PUBLICATIONS

G. Chiritescu, K. Dumon, C. Verslype, G. Houbiers, M. Peeters, J. Janssens, D. van Daele, S. Laurent, J. Arts, K. Hendrickx, I. Borbath, M. Ferrante1, F.M. Bastin, JC. Goeminne, J-L. van Laethem, E. Vanderstraeten, J. Decaestecker, W. van Vaerenbergh, B. Delhougne, E. Van Cutsem. (2018). Final results of a phase II quality of life (QOL) randomized, cross-over (CO) study with gemcitabine (Gem) and nab-paclitaxel (n-P) in locally advanced or metastatic pancreatic ductal adenocarcinoma (PDAC): QOLINPAC. Annals of Oncology. Volume 29, Supplement 8, October 2018. Poster presentation 740P, ESMO Congress, Munich, Germany, 2018.

Abstract:

Background: QOL parameters may be predictive of treatment efficacy in PDAC.

Methods: Eligible consenting patients (pts) received n-P/Gem or Gem in standard regimens. CO was possible at progression. Monthly EORTC QLQ-C30 v3.0 QOL questionnaires were used. Deterioration-free rate of global health status (GHS) at 3 months (mths) was the primary endpoint. Safety, efficacy and molecular studies on blood were secondary endpoints.

Results: One hundred forty-six pts (125 metastatic), median age 65, were included in 17 hospitals of the Belgian Group of Digestive Oncology network between May 2014 and Nov 2015 and randomized to n-P/Gem (72) or Gem (74); 37 crossed-over. Median duration on treatment was 5mths (0-28). Ninety-nine pts (68%) experienced at least one serious adverse event; 6 events had fatal outcome, one was possibly related to Gem (sepsis). Gastrointestinal toxicity and infections were frequent. Hemolytic uremic syndrome occurred in 5 pts. Overall, 1465 QOL questionnaires were completed; 85%of pts responded to a series of at least three. Deterioration-free rate of GHS at 3 mths was 83% (60/72) with n-P/Gem, 60% (28/47) with Gem alone and 96% (26/27) after CO. Median times to definitive deterioration were 12.8, 8.9 and 12.3 mths respectively. Baseline GHS scores correlated at 0.05 significance level with survival time in the n-P/Gem group. Other QOL indicators showed equivalent patterns. Tumour response was locally assessed in 43% of pts (95%CI 31-55) with n-P/Gem, 19% (95%CI 6-32) with Gem and 24% (95%CI 10-39) in the CO group (p¼0.006) with 2 pts in complete response. Median PFS was 6.8 mths (95%CI 5.5-8.1) in all pts, with 7.4 in n-P/Gem, 7.2 in Gem and 5.4mths in CO (1st progression). Median PFS for 2nd progression in CO was 10.8mths. Overall survival was 11.9 mths (95%CI 10-14) with 10.7, 8.8 and 13mths in the three groups.

Conclusions: Survival was long and response rates significantly higher in pts receiving the combination. Pts receiving n-P/Gem reported better quality of life scores for longer duration compared to pts on Gem alone. QOL analyses and translational studies will be presented at the congress. Academic study with support from Celgene.

Clinical trial identification: EudraCT: 2013-004101-75, NCT02106884.

Legal entity responsible for the study: Academic study governed by the Belgian Group of Digestive Oncology network. Sponsored and coordinated by University Hospitals Leuven.

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G Chiritescu, K Dumon, C Verslype, H Prenen, G Houbiers, M Peeters, J Janssens, D Van Daele, S Laurent, J Arts, K Hendrickx1, I Borbath, M Ferrante, F Bastin, J Goeminne, J Van Laethem, E Vanderstraeten, J Decaestecker, W Van Vaerenbergh, B Delhougne, E Van Cutsem. 2018. Gemcitabine with nab-paclitaxel in patients with locally advanced or metastatic pancreatic ductal adenocarcinoma (PDAC): A quality of life randomized cross-over study (QOLINPAC). Annals of Oncology. Volume 29, Supplement 5, Jul 2018. Oral and poster presentation O-003, ESMO GI Congress, Barcelona, Spain, 2018.

Abstract:

Introduction: Nab-paclitaxel added to standard gemcitabine significantly improves overall survival, progression-free survival and response rates when compared to gemcitabine alone in metastatic PDAC. Baseline quality of life (QOL) indicators such as global health status (GHS) may be predictive for survival in this disease setting, together with clinical variables and tumour markers.

Methods: In an academic multicentric phase II study, patients with locally advanced or metastatic PDAC were randomized to receive gemcitabine 1000mg/m2 alone or with nab-paclitaxel 125mg/m2 in standard schedules. Patients progressing on monotherapy could cross-over to combination. The EORTC QLQ-C30 v. 3.0 questionnaire was applied monthly. Deterioration-free rate of GHS at three months was the primary endpoint. Clinically significant deterioration was considered at first 10-point score decrease from baseline without further improvement. Safety, response rates, progression free and overall survival, exploratory biomarker and hypoxia studies on blood samples were secondary endpoints.

Results: One hundred forty-six consenting patients (21 locally advanced and 125 metastatic) with median age 65 were included in 17 hospitals of the BGDO network between May-2014 and Nov-2015 and randomized to combination (72) versus monotherapy (74). Thirty-seven patients crossed-over. Total cumulative drug exposure to nab-paclitaxel was 73% from planned dose in the combination group and 67% in cross-overs. Median duration on treatment was 5 months (range 0-28), 10 patients being on treatment >18 months. One hundred and eighty-three serious adverse events were reported in 98 unique patients (67%), 51% occurring in the combination group vs 37% in monotherapy and 12% after cross-over. Six had fatal outcome, one was possibly related to gemcitabine (sepsis). Most frequent toxicities were gastrointestinal or infections. Five gemcitabine-related cases of hemolytic uremic syndrome occurred. Overall, 1465 QOL questionnaires were completed, 85% of patients responded to at least three. Unweighted analysis of GHS showed a deterioration-free rate at three months of 83% (60/72) in the combination group, 60% (28/47) in patients on monotherapy at the time of definitive deterioration and 96% (26/27) in cross-overs. Median times to definitive deterioration were 12.8, 8.9 and 12.3 months in combination, monotherapy and crossovers respectively. Baseline GHS scores correlated at 0.05 significance level with survival times in the combination group. Other QOL indicators showed equivalent patterns. Tumour response (locally assessed) was observed in 43% of patients (95%CI_31-55) in combination, 19% (95%CI_6-32) in monotherapy and 24% (95%CI_10-39) in crossover, the difference being statistically significant (p¼0.006). Two patients had complete response. Disease control was observed in 116 patients (79%) for a median duration of 6.8 (0.7-28.1) months. Median progression free survival was 6.8 months (95%CI_5.5-8.1) with 7.4, 7.2 and 5.4 in the three groups. Overall survival was 11.9 months (95%CI_10-14) with 10.7, 8.8 and 13 months respectively.

Conclusion: Median survival was long and response rates significantly higher in combination groups. Patients receiving the combination nab-paclitaxel/gemcitabine seem to report better quality of life scores for longer duration compared to patients on gemcitabine monotherapy. Further QOL analyses and translational studies are ongoing.

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Clinical trial registration: EudraCT 2013-004101-75; NCT02106884.