
GI
connect®
POWERED BY COR2ED

MEETING SUMMARY
ESMO 2021, VIRTUAL MEETING

Prof. Armin Gerger, MD
Medical University of Graz, Austria

HIGHLIGHTS ON NON-COLORECTAL CANCER
SEPTEMBER 2021

DISCLAIMER

Please note: Views expressed within this presentation are the personal opinions of the author.

They do not necessarily represent the views of the author's academic institution or the rest of GI CONNECT group.

This content is supported by an independent educational grant from Bayer.

Disclosures: Prof. Armin Gerger has the following disclosures:

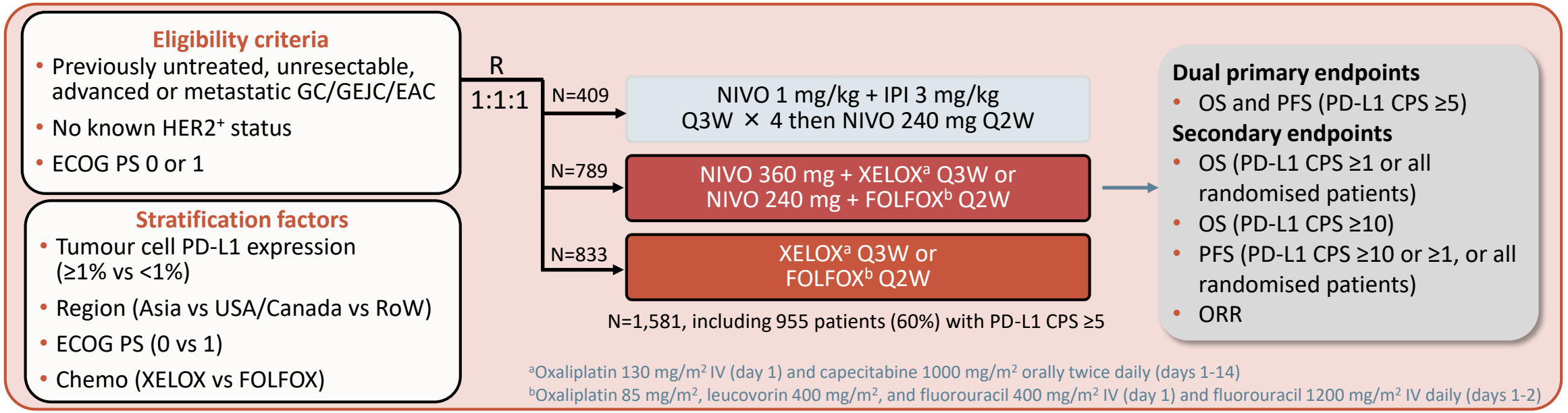
- Speaker's honoraria: BMS, MSD, Roche, Bayer
- Advisory Role: BMS, MSD, Roche, Bayer
- Research grants BMS, MSD, Roche

NIVOLUMAB PLUS CHEMOTHERAPY OR IPILIMUMAB VS CHEMOTHERAPY AS FIRST-LINE TREATMENT FOR ADVANCED GASTRIC CANCER/GASTROESOPHAGEAL JUNCTION CANCER/ESOPHAGEAL ADENOCARCINOMA: CHECKMATE 649 STUDY

Yelena Janjigian. ESMO 2021, Abstract #LBA7

DESIGN OF THE STUDY

CheckMate-649 study (NCT02872116): randomised, open-label, Phase 3 study comparing OS in patients with GC or GEJC treated with nivolumab + ipilimumab or nivolumab + chemo compared with chemo alone



Moehler M. et al, reported during ESMO 2020 the first results of NIVO + chemo vs chemo[1]
Long-term follow up results of NIVO + chemo vs chemo and first results from the NIVO + IPI vs chemo

chemo, chemotherapy; CPS, combined positive score; EAC, oesophageal adenocarcinoma; ECOG, Eastern Cooperative Oncology Group; FOLFOX, folinic acid + fluorouracil + oxaliplatin; GC, gastric cancer; GEJC, gastro-oesophageal junction cancer; HER2, human epidermal growth factor receptor 2; IV, intravenous; IPI, ipilimumab; NIVO, nivolumab; ORR, objective response rate; OS, overall survival; PD-L1, programmed death-ligand 1; PFS, progression-free survival; PS, performance status; Q2W, every 2 weeks; Q3W, every 3 weeks; R, randomisation; RoW, rest of the world; XELOX, capecitabine + oxaliplatin. 1. Moehler M, et al. Ann Oncol. 2020;31(suppl_4):abstr LBA6

RESULTS: IMPROVED OS AND ROBUST DOR WITH NIVO + CHEMO VS CHEMO

Data cut-off date: 27 May 2021 – minimum follow-up duration 24 months in the NIVO + chemo arm and 35.7 months in the NIVO + IPI arm

	PD-L1 CPS ≥5		All randomised patients	
	NIVO + chemo (N=473)	**Chemo (N=482)**	**NIVO + chemo (N=789)**	**Chemo (N=792)**
Median OS, months (95% CI)	14.4 (13.1-16.2)	11.1 (10.0-12.1)	13.8 (12.4-14.5)	11.6 (10.9-12.5)
HR (95% CI)	0.70 (0.61-0.81)		0.79 (0.71-0.88)	
12-month OS rate, %	57	46	55	48
24-month OS rate, %	31	19	28	19
	NIVO + chemo (N=226)	**Chemo (N=176)**	**NIVO + chemo (N=350)**	**Chemo (N=279)**
Median DOR, months (95% CI)	9.7 (8.2-12.4)	7.0 (5.6-7.9)	8.5 (7.7-10.2)	6.9 (5.8-7.2)

chemo, chemotherapy; CI, confidence interval; CPS, combined positive score; DOR, duration of response; HR, hazard ratio; IPI, ipilimumab; NIVO, nivolumab; OS, overall survival; PD-L1, programmed death-ligand 1

RESULTS: NIVO + IPI VS CHEMO

SECONDARY ENDPOINT: OS NOT MET

Data cut-off