P-4 Efficacy and safety of sintilimab combined nab-paclitaxel and gemcitabine as first-line treatment for metastatic pancreatic ductal adenocarcinoma (PDAC): A retrospective analysis

J. Wang[1], Y. He[1], H. Lv[1], B. Chen[1], C. Nie[1], W. Xu[1], J. Zhao[1], B. Zhang[2], X. Cheng[2], Q. li[2], S. Tu[2], X. Chen[1]

[1]Affiliated Cancer Hospital of Zhengzhou University/Henan Cancer Hospital, Zhengzhou, China; [2]Renji Hospital of Shanghai Jiaotong University School of Medicine, Shanghai, China

Background: Advanced pancreatic cancer is a devastating disease with a short survival time. Chemotherapy is one of the most important treatments for advanced pancreatic cancer, which has a synergistic mechanism with immunotherapy on the basis of theory. Exploring more effective combination regimens based on immunotherapy is a research hotspot in recent years. We evaluated the efficacy and safety of sintilimab combined with nab-paclitaxel/gemcitabine as first-line treatment to provide new evidence for chemotherapy combined immunotherapy of advanced PDAC.

Methods: This was a retrospective study in patients with advanced PDAC performed from September 20, 2020 to February 10, 2022. Patients who received first-line sintilimab plus nab-paclitaxel/gemcitabine treatment were enrolled. The primary end point was progression free survival (PFS). Secondary end points included objective response rate (ORR), disease control rate (DCR), and safety.

Results: A total of 20 patients were eligible for response assessment. In the general population, complete response (CR) was not observed, 6 patients achieved partial response (PR), 12 patients had stable disease (SD) and 2 patients had progression disease (PD). The ORR and DCR were 6(30%) and 18(90%), respectively. Median PFS was 5.2 months(95%CI:2.916-7.484).The most common grade 3 treatment related AEs (trAEs) were hematological toxicity, however, the incidence is $\leq$10%, anemia(10%), leukopenia(10%), neutropenia(10%), thrombocytopenia(5%).Non-hematological toxicity were hand-foot syndrome(10%) and nausea(10%). Only one patient had grade 4 oral mucositis.

Conclusions: Sintilimab combined with nab-paclitaxel and gemcitabine can be used a feasible first-line treatment strategy for patients with metastatic pancreatic cancer, and the toxicity is tolerable. More data are needed in the future to explore the correlation between biomarkers and efficacy and to identify people who can benefit from combined strategy.

Legal entity responsible for the study: The author.

Funding: This work was financially supported by the Science and Technique Foundation of Henan Province (No. 202102310121 for J.-Z. W), the Medical Science and Technology Co-construction Project of Henan Province (No. LHGJ20200167), the 1000 Talents Program of Central plains (No. 204200510023 for X.-B. C), and the Sate Key Laboratory of Esophageal Cancer Prevention & Treatment (No. Z2020000X for X.-B. C).

Disclosures: All authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2022.04.096

P-5 Phase II study (daNIS-1) of the anti-TGF-β monoclonal antibody (mAb) NIS793 +/- spartalizumab in combination with nab-paclitaxel/gemcitabine (NG) versus NG alone in patients with first-line metastatic pancreatic ductal adenocarcinoma (mPDAC)

S. Sivakumar[1], T. Macarulla[2], P. Grell[3], C. Chee[4], A. Krishnamurthy[5], M. Ka Wong[6], M. Michael[7], M. Milella[8], G. Prager[9], C. Springfeld[10], J. Collignon[11], J. Siveke[12], A. Santoro[13], C. Lin[14], K. Peltola[15], G. Bostel[16], D. Jankovic[16], M. Altzerinakou[17], C. Fabre[16], L. Bai[18]

