresponded to toxicities typically observed with pemetrexed and overall resource use was low. Patients can tolerate long term maintenance pemetrexed treatment without significant decreases in QOL.

In the Lux-Lung1 trial, patients with metastatic NSCLC were randomized to receive either afatinib with BSC or placebo. There was a 3 fold increase in median PFS (1.1 to 3.3 months) No effect on OS was noted. The results of patient reported symptom and health related quality of life results were presented. Compared to placebo, a significantly higher proportion of afatinib treated patients showed a significant improvement in cough, pain and dyspnoea. Interestingly its effects on cough and dyspnoea relief were more pronounced in patients with worse baseline performance status. There was however more significant diarrhea, sore mouth, dysphagia and loss of appetite with afatinib versus placebo. Overall this trial showed that there was significant improvement in global HRQoL and physical functioning in patients of afatinib+BSC vs. placebo+BSC.

Figure 1: BTOG2 Trial Design

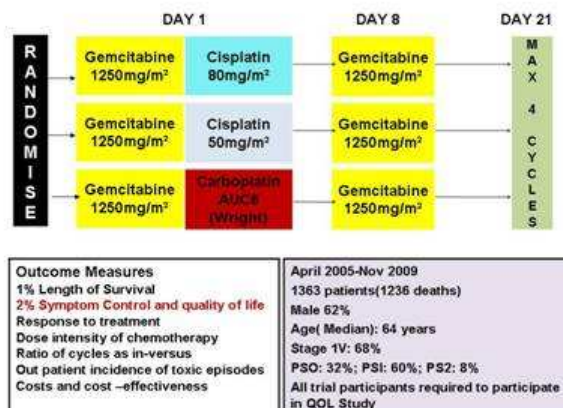
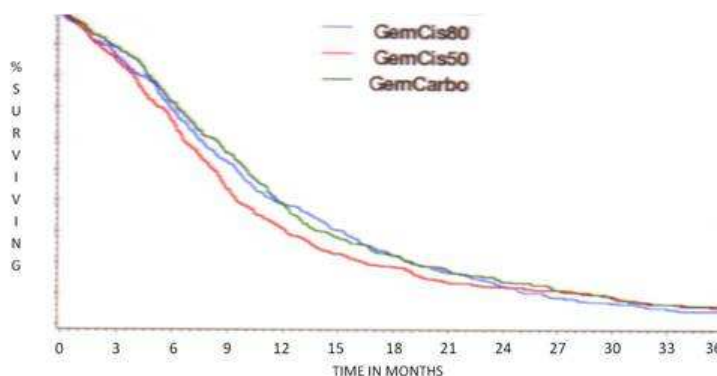


Figure 2: B2GO2 Primary Analysis – Survival Time



Final thoughts...

- It's more important to choose the right dose rather than what platinum to use in the first line treatment of NSCLC. Carboplatin AUC 6 is equal in efficacy to cisplatin 80 mg/m<sup>2</sup>
- Pemetrexed appears to be effective in the maintenance setting even after first line treatment with platinum and pemetrexed, however we need to await OS data before considering this strategy
- The data from the LUX Lung 1 trial highlights that in addition to PFS benefits seen with afatinib, there is also an improvement in lung cancer related symptoms and quality of life

We look forward to sending you our postcard tomorrow which will highlight novel therapies including some data from key EGFR trials.

Have a good night!

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