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Progress Report

Trifluridine/tipiracil + oxaliplatin ± nivolumab vs FOLFOX ± nivolumab in HER2 negative advanced oesogastric adenocarcinoma: The PRODIGE73-UCGI40-LOGICAN trial [☆]



Damien Botsen^a, Sylvie Chabaud^b, Hervé Perrier^c, Hanifa Ammarguella^d,
Véronique Jestin-Le-Tallec^e, Jonathan Olesinski^f, Clémence Toullec^g, Thomas Aparicio^h,
Meher Ben Abdelghaniⁱ, Christophe Borg^j, Olivier Bouche^k, Clélia Coutzac^l,
Hervé Devaud^m, Frédéric Di Fioreⁿ, Olivier Dubreuil^o, Ludovic Evesque^p, Bruno Huguenin^q,
Marie Muller^r, Pierre-Guillaume Poureau^s, Emilie Oularue^t, David Tougeron^u,
Aziz Zaanani^v, Samy Ammari^{w,x}, Nicolas De Sousa Carvalho^y, Pierre Decazes^{z,aa},
Christelle De La Fouchardiere^{ab,*}

^a Medical Oncology Department, Godinot Cancer Institute, 1 avenue General Koenig, Reims 51100, France

^b Department of Clinical Research and Innovation, Centre Léon Bérard, Lyon, France

^c Medical Oncology Department, Saint-Joseph Hospital, Marseille, France

^d Medical Oncology Department, Beauvais Hospital, Beauvais, France

^e Clinique Pasteur Lanroze, Brest, France

^f Gastroenterology Department, Villefranche Sur Saone North West Hospital, Gleize, France

^g Medical Oncology Department, Sainte Catherine Institute, Avignon, France

^h Gastroenterology Department, Saint Louis Hospital, Paris, France

ⁱ Medical Oncology Department, ICANS, Strasbourg, France

^j Medical Oncology Department, Hopital Nord Franche Comté, Montbeliard France

^k Hepato-Gastroenterology and Digestive Oncology Department, CHU, Reims, France

^l Medical Oncology Department, Centre Léon Bérard, Lyon France

^m Medical Oncology Department, Centre Jean Perrin, Clermont Ferrand, France

ⁿ Hepato-Gastroenterology Department, Charles Nicolle Hospital, Rouen, France

^o Oncology Department, GH Diaconesses – Croix St Simon, Paris, France

^p Medical Oncology Department, Centre Antoine Lacassagne, Nice, France

^q Hepato-Gastroenterology Department, Private Hospital Arras Les Bonnettes, Arras, France

^r Gastroenterology and Hepatology Department, Nancy University Hospital, Vandoeuvre Les Nancy, France

^s Medical Oncology Department, Morvan Hospital, Brest, France

^t Medical Oncology Department, Institut Mutualiste Montsouris, Paris, France

^u Hepato-Gastroenterology Department, Poitiers University Hospital, Poitiers, France

^v Hepato-Gastroenterology and Digestive Oncology Department, Hopital Européen Georges Pompidou, Paris, France

^w Biomaps, UMR1281 INSERM, CEA, CNRS, University of Paris-Saclay, 94800 Villejuif, France

^x Department of Imaging, Gustave Roussy Cancer Campus, University of Paris-Saclay, 94800 Villejuif, France

^y Unicancer, Paris, France

^z Department of Nuclear Medicine, Henri Becquerel Cancer Center, 76000 Rouen, France

^{aa} QuantIF-LITIS (EA[Equipe d'Accueil] 4108), Faculty of Medicine, University of Rouen, 76000 Rouen, France

^{ab} Medical Oncology Department, Paoli-Calmettes Cancer Institute, Marseille, France

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* Corresponding author.

E-mail address: delafouchardiere@ipc.unicancer.fr (C. De La Fouchardiere).

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ABSTRACT

Background: Trifluridine/tipiracil (FTD/TPI) is approved in third-line treatment of patients with advanced/metastatic gastric and gastroesophageal junction adenocarcinomas (aGA/GEJA). The association of oxaliplatin with FTD/TPI is promising and the combination of FTD/TPI + oxaliplatin + nivolumab has shown a predictable and manageable safety profile.