[1]Department of Oncology, University of Oxford, Oxford, United Kingdom; [2]Hospital Vall D'Hebron, Barcelona, Spain; [3]Masaryk Memorial Cancer Institute, Brno, Czech Republic; [4]National University Hospital, Singapore, Singapore; [5]University of Pittsburgh Cancer Institute, Pittsburgh, United States; [6]Westmead Hospital, Sydney, Australia; [7]Peter MacCallum Cancer Centre, Melbourne, Australia; [8]Section of Oncology, University of Verona, Azienda Ospedaliera Universitaria Integrata Verona, Verona, Italy, Verona, Italy; [9]Uni Klinik fuer Innere Medizin, Vienna, Austria; [10]Universitaetsklinikum Heidelberg, Heidelberg, Germany; [11]Centre Hospitalier Universitaire du Sart-Tilman, Liège, Belgium; [12]Universitaetsklinikum Essen, Essen, Germany; [13]Humanitas Clinical and Research Center - IRCCS, Humanitas Cancer Center, Rozzano; Department of Biomedical Sciences, Humanitas University, Pieve Emanuele, Milan, Italy; [14]National Taiwan University Hospital, Taipei, Taiwan; [15]Helsingin yliopistollinen keskussairaala, Helsinki, Finland; [16]Novartis Institutes for BioMedical Research, Basel, Switzerland; [17]Novartis Pharmaceuticals Corporation, Basel, Switzerland; [18]China Medical University Hospital, Taichung, Taiwan

Background: Overall survival remains low for patients (pts) with mPDAC despite approved therapies, highlighting the need for further innovative treatment options. Intra-tumoral fibrosis that characterizes PDAC has been associated with a state of immune exclusion and may constitute a mechanical obstacle to the intra-tumoral penetration of chemotherapy as well as contribute to the lack of efficacy of immunotherapy. TGF-β plays a key role in regulating the tumor microenvironment and emerging evidence points to its role as a pivotal activator of cancer-associated fibroblasts, leading to the development of fibrotic networks. Preclinical data in murine models have shown that TGF-β blockade augmented the antitumor activity of both NG and anti-PD-1 therapy, leading to tumor regression. These data provide the rationale for combining TGF-β-targeting agents with immunotherapy and chemotherapy. NIS793 is a human IgG2 mAb that binds to TGF-β. This study investigates NIS793 with and without spartalizumab (PD-1 antagonist) combined with NG in treatment naïve mPDAC.

Trial design: This is a phase II open-label, randomized, multicenter study (NCT04390763) beginning with a safety run-in period followed by randomization. Eligible pts are adults with previously untreated mPDAC and ECOG performance status score $\leq$1. Pts are excluded if they have a microsatellite-unstable tumor. The safety run-in data will be analyzed after $\geq$6 pts have received NIS793 (intravenously [IV] 2100 mg Q2W) + spartalizumab (IV 400 mg Q4W) + nab-paclitaxel (IV 125 mg/m2 on Days 1, 8 and 15) + gemcitabine (IV 1000 mg/m2 on Days 1, 8 and 15) for 1 cycle (28 days) to assess the safety and tolerability of the combination. In the randomized part, pts will be randomized 1:1:1 to NIS793 + spartalizumab + NG (n=50) or NIS793 + NG (n=50) or NG (n=50). Treatment will continue until unacceptable toxicity, disease progression, discontinuation by investigator's/pt's choice, or withdrawal of consent. The primary objective is to evaluate the progression-free survival per RECIST 1.1, of NIS793 + NG $\pm$ spartalizumab versus NG alone. Secondary objectives include safety and tolerability, antitumor activity, overall survival, change in tumoral CD8 and PD-L1 status, and characterization of immunogenicity and pharmacokinetics. Efficacy will be assessed locally per RECIST v1.1 and iRECIST at screening, every 8 weeks for 1 year and then every 12 weeks until disease progression. Blood and tumor samples will be taken at baseline and during study treatment for pharmacokinetic, immunogenicity and biomarker assessments. This study is ongoing and will enroll pts from 31 sites across 14 countries. The first pt was treated on October 22, 2020. Enrollment for the randomized part of the study started on August 09, 2021.

Clinical trial identification: NCT04390763.

Editorial acknowledgement: Editorial assistance was provided by Sivanjaa Manoj of ArticulateScience Ltd and was funded by Novartis Pharmaceuticals Corporation.

Legal entity responsible for the study: Novartis Pharmaceuticals Corporation.

Funding: This study is sponsored by Novartis Pharmaceuticals Corporation.

