Phase II, randomized, double-blind placebo-controlled trial of nimotuzumab plus gemcitabine compared with gemcitabine alone in patients (pts) with advanced pancreatic cancer (PC).

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Background: FOLFIRINOX significantly increases survival in metastatic PC compared to gemcitabine, but its use is limited to selected pts, due its high toxicity. In the majority of cases, gemcitabine (gem) remains the mainstay of palliative treatment, although its modest impact on survival and disease progression. The addition of the EGFR tyrosine kinase inhibitor erlotinib prolonged median survival for only 2 weeks. This study was aimed to investigate the effect of adding Nimotuzumab (nimo), an anti-EGFR monoclonal antibody, to first-line gemcitabine, in PC.

Methods: Pts with previously untreated, unresectable, locally-advanced or metastatic PC were randomly assigned to receive gem: 1000 mg/m²/30-min iv once weekly (d1, 8, 15; q28) and nimo: fixed dose of 400 mg once weekly as a 30-min infusion, or placebo, until progression or unacceptable toxicity. Primary endpoint was overall survival (OS) in the intention-to-treat (ITT) population. Secondary endpoints included PFS, safety, objective response rate (ORR), QoL. Results: Between 9/2007-10/2011 a total of 192 pts were randomized (average age 63.6 ± 10 years; 60% male; 69% ECOG PS 0), and 186 were evaluable at the ITT analysis. One-year OS was 19.5 % with gem+placebo and 34.4% with gem+nimo (HR=0.69; p=0.034). Median OS and PFS were 6.0 mo in the gem+placebo group, vs. 8.7 mo in gem+nimo (HR=0.83; p=0.21), and 3.7 vs. 5.4 mo, respectively (HR=0.73; p=0.06). One-year PFS was 9.5 % for gem+placebo, compared with 21.5% for gem+nimo (HR=0.71; p=0.05). Significantly, in pts ≥ 62 years (60% of the population), median OS and PFS were 5.2 mo in the gem+placebo group vs. 8.8 mo in gem+nimo (HR=0.66; p=0.034), and 3.2 in gem+placebo vs. 5.5 mo in gem+nimo group, respectively (HR=0.55; p=0.0096). Nimo was safe and well tolerated, and no grade 3/4 toxicities were observed. Thirteen % of pts experienced grade 1/2 skin toxicity. Conclusions: This randomized study clearly showed that nimo in combination with gem is safe and well tolerated. The 1-year survival rate is significantly improved. Especially pts ≥ 62 years seem to benefit, possibly due to a more aggressive biology in younger pts. Clinical trial information: NCT00561990.