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502O Pembrolizumab in combination with CAPOX and bevacizumab in patients with microsatellite stable metastatic colorectal cancer and a high immune infiltrate: Preliminary results of FFCD 1703 POCHI trial

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Background: Immune checkpoint inhibitors (ICI) are considered ineffective in pMMR/MSS mCRC. About 15% of pMMR/MSS CRCs are infiltrated by tumor infiltrating lymphocytes and may be sensitive to ICIs. Some immune scores based on CD3+ and/or CD8+ T-cells infiltration are validated and reproducible to assess lymphocyte infiltration in CRC.

Methods: POCHI is a multicentre, single-arm phase II trial aiming to evaluate efficacy of Pembrolizumab in combination with CAPOX and bevacizumab as first-line treatment of unresectable pMMR/MSS mCRC patients with a high immune infiltrate defined by at least one positive immune score (Immunoscore® and/or TuLIS) on primary tumor resection specimens. Primary objective was progression-free survival (PFS) at 10 months. Main secondary objectives were overall survival, disease control rate (DCR), overall response rate (ORR), safety and duration of response (DoR). The clinical hypotheses are to increase PFS at 10 months from 50% to 70%. With a type one error α of 5%, a power of 85%, 55 pts were required.

Results: Between April 2021 and April 2024, 176 pts were screened in 39 active centres and 25 had at least one positive immune score (14%) and were enrolled. Median age was 66 y, 68% of pts were men and 84/16% were respectively ECOG PS 0/1. Pts baseline characteristics were: right-sided primary tumour (42%), RAS-mutated tumour (68%) and lung (29%) and liver metastases (46%). At the time of this preliminary analysis (cut-off date May 2, 2024), median follow-up was 17 months and 11 pts (44%) were still on treatment. A high DCR of 100% and ORR of 75% were observed including 25% of complete response. Median DoR was 12.7 months. Overall, 52% of pts had at least one grade 3-4 treatment-related adverse events. No toxic death was observed. Only 2 patients were dead and PFS at 12 months is 57.9%.

Conclusions: Preliminary results of the POCHI trial demonstrate a good safety profile and a high efficacy of Pembrolizumab combined to a standard regimen (CAPOX+bevacizumab). To our opinion the impressive ORR and DCR observed justify further evaluation in a randomized phase III trial dedicated to pMMR/MSS mCRC pts with a high immune infiltrate.

Clinical trial identification: NCT04262687.

Legal entity responsible for the study: Fédération Francophone de Cancérologie Digestive (FFCD).

Funding: MSD and Veracyte.

Disclosure: D. Tougeron: Financial Interests, Personal, Advisory Board: AstraZeneca, Sanofi, Amgen, MSD, Roche, Servier, Pierre Fabre, BMS, Bayer; Non-Financial Interests, Member of Board of Directors: Federation Francophone de Cancerologie Digestive. J. Emile: Financial Interests, Personal, Invited Speaker, pPresentations on digital PCR (Qiacuity): Qiagen; Financial Interests, Personal, Invited Speaker, Presentation on GIST pathology: Deciphera; Financial Interests, Personal, Advisory Board, Board on Lung cancer: AstraZeneca; Financial Interests, Personal, Invited Speaker, Presentation on Molecular Analysis of Cancers: Servier. B. Chibaudel: Financial Interests, Personal, Advisory Board: Amgen, Bayer, BeiGene, Biocartis, Lilly, Merck, MSD, Pfizer, Pierre Fabre, Roche, SeqOne, Sanofi, Servier, Takeda. F. Khemissa Akouz: Financial Interests, Personal, Invited Speaker: Servier, AstraZeneca; Other, Fees for Congress (JFHOD): MSD; Other, Fees for congress: Servier. J. Hartwig: Financial Interests, Personal, Stocks/Shares: MaaT Pharma. A. Lievre: Financial Interests, Personal, Invited Speaker: Amgen, Astellas, AstraZeneca, BMS, Esteve, Pierre Fabre Oncologie, Servier, Viatris; Financial Interests, Personal, Advisory Board: Astellas, BMS, Bayer, Servier; Financial Interests, Institutional, Research Grant, RePERSO trial: Bayer; Financial Interests, Institutional, Coordinating PI, SOCRATE trial (FFCD promotion): Lilly; Non-Financial Interests, Principal Investigator: AstraZeneca, BMS, Bayer, Incyte, Lilly; Non-Financial Interests, Travel and Meeting Registration: Bayer, Pierre Fabre, Servier, Viatris. C. Toullec: Financial Interests, Personal, Invited Speaker: Amgen, BMS, MSD, Pierre Fabre, Viatris; Financial Interests, Personal, Advisory Board: Bayer, Merck Serono, Sanofi, Servier, AstraZeneca, Oncoscience. P. Laurent-Puig: Financial Interests, Personal, Invited Speaker: Amgen, Sanofi; Financial Interests, Personal, Advisory Board: Biocartis, Pierre Fabre; Financial Interests, Personal, Ownership Interest: Methys DX; Financial Interests, Institutional, Research Grant, PI of translational research: Federation Francophone de Cancerologie Digestive; Non-Financial Interests, Leadership Role: President of Canceropole Ile de France. C. Lepage: Financial Interests, Personal, Advisory Board: AAA; Financial Interests, Personal, Invited Speaker: Amgen, Pierre Fabre, Ipsen. J. Taieb: Financial Interests, Personal, Advisory Board: MSD, Astellas, Merck, Servier, Pierre Fabre, Amgen, BMS, Novartis, Pfizer, Sanofi, Rottapharm, Takeda; Financial Interests, Personal, Invited Speaker: Amgen, BMS, Merck, MSD, Novartis; Financial Interests, Personal, Invited Speaker, symposia: Astellas; Financial Interests, Personal, Other, Steering Committee of clinical trial: Novartis; Non-Financial Interests, Leadership Role, President of the Scientific Committee of the ARCAD foundation until end 2022: ARCAD Foundation; Non-Financial Interests, Leadership Role, Chair of the ARCAD Pancreas Research group: ARCAD Foundation; Non-Financial Interests, Leadership Role, Member of the Administrative Council, Scientific Committee, Executive Board and Responsible for the International Relationships/Partnership for FFCD in the Prodige Intergroup: Federation Francophone de Cancerologie Digestive (FFCD); Non-Financial Interests, Other, Steering Committee of clinical trials: Pfizer, Servier. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2024.08.571

503O Neoadjuvant nivolumab (nivo) plus relatlimab (rela) in MMR-deficient colon cancer: Results of the NICHE-3 study

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Background: Immune checkpoint inhibitors (ICI) have shown unprecedented responses in MMR-deficient (dMMR) colorectal cancers. In the NICHE-2 study, major pathologic responses (MPR) and pathologic complete responses (pCR) were observed in 95% and 68% of patients, respectively, following a short neoadjuvant regimen of nivolumab/ipilimumab. Data on nivo/rela in patients with melanoma suggest a favorable toxicity profile. Here we present data from NICHE-3, in which we investigated the efficacy and safety of nivo/rela in locally advanced resectable dMMR colon cancer (CC).

Methods: Patients with dMMR CC were treated with 2 doses of nivo/rela (480mg/480mg) on day 1 and 29, followed by surgery within 8 weeks of enrollment. A Simon's 2 stage design was used where $>$46/59 responders were needed in stages 1+2 for the study to be deemed successful. Pathologic response was defined as $\leq$50% residual viable tumor (RVT). Secondary endpoints included pCR, MPR ($\leq$10% RVT), safety and survival. We previously showed data from stage 1 (19pts). Here we present the primary endpoint from the fully accrued study.

Results: A total of 59 patients were treated. Median age was 65 years and 78% of patients had clinical stage III disease. Of the 59 patients, 56 have undergone surgery, and surgery is scheduled for 3 treated patients. Pathologic response was observed in 54/56 (96%) patients and included 91% MPR and 68% pCR. Grade 3-4 immune related adverse events were observed in 6/59 (10%) patients and led to delay of surgery in 3 patients. Endocrinopathies requiring long-term suppletion occurred in 14 (24%) patients consisting of 10 cases of hypothyroidism (17%) and 5 (8%) of adrenal insufficiency. To date, one patient had recurrence of disease.