Disclosures: S. Sivakumar: Research grant / Funding (institution): Bristol-Myers Squibb, Celgene. T. Macarulla: Advisory / Consultancy: (SOBI) Swedish Orpahn Biovitrum AB, Ability Pharmaceuticals SL, Aptitude Health, AstraZeneca, Basilea Pharma, Baxter, BioLineRX Ltd, Celgene, Eisai, Ellipses, Genzyme, Got It Consulting SL, Hirslanden/GITZ, Imedex, Incyte, Ipsen Bioscience, Inc, Janssen, Lilly. Marketing Farmacéutico & Investigación Clínica, S.L, MDS, Medscape, Novocure, Paraxel, PPD Development, Polaris, QED Therapeutics, Roche Farma, Sanofi-Aventis, Servier, Scilink Comunicación Científica SC, Surface Oncology, TRANSWORLD EDITORS, SL and Zymeworks. C. Chee: Honoraria (self): Roche, Genentech, AstraZeneca; Advisory / Consultancy: Guardant Health AMEA; Travel / Accommodation / Expenses: Taiho Pharmaceutical. M. Michael: Advisory / Consultancy: NOVARTIS AUSTRALIA; Speaker Bureau / Expert testimony: NOVARTIS AUSTRALIA. M. Milella: Honoraria (self): Pfizer, MSD, AstraZeneca, Roche, EUSA Pharma, Boehringer Ingelheim, Ipsen; Advisory / Consultancy: Novartis; Research grant / Funding (institution): Roche. G. Prager: Advisory / Consultancy: Merck, Roche, Amgen, Sanofi, Lilly, Bayer, Servier, CECOG, MSD, BMS, Pierre Fabre, Incyte, Novartis. J. Siveke: Advisory / Consultancy: Celgene, AstraZeneca, Immunocore, Bayer, Roche; Research grant / Funding (institution): Celgene, Bristol-Myers Squibb, Roche; Shareholder / Stockholder / Stock options: Pharma 15. A. Santoro: Advisory / Consultancy: ARQULE / SANOFI/ INCYTE/BMS (BRISTOL-MYERS-SQUIBB) / SERVIER / GILEAD / PFIZER / EISAI / BAYER / MSD (MERCK SHARP & DOHME); Speaker Bureau / Expert testimony: TAKEDA / BMS (BRISTOL-MYERS-SQUIBB) / ROCHE / ABBVIE / AMGEN / CELGENE / SERVIER / GILEAD / ASTRAZENECA / PFIZER / ARQULE / ELI-LILLY / SANDOZ / EISAI / NOVARTIS / BAYER / MSD (MERCK SHARP & DOHME). K. Peltola: Honoraria (self): Pfizer, Ipsen, BMS, Roche, Novartis, MSD; Advisory / Consultancy: Pfizer, Ipsen, BMS, Roche, MSD, Novartis; Travel / Accommodation / Expenses: Roche, Pfizer; Shareholder / Stockholder / Stock options: Faron Pharmaceuticals. G. Bostel: Shareholder / Stockholder / Stock options: Novartis; Full / Part-time employment: Novartis. D. Jankovic: Shareholder / Stockholder / Stock options: Novartis; Full / Part-time employment: Novartis. M. Altzerinakou: Full / Part-time employment: Novartis Pharma. C. Fabre: Shareholder / Stockholder / Stock options: Novartis; Full / Part-time employment: Novartis. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2022.04.097

P-6 Prognostic value of the lymphocyte/monocyte ratio in advanced pancreatic cancer

W. Ben Kridis, M. Lajnef, A. Feki, S. Khmiri, A. Khanfir

Habib Bourguiba University Hospital, Sfax, Tunisia

Background: Several studies have evaluated the interest of inflammatory markers as prognostic indicators for pancreatic cancer. The aim of this work was to investigate the utility of the lymphocyte/monocyte ratio (LMR) as a prognostic factor in Tunisian advanced pancreatic cancer.

Methods: This is a retrospective study including 31 patients diagnosed and treated for locally advanced or metastatic pancreatic cancer, at the medical oncology department at Habib Bourguiba university hospital in Sfax, between 2011 and 2017. LMR was calculated by using the equation: LMR = absolute lymphocyte count/absolute monocyte ratio. Value cutoffs were adopted to discriminate patients as follows: low LMR $<$ 4.6 and high LMR$\geq$4.6.

Results: The median age of our patients was 60 years (36 -77). A male predominance was observed (61%). The average consultation time was 2.7 months, and the most common reason was abdominal pain (87%) followed by the onset of jaundice (29%). Nine patients had a performance status (PS) $\geq$2. On imaging, the average tumor size was estimated at 4.5 cm. The presence of metastases was observed in 16 patients (51.6%). Chemotherapy was indicated in 19 patients, as a neoadjuvant situation (38%) and in 51% in case of metastatic disease. A high LMR was found in 9 patients (29%). The mean overall survival was 7 months. Survival at 1 and 2 years were 12.9% and 3.2% respectively. The LMR $<$ 4.6 was associated with a worse overall survival (OS) at 1 year (3.2% vs 13%, p =0.002). The other poor prognostic factors were PS $\geq$2, high CA19-9 level and stage IV (p=0.001, p=0.021 and p=0.027 respectively).

Conclusions: The findings from our study suggest that low LMR is associated with worse OS in Tunisian patients with advanced pancreatic cancer, in addition to the other prognosis factors.

Legal entity responsible for the study: The authors.

Funding: Has not received any funding.

Disclosures: All authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2022.04.098

P-7 Encorafenib and cetuximab in patients with metastatic, BRAF V600E-mutated, colorectal cancer: Update on the first real-world study in Germany and Austria – BERING CRC

E. von der Heyde[1], D. Bürkle[2], H. Forstbauer[3], G. Hübner[4], B. Schmidt[5], J. Schröder[6], A. Distelrath[7], J. Wierecky[8], P. Stübs[9], J. Kisro[10], M. Welslau[11], H. Müller-Huesmann[12], T. Göhler[13], B. Krammer-Steiner[14], I. Schwaner[15], C. Hering-Schubert[16], A. Gerger[17], R. Greil[18], L. Jacobasch[19], F. Reichenbach[20], S. Stintzing[21], G. Prager[22]

[1]Onkologische Praxis am Raschplatz, Hannover, Germany; [2]Oncological Practice Schorndorf, Schorndorf, Germany; [3]Practice network hematology/oncology, Troisdorf, Germany; [4]Oho! Ostholstein-Onkologie, Oldenburg i.H., Germany; [5]Oncological Practice Munich, Munich, Germany; [6]Outpatient Center for Hematology – Oncology – Palliative Care, Muelheim, Germany; [7]Joint Practices for Urology and Oncology, Wilhelmshaven, Germany; [8]Überörtliche Gemeinschaftspraxis, Schwerpunkt Hämatologie, Onkologie und Palliativmedizin, Hamburg, Germany; [9]DRK-Hospital Berlin-Koepenick, Berlin, Germany; [10]Oncological Practice Lübeck, Lübeck, Germany; [11]Oncological Practice Aschaffenburg, Aschaffenburg, Germany; [12]Medizinisches Versorgungszentrum im Medico, Paderborn, Germany; [13]Onkozentrum Dresden/Freiberg, Dresden, Germany; [14]Department of Hematology and Oncology, Rostock South City Medical Center, Rostock, Germany; [15]Onkologische Schwerpunktpraxis Kurfürstendamm, Berlin, Germany; [16]St. Georg Hospital Eisenach, Eisenach, Germany; [17]Medical University of Graz, Graz, Austria; [18]Paracelsus Medical University Salzburg, Salzburg Cancer Research Institute-CCCIT and Cancer Cluster Salzburg, Salzburg, Austria; [19]Gemeinschaftspraxis Hämatologie und Onkologie, Dresden, Germany; [20]Pierre Fabre Pharma GmbH, Freiburg, Germany; [21]Department of Hematology, Oncology and Tumorimmunology, Charité-Universitatsmedizin Berlin, Freie Universitat Berlin, Humboldt-Universitat zu Berlin, and Berlin Institute of Health, Berlin, Germany; [22]Uni Klinik fuer Innere Medizin, Vienna, Austria

Background: For the therapy of previously treated BRAF V600E-mutant metastatic colorectal cancer, the combination of encorafenib with cetuximab represents a new standard of care. The combination of encorafenib plus cetuximab was approved in the EU in June 2020. The approval was based on positive results from the BEACON CRC trial, which demonstrated a median overall survival (OS) of 8.4 mo (second data cut off 9.3 mo) and an objective response rate of 20% (both data cut offs). The observed tolerability profile was consistent with the known safety profile of each agent. Since data from controlled clinical trials are based on a selected patient population, the present non-interventional study (NIS) investigates the use of encorafenib + cetuximab under real-world conditions in a broader patient population.

Trial design: BERING CRC is an ongoing, multi-national, multi-centric, prospective, longitudinal NIS. It represents the first NIS to investigate the real-world use of the targeted therapy encorafenib + cetuximab in BRAF V600E-mutant metastatic colorectal cancer after prior systemic treatment in Germany and Austria. The project aims to enroll up to 500 patients from 90 German and Austrian sites with a total study duration of approx. 6 yrs. From Sep 2020 to Feb 2022, 72 patients have been included from 80 open sites. The study follows patients treated according to the SmPCs (Summary of Product Characteristics) and the primary objective is to assess the 1-year OS rate. Additional analyses include efficacy, quality of life, safety and tolerability of encorafenib + cetuximab treatment. The influence of prognostic factors on efficacy, safety and tolerability will also be analyzed.

Clinical trial identification: NCT04673955.

Legal entity responsible for the study: Pierre Fabre Pharma.

Funding: This study is funded by Pierre Fabre Pharma GmbH (Freiburg, Germany) and Pierre Fabre Pharma Austria (Wels, Austria).

Disclosures: R. Greil: Honoraria (self): Celgene, Roche, Merck, Takeda, AstraZeneca Novartis, Amgen, BMS, MSD, Sandoz, Abbvie Gilead, Daiichi Sankyo, Sanofi; Advisory / Consultancy: Celgene, Novartis, Roche, BMS, Takeda, Abbvie, Astra Zeneca, Janssen, MSD Merck, Gilead, Daiichi Sankyo, Sanofi; Research grant / Funding (self): Celgene, Roche, Merck, Takeda, AstraZeneca Novartis, Amgen, BMS, MSD, Sandoz, Abbvie Gilead, Daiichi Sankyo; Travel / Accommodation / Expenses: Roche, Amgen, Janssen, Astra Zeneca Novartis, MSD, Celgene, Gilead, BMS, Abbvie, Daiichi Sankyo. F. Reichenbach: Full / Part-time employment: Pierre Fabre Pharma GmbH. S. Stintzing: Honoraria (self): Amgen, Pierre-Fabre, Merck KGaA; Advisory / Consultancy: Amgen, Pierre-Fabre, Merck KGaA; Research grant / Funding (institution): Roche, Pierre-Fabre, Merck KGaA; Travel / Accommodation / Expenses: Amgen, Pierre-Fabre, Merck KgaA. G. Prager: Advisory / Consultancy: Merck, Roche, Amgen, Sanofi, Lilly, Bayer, Servier, CECOG, MSD, BMS, Pierre Fabre, Incyte, Novartis. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2022.04.099

P-8 Long-term survival in patients with pancreatic cancer (PAC) treated with liposomal irinotecan in combination with 5-fluorouracil and leucovorin (nal-IRI+5-FU/LV)

G. Prager[1], K. Potthoff[2], C. Yoo[3], S. Lonardi[4], F. Hédouin-Biville[5], T. Macarulla[6]

[1]Uni Klinik fuer Innere Medizin, Vienna, Austria; [2]iOMEDICO AG, Freiburg im Breisgau, Germany; [3]Asan Medical Centre, University of Ulsan, Seoul, South Korea; [4]Medical Oncology, Veneto Institute of Oncology IRCCS, Padua, Italy; [5]Servier, Suresnes, France; [6]Hospital Vall D'Hebron, Barcelona, Spain

Background: PAC is an aggressive disease with 85% of patients being diagnosed at a locally advanced or metastatic (mPAC) stage; the prognosis is poor, as only 10% survive beyond 5 years after diagnosis. Current treatments include the use of gemcitabine (GEM)-based therapies in first line, followed by liposomal irinotecan (nal-IRI+5-FU/LV) after failure. Despite poor survival outcomes, some patients survive $>$1 year from the start of nal-IRI+5-FU/LV. No clear recommendations exist for the optimal treatment sequence with no precise characteristics or molecular markers to help select a chemotherapy regimen or personalized treatment. Nevertheless, a nomogram derived from the pivotal NAPOLI-1 trial identified 8 factors that were significantly associated with overall survival, including baseline Karnofsky score (KPS), albumin (g/dL), neutrophil-to-lymphocyte ratio (N/L), liver metastasis, CA19-9 (U/mL), disease stage at diagnosis, body mass index (kg/m2), treatment arm (nal-IRI+5-FU/LV). While the identification of these factors has greatly helped in determining who will be a long-term survivor, they are not exhaustive and there is a need to further identify predictive markers. This abstract will report some published experiences of long-term survivors following nal-IRI+5-FU/LV treatment.

Methods: A descriptive analysis on the experiences of patients with mPAC who were treated with nal-IRI+5-FU/LV from several countries and who are considered long-term survivors ($>$1 year from start of nal-IRI treatment) was conducted.

Results: NAPOLI-1 survival data are replicated in the clinical practice and several data are already published (Drugs 2020). A retrospective observational database study evaluating patients treated with nal-IRI between Nov-2015 and Jul-2020, was presented during ASCO-GI (Kim 2021). This analysis from $>$280 cancer clinics in the US that examined 1-year survival for 699 patients treated with nal-IRI—based regimens showed that, when compared to NAPOLI-1, these patients were older, had more prior lines of therapy, and worse ECOG PS, but a similar treatment exposure. Despite these characteristics, the 1-year OS among patients who received at least 4 treatment cycles was similar to the intent-to-treat (25%) and per-protocol (34%) treated patients in NAPOLI-1. Among all patients, 1-year OS was 17.2% (14.3-20.7), 31.5% (22.1—41.3) for patients treated in first line, 16.4% (12.2 -21.1) in second line, and 12.2% (7.5 -18.0) in third line. Among those who received at least 4 and 8 cycles, the 1-year OS estimates were 29.1% (24.0-34.3) and 47.9% (39.7-55.7), respectively. Additionally, four published clinical cases of patients with unfavorable profiles at baseline were successfully treated with nal-IRI+5-FU/LV without any specific common factors (except age $<$ 60 years old). Additional experiences coming from other countries will be presented during the congress.

Conclusions: A subset of mPAC patients may derive exceptional benefit from nal-IRI+5-FU/LV. The currently presented evidence from real-world data and specific clinical cases highlight the need to identify and better characterize predictive factors for long-term survival. Future studies elucidating predictive factors of response to nal-IRI+5-FU/LV are needed to enable better patient selection.

Legal entity responsible for the study: Servier Affaires Médicales.

Funding: Servier Affaires Médicales.

Disclosures: G. Prager: Advisory / Consultancy: Merck, Roche, Amgen, Sanofi, Lilly, Bayer, Servier, CECOG, MSD, BMS, Pierre Fabre, Incyte, Novartis. C. Yoo: Honoraria (self): Ipsen, Servier, Eisai, Bayer, AstraZeneca, Roche, Novartis; Research grant / Funding (self): Ipsen, Servier, Bayer, AstraZeneca. F. Hédouin-Biville: Full / Part-time employment: SERVIER. T. Macarulla: Advisory / Consultancy: (SOBI) Swedish Orpahn Biovitrum AB, Ability Pharmaceuticals SL, Aptitude Health, AstraZeneca, Basilea Pharma, Baxter, BioLineRX Ltd, Celgene, Eisai, Ellipses, Genzyme, Got It Consulting SL, Hirslanden/GITZ, Imedex, Incyte, Ipsen Bioscience, Inc, Janssen, Lilly. Marketing Farmacéutico & Investigación Clínica, S.L, MDS, Medscape, Novocure, Paraxel, PPD Development, Polaris, QED Therapeutics, Roche