Aims: The aim is to evaluate the efficacy and safety of FTD/TPI plus oxaliplatin with or without nivolumab in patients, with HER2 negative aGA/GEJA, unfit for triplet chemotherapy (TFOX/mFLOT regimen), in the first-line metastatic setting in comparison with the standard of care FOLFOX with or without nivolumab.

Methods: This study is a prospective randomised, open label, comparative, multicentre, phase II trial designed to include 118 patients. The primary objective is to evaluate the superiority of FTD/TPI plus oxaliplatin with or without nivolumab over FOLFOX regimen with or without nivolumab in terms of PFS in a population of patients non candidate for triplet chemotherapy. Nivolumab will be used for patients whose tumour express PD-L1 with a CPS score ≥ 5 .

Discussion: PRODIGE73-UCGI40-LOGICAN study will provide efficacy and safety data on the association of FTD/TPI plus oxaliplatin with or without nivolumab versus FOLFOX regimen with or without nivolumab in first-line palliative setting, in patients with aGA/GEJA (NCT05476796).

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1. Background

Cytotoxic chemotherapy based on a fluoropyrimidine and a platinum agent (cisplatin or oxaliplatin) with or without the adjuvant of anti-Programmed Death - Ligand 1 (PD-L1) or anti-human epidermal growth factor receptor 2 (HER2) is the cornerstone of first-line treatment for advanced/metastatic gastric and gastroesophageal junction adenocarcinomas (aGA/GEJA). Treatment choice is mainly driven by patient's performance status (PS), HER2 expression, and Combined Positive Score (CPS) PD-L1 [1,2]. The 5FU-oxaliplatin combination demonstrated a particularly favourable toxicity profile compared with the 5FU-cisplatin combination [3]. Adding immune checkpoint inhibitors (nivolumab or pembrolizumab) to chemotherapy showed a superiority over chemotherapy alone with an improved progression-free survival (PFS) and overall survival (OS) in the PD-L1 CPS >1 or ≥ 5 and the overall populations [4,5]. Consecutively, the Food and Drug Administration (FDA) and the European Medicines Agency (EMA) approved monoclonal antibodies against PD-L1, nivolumab then pembrolizumab, in these indications in 2021 and 2023 respectively. Combination with FOLFOX or XELOX has become the standard first-line treatment for patients with advanced/metastatic HER2-negative, PD-L1 CPS ≥ 5 GEJA or oesophageal adenocarcinoma patients. Recently, the GASTFOX-PRODIGE 51 randomised phase III trial [6] demonstrated the superiority of a triplet chemotherapy regimen, TFOX/mFLOT (docetaxel, 5FU and oxaliplatin), versus doublet FOLFOX in aGA/GEJA [7]. However, there are still unmet clinical needs in this disease. One of them is to develop specific study protocols to evaluate treatments in patients usually excluded from clinical trials because to their age, ECOG-PS, or nutritional status and not candidate for triplet chemotherapy [8]. In the randomised GO2 phase III trial, Hall et al. evaluated the efficacy and safety of three different dose levels of capecitabine-oxaliplatin regimen in patients with advanced gastroesophageal cancer, considered unfit for conventional dose chemotherapy [9]. The non-inferiority of PFS was confirmed between lower chemotherapy doses vs standard dose administration. Another step towards improving patient outcomes is to find alternative options for first-line chemotherapy backbone. Trifluridine/tipiracil (FTD/TPI) (Lonsurf®) is an orally active agent composed of a thymidine-based nucleoside analog (trifluridine) and a thymidine phosphorylase (TPase) inhibitor (tipiracil). First developed in metastatic colorectal cancer (mCRC), FTD/TPI was approved for third-line treatment of patients with refractory mCRC [10,11]. Moreover, Prager et al. recently shown that the combination of bevacizumab with FTD/TPI

improved OS and PFS compared with FTD/TPI alone in this mCRC population [12]. In metastatic gastroesophageal adenocarcinoma, the TAGS study, showed a clinically meaningful improvement in OS and PFS in patient treated with FTD/TPI compared with placebo and with an acceptable safety profile [13]. FTD/TPI is now approved in third-line treatment of patients with refractory metastatic gastroesophageal adenocarcinoma [14]. It has also already been evaluated in less-heavily pre-treated gastric cancer patients, in combination with irinotecan in a phase Ib study [15] and in combination with ramucirumab (an anti-VEGFR2) in a two-cohort, single arm phase II study [16] with a good safety profile and promising potential efficacy. Furthermore, oxaliplatin was shown to be a promising combination partner for FTD/TPI [17]. Two phase I studies of FTD/TPI in combination with oxaliplatin were conducted (NCT02848443, NCT02848079) and preliminary efficacy results were promising [17]. The combination of FTD/TPI + oxaliplatin + nivolumab was also evaluated in a phase I study and has shown a predictable and manageable safety profile [18].

Thus, the aim of the PRODIGE73-UCGI40-LOGICAN study (NCT05476796) is to evaluate the efficacy and safety of FTD/TPI plus oxaliplatin with or without nivolumab combination in patients, with aGA/GEJA, unfit for triplet chemotherapy, in the first-line metastatic setting in comparison with the standard of care, FOLFOX with or without nivolumab.

2. Materials and methods

2.1. Trial design

This study is a prospective randomised, open label, comparative, multicentre, phase II trial comparing FTD/TPI plus oxaliplatin with or without nivolumab vs FOLFOX regimen with or without nivolumab in first-line palliative setting, in patients with HER2 negative aGA/GEJA, ineligible for triplet chemotherapy. Nivolumab will be used for patients whose tumour express PD-L1 with a CPS score ≥ 5 as already approved in France. In both arms, oxaliplatin will be stopped after eight cycles (or before in case of toxicity) and FTD/TPI or 5-FU with or without nivolumab will be continued until disease progression, death, patient's refusal, or intolerable toxicity.

2.2. Study objectives

The primary objective is to evaluate the superiority of FTD/TPI plus oxaliplatin with or without nivolumab over FOLFOX regimen

with or without nivolumab in terms of PFS, in first-line palliative setting, in patients with HER2 negative aGA/GEJA, ineligible for triplet chemotherapy. The reason of ineligibility to triplet chemotherapy will be collected in the CRF.

The secondary objectives are to evaluate treatments efficacy in terms of objective response rate (ORR), OS, safety and tolerability of treatment, time to PS deterioration >2 , and the effect of treatments on Quality of Life (QoL).

2.3. Study endpoints

PFS is defined as the time from the date of randomisation to date of disease progression (radiological or clinical) or death from any cause, whichever occurs first. ORR (according to response evaluation criteria in solid tumours version 1.1 [RECIST v1.1]) is defined as the percentage of patients with Complete Response (CR) or Partial Response (PR). OS is defined as the time from date of randomisation to the date of death from any cause. Time to PS deterioration >2 was defined as the time between patient randomisation and the first date when PS >2 . Safety and tolerability of treatment (graded according to the National Cancer Institute - common terminology criteria for adverse events [NCI-CTCAE] version 5.0) will be determined through the incidence of adverse events, treatment-related adverse events, serious adverse events (SAE), and death. QoL will be evaluated using the EORTC QLQ-C30 questionnaire.

2.4. Ancillary studies

Ancillary studies are pre planned to evaluate prognostic and predictive values of several radiological and biological biomarkers. Body composition analysis will be based on pre-therapeutic CTscan to measure 3D fat body mass (FBM), subcutaneous fat mass (SFM), visceral fat mass (VFM), muscle body mass (MBM), and lean body mass (LBM) (in kilograms) as previously described [19,20]. Specific pathological features and expression of the biomarkers including microsatellite status (MS), PD-1/PD-L1, claudin 18.2 and FGFR2b expression, Tumour Mutational Burden (TMB), CD8+ and CD3+ cell infiltration, Epstein Barr Virus (assessed by in situ hybridization), TP53, E-cadherin, HER3 and other will also be analysed. Molecular genotyping will be analysed on both tumour and circulating tumour DNA (ctDNA). The ctDNA value for prognosis and treatment monitoring (monitoring of ctDNA levels at different time point during the treatment: pretreatment then every two months during the first year or until disease progression whatever occurs first) will be measured and genetic changes on several genes will be evaluated. Specific geriatric analyses will be done including a correlation with Geriatric Core Dataset (G-CODE) and overall treatment utility (OTU) (Hall's index) in patients ≥ 70 years old. Correlation of G-CODE (including social assessment, functional autonomy, mobility, nutrition, cognition, mood and comorbidity analysis) with OS and correlation of different biological prognostic scores (Glasgow and modified Glasgow Prognostic Score and Neutrophil to Lymphocyte Ratio) with patient outcome will also be assessed.

2.5. Sample size calculation

The median PFS in the control arm was set to those observed in the subgroup of patients with PD-L1 CPS ≥ 5 of the CHECKMATE 649 study [4]. The PRODIGE73-UCGI40-LOGICAN study was calibrated to detect a treatment effect hazard ratio (HR) of 0.65 under the proportional hazard assumption, translating in an improvement in median PFS from 7.7 months (control arm) to 11.8 months (experimental arm). With a 1:1 randomisation, a total of 97 events observed in the study would have 80 % power to show statistically significant PFS at a 1-sided alpha level of 10 %. Considering a recruitment duration of 36 months and a 24-month

follow-up for the last included patient (estimated total duration of the study: 60 months), and assuming a common exponential dropout rate of 1 %, 118 patients should be randomised in the study (59 patients by arm) so that maturity of the PFS data is approximately 82 % at the time of the analysis. Sample size was performed using nQuery software version 8.7.2, module STT2-1 (two sample Log-rank test of exponential survival with exponential dropout). Given that this study can be considered as a screening phase II trial, we allow α to be set at 10 % as proposed by Rubinstein [21]. Randomisation will be stratified on PS 0-1 vs 2, age <75 vs ≥ 75 years, and CPS <5 vs between ≥ 5 and <10 vs ≥ 10 . No interim analysis is planned. Final analysis will be performed after the required number of events (97 progression or death) are notified in order to ensure the expected statistical power and will be performed on frozen database after blind review.

2.6. Inclusion and non-inclusion criteria

Eligible patients must be 18 years or older, have an ECOG PS ≤ 2 , with histologically confirmed locally advanced, recurrent or metastatic non resectable aGA/GEJA ineligible to curative treatment, no dysphagia or difficulty in swallowing, no overexpression/amplification of HER2 (IHC 0 or 1+; if IHC is 2+, ISH must be negative), and known PD-L1 CPS. The microsatellite and MMR status of patient's tumour (MSI/MSS and pMMR/dMMR) must also be known at the time of screening (IHC and PCR or NGS tests have to be done). In addition, patient must be unfit for triplet chemotherapy (ECOG-PS=2 or age ≥ 70 years old PLUS one frailty criteria on ADL/IADL score or denutrition defined by albumin <30 g/L).

Patient who completed chemotherapy or radio-chemotherapy within 6 months before inclusion, previous treatment with FTD/TPI, with Human Immunodeficiency Virus or Hepatitis (HBV or HCV) infection, active systemic autoimmune disease, or lung, coronary artery disease or history of myocardial infarction are not eligible to the study.

All other inclusion and exclusion criteria are summarized in Table 1.

2.7. Procedures

2.7.1. Description of trial treatments (Flow chart Fig. 1)

Experimental arm (FTD/TPI plus oxaliplatin with or without nivolumab): FTD/TPI will be administered with a 14-day schedule (35 mg/m² twice-daily [BID] per os for 5 days followed by 9 days of recovery) with or without nivolumab 240 mg (30-minute infusion) every 2 weeks until disease progression or intolerable toxicity. Oxaliplatin will be administered intravenously on day 1 of each treatment cycle (2-hour infusion) every 2 weeks. The first cycle will be administered at 70 mg/m² then increased to 85 mg/m² (if feasible) from cycle 2 to 8 or until disease progression, whatever occurs first. In case of limitant oxaliplatin neuropathy and in all cases after 8 cycles, oxaliplatin will be stopped and FTD/TPI will be continued with or without nivolumab until disease progression or intolerable toxicity.

Control arm (FOLFOX with or without nivolumab): folinic Acid 400 mg/m² (or 200 mg/m² if l-folinic acid) + oxaliplatin 85 mg/m² (2-hour infusion) followed by 5-FU bolus 400 mg/m² then 5-FU 2400 mg/m² as a 46-hour continuous infusion with or without nivolumab 240 mg (30-minute infusion). Treatment will be repeated every 14 days. In case of limitant oxaliplatin neuropathy and in all cases after 8 cycles, oxaliplatin will be stopped and 5-FU (simplified LV5FU2 regimen) or capecitabine (1000 mg/m² BID during 2 weeks every 3 weeks) with or without nivolumab will be continued until disease progression or intolerable toxicity.

Table 1
Inclusion and exclusion criteria.

Inclusion Criteria

- 1) Histologically confirmed locally advanced, recurrent or metastatic non resectable adenocarcinoma of the stomach, oesophagus or gastroesophageal junction (GEJ) ineligible to curative treatment.
- 2) No dysphagia or difficulty in swallowing.
- 3) No overexpression/amplification of HER2 (IHC 0 or 1+; if IHC is 2+, HIS must be negative). Known CPS PD-L1 score. The microsatellite and MMR status of patient's tumour (MSI/MSS and pMMR/dMMR) must also be known at the time of screening (IHC and PCR tests have to be done).
- 4) At least one evaluable lesion according to RECIST v1.1 outside any previously irradiated area.
- 5) No prior palliative chemotherapy.
- 6) Age ≥18 years old.
- 7) Patient unfit for triplet chemotherapy = ECOG-PS=2 or age ≥70 year old PLUS one frailty criteria on ADL/IADL score or denutrition defined by albumin <30 g/L
- 8) Adequate organs function:
 - a. Absolute neutrophils count $\geq 1.5 \times 10^9/L$
 - b. Platelets count $\geq 100 \times 10^9/L$
 - c. Haemoglobin ≥ 9 g/L
 - d. Serum bilirubin levels <2 times upper limit of normal (ULN), up to 2.5 times ULN in case of hepatic metastasis (biliary drainage allowed)
 - e. Transaminases <5 times ULN
 - f. Creatinine clearance >40 mL/min
- 9) No Dihydropyrimidine dehydrogenase (DPD) deficiency (uracilemia <16 ng/ml)
- 10) Women of childbearing potential must have a negative serum or urine pregnancy test done within 14 days before the first study treatment.
- 11) Patients must agree to use adequate contraception methods for the duration of study treatment and within 6 months after completing treatment.
- 12) Patients must be affiliated to a Social Security System (or equivalent).
- 13) Patient must have signed and dated a written informed consent form prior to any trial specific procedures. When the patient is physically unable to give their written consent, a trusted person of their choice, independent from the investigator or the sponsor, can confirm in writing the patient's consent.
- 14) Availability of archived tumour material for ancillary studies

Exclusion Criteria

- 1) Patient with a performance status ECOG PS >2.
- 2) Other current or previous malignancy within the past 3 years (with the exception of squamous cell carcinoma of the skin treated by surgery).
- 3) Adjuvant chemotherapy or radio-chemotherapy completed for less than 6 months.
- 4) Peripheral neuropathy of NCI-CTCAE grade ≥ 2 at baseline.
- 5) Patients with known allergy or severe hypersensitivity to any of the trial drugs or any of the trial drug excipients.
- 6) Patients unwilling or unable to comply with trial obligations for geographic, social, or physical reasons, or who are unable to understand the purpose and procedures of the trial.
- 7) Previous treatment with trifluridine/tipiracil.
- 8) Known Human Immunodeficiency Virus (HIV) infection.
- 9) Active Hepatitis B virus (HBV, defined as having a positive hepatitis B surface antigen [HBsAg] test prior to inclusion) or hepatitis C virus (HCV).
- 10) Interstitial lung disease.
- 11) Prior pneumonitis requiring systemic corticosteroid therapy.
- 12) Active infections.
- 13) Pregnant or breastfeeding woman.
- 14) Participation in another therapeutic trial within the 30 days prior to randomisation.
- 15) Persons deprived of their liberty or under protective custody or guardianship.
- 16) Clinically relevant coronary artery disease or history of myocardial infarction in the last 12 months, or high risk of uncontrolled arrhythmia (for men: QTc ≥ 450 msec, for women: QTc ≥ 470 msec)
- 17) Active systemic autoimmune disease. Subjects with vitiligo, type I diabetes mellitus, residual hypothyroidism due to autoimmune condition only requiring hormone replacement, psoriasis not requiring systemic treatment, or conditions not expected to recur in the absence of an external trigger are permitted to enrol.
- 18) Subjects with a condition requiring systemic treatment with either corticosteroids (> 10 mg daily prednisone equivalents) or other immunosuppressive medications within 14 days prior to first study drug administration (Inhaled or topical steroids are permitted in the absence of active autoimmune disease)
- 19) History of anterior organ transplant, including stem cell allograft

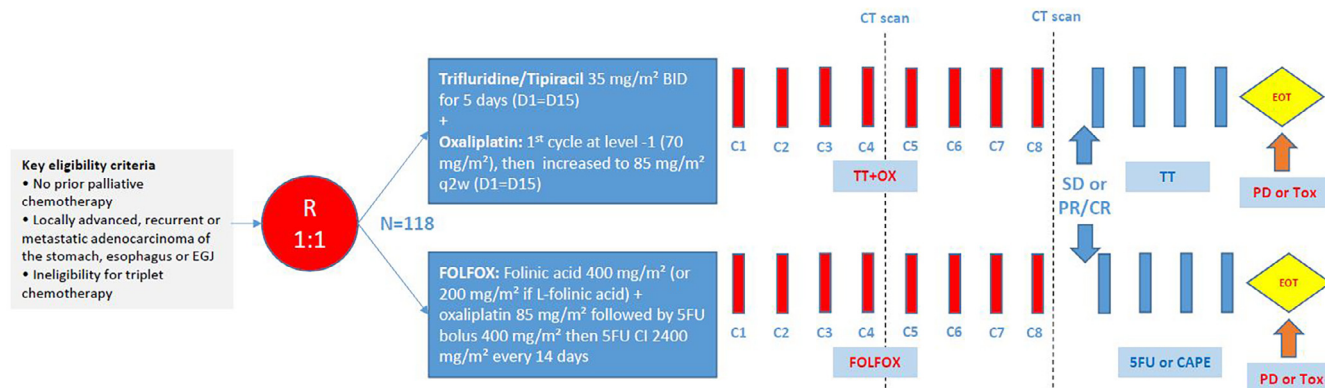


Fig. 1. Flow chart.

Nivolumab will be used within the indication of its marketing authorization for a maximum of 2 years in both arms. An amendment will be submitted during the study if pembrolizumab, which is FDA- and EMA-approved in advanced HER2-negative gastric or GEJ adenocarcinoma in tumours expressing PD-L1 (CPS ≥ 1), is reimbursed in France in this indication.

2.7.2. Evaluation of treatment efficacy and safety

Treatment efficacy will be evaluated by measuring changes in tumour size in response to treatment; using CT-scan (thorax, abdomen, pelvis) performed at baseline then every 8 weeks from D1C5 until disease progression, and assessed by RECIST v1.1. In addition, tumour markers (CA19-9, CEA) will be assessed with the same schedule. Treatment safety evaluation will be based on adverse event (AE) occurrence, the use of concomitant treatments, and changes occurring during treatment including those observed during physical examinations, in vital signs (blood pressure, pulse, body temperature), in electrocardiogram (ECG) results, and with blood chemistry and cytology analysis. Safety criteria will be evaluated using the NCI-CTCAE version 5.0.

2.7.3. Follow up

First follow-up visit will be done 2 months after the end of treatment visit. In absence of disease progression, patients will perform follow-up visits every 8 weeks (± 2 weeks) until documented progressive disease, start of new anticancer therapy, death, or end of study, whatever occurs first. The following assessments will be performed during the follow-up period: physical examination, WHO Performance status, information on safety data, pregnancy test (at the first two follow-up visits for women of child bearing potential receiving nivolumab), and QLQ-C30 and G-CODE evaluation (only at the first follow-up visit). For patients without disease progression, tumour biological markers (CEA and CA19-9), CT-Scan (Thorax Abdomen Pelvis), tumour assessment (RECIST v1.1) will also be performed. In addition, information on further anticancer therapy and optional tumour biopsy (if patient consented) will be collected at disease progression. After disease progression or starting of a new anticancer therapy (whatever occurs first), follow-up will only be performed every 12 weeks (± 2 weeks) until patient's death or the end of study, whatever occurs first, and will consist in the collection of overall survival and safety data.

2.8. Data analysis

The Intention To Treat (ITT) population is defined as all patients randomised in the trial. The Per-Protocol population is a subgroup of the ITT population containing all randomised patients with no major protocol violation who received at least one dose of study treatments. The safety analysis is defined as all randomised patients having received at least one dose of study treatment, whether withdrawn prematurely or not. Baseline characteristics and efficacy endpoints will be described among the ITT population. The safety population will be used for safety analyses.

Qualitative variables will be described using frequency and percentage distributions. The number of missing data will be given, but will not be considered for the calculation of proportions. Quantitative data will be described using the number of observations, mean, standard deviation, median, minimum and maximum values. The date of randomisation will serve as a reference for calculation of durations unless otherwise indicated. Statistical analyses will be performed using SAS® software version 9.4 or later.

PFS will be estimated using the Kaplan-Meier method, and will be described in terms of median PFS and 1-year PFS rate, along

with the associated 1-sided 90 % confidence interval (CI; in accordance with sample size calculation) for the estimates. OS will be estimated using the Kaplan-Meier method, and will be described in terms of median OS and 2-year OS rate, along with the associated 2-sided 95 % CIs for the estimates. PFS and OS analyses will be supplemented by a Cox model in order to measure the effect of the treatment throughout the follow-up (Hazard Ratio and its 95 % CI). Patients without disease progression or death at the time of analysis will be censored at the date of their last tumour assessment and patients alive at the database cut-off date will be censored at the last date of follow-up for PFS and OS analysis, respectively. ORR will be assessed according to RECIST v1.1 criteria and patients who discontinue treatment without a tumour assessment will be considered non-responders for the analysis. Percentage of responders will be presented with its 95 % CI.

Safety will be assessed in terms of AEs, SAEs, and toxic deaths. AE will be described according to MedDRA terms and graded according to CTCAE version 5.0. Descriptive statistics will be provided for characterizing and assessing patient tolerance to treatment. QoL analysis will be performed according to the QLQ-C30 scoring manual provided by EORTC. Descriptive statistics will be used to summarize the scored scales at each scheduled assessment time point. Variation from baseline will be described.

2.9. Ethical and regulatory aspects

The study, sponsored by UNICANCER is performed with the PRODIGE intergroup. The study was registered under EudraCT (2022-000273-81) and ClinicalTrials.gov (NCT05476796) database. This trial is conducted in accordance with the ethical principles of the Helsinki declaration of 1964 and its subsequent revisions and with good clinical practice of the international conference on harmonization (ICH-E6, 17/07/96). The initial protocol received approval from the National Agency for the Safety of Medicines and Health Products (ANSM) on 12/09/2022 and from French ethic committee on 13/09/2022.

2.10. Independent data monitoring committee

An Independent Data Monitoring Committee, composed of two oncologists and one statistician without direct involvement in the conduct of the trial, will meet 6 months after the first patient's randomisation to evaluate Benefit/Risk ratio of the study. Further meetings will be set up at least once a year to guarantee effective protection of the patients, insure the ethical conduct of the trial, and to ensure the independent review of the scientific results during the trial and at the end of the trial.

3. Discussion

While major progresses have been made for the treatment of aGA/GEJA patients, there is still an urgent need for new first-line palliative treatments [22]. In HER2-negative aGA/GEJA, PD-1 inhibitors have demonstrated their efficacy in combination with chemotherapy and are now considered as standard therapy in PD-L1 expressing tumours [4,5]. Recently, a broad new spectrum of actionable alterations has also emerged enlarging the therapeutic landscape in aGA/GEJA. Targeted anti-claudin 18 isoform 2 therapy (zolbetuximab) in combination with cytotoxic chemotherapy has recently demonstrated longer PFS and OS than chemotherapy + placebo in two clinical phase III trials and will become the future treatment combination in claudin 18.2 expressing tumours [23,24]. Moreover, the FGFR2b inhibitor bemarituzumab seems to be novel promising agent in patients with FGFR2b-selected aGA/GEJA [25]. However, these major therapeutic advances focus

on aGA/GEJA patients with relatively young age, ECOG-PS 0-1 and favourable nutritional status, who could also benefit from intense chemotherapy regimen like FLOT or TFOX [6,7]. Meanwhile, frail and/or older patients constituting the main part of aGA/GEJA population in the routine clinical setting are under-represented in clinical trials. Only one randomised phase III trial demonstrated non-inferiority of low-dosed chemotherapy with standard doublet regimen of capecitabine and oxaliplatin, in terms of PFS [9]. No specific trial with immune checkpoint inhibitors has been performed in older and/or frail patients whereas their benefit/adverse events ratio make them attractive candidates in this patient's population. To our knowledge, the PRODIGE73-UCGI40-LOGICAN phase II trial evaluating the efficacy and tolerance of FTD/TPI in association with oxaliplatin with or without nivolumab, is the first study to assess a combination of chemotherapy plus nivolumab in older/frail patients and it will be of great value for patients management. A large analysis of prognostic or predictive biomarkers (MS status, PD-1 and PD-L1 expression, TMB, CD8+ and CD3+ cell infiltration, Epstein Barr Virus, TP53, E-cadherin, HER3, circulating tumour DNA, Claudin 18.2, FGFR2b...) is planned to better characterize molecular somatic characteristics in this specific population and to correlate their expression to patient's outcome. Correlation of nutritional status, sarcopenia and patient's outcome will highlight the hypothesis of body composition/plasmatic exposure and treatment's efficacy/tolerance [26]. Furthermore, geriatric analyses will allow us to explore the heterogeneity characterizing the older patient population.

In conclusion, PRODIGE73-UCGI40-LOGICAN study will provide valuable data on the association of FTD/TPI plus oxaliplatin with or without nivolumab versus FOLFOX regimen with or without nivolumab in terms in first-line palliative setting, in patients with aGA/GEJA (NCT05476796).

Conflict of interest

D.B. reports personal fees as a speaker and/or in an advisory role from Accord Healthcare, Amgen, Sanofi, Servier, and Pierre Fabre, outside the submitted work.

O.B. reports personal fees as a speaker and/or in an advisory role from Merck, Bayer, Apmonia Therapeutics, Deciphera, Takeda, MSD, Amgen, Servier, and Pierre Fabre, outside the submitted work.

C.C. reports personal fees as speaker and/or in an advisory role from Amgen, Astra-Zeneca, Pierre Fabre, Daiichi Sankyo, BMS, MSD, Merck Serono, Servier, outside the submitted work.

O.D. reports personal fees as speaker and/or in an advisory role from Astra-Zeneca, BMS, MSD, Merck Serono, Sanofi, Servier outside the submitted work.

DT: Honoraria: Amgen, Roche, Sanofi, Bristol Myers Squibb, Merck Serono, MSD, Bristol Myers Squibb, Servier, Ipsen, Pierre Fabre, AstraZeneca, Takeda, BeiGene, Astra Zeneca.

Consulting or Advisory Role: Sanofi, MSD, Pierre Fabre, AstraZeneca, Novartis, Takeda.

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Travel, Accommodations, Expenses: Roche, Amgen, Bristol Myers Squibb, MSD, Pierre Fabre.

CDLF: Honoraria: Amgen, AstraZeneca, Bayer, BeiGene, Bristol Myers Squibb, Ipsen, Merck, MSD, Pierre Fabre, Servier, Roche, Sanofi, Takeda.

Consulting or Advisory Role: MSD, Pierre Fabre, AstraZeneca, Takeda.

Research Funding: Servier (Inst), Roche (Inst), MSD (Inst).

Travel, Accommodations, Expenses: Roche, Amgen, MSD, Pierre Fabre, Servier.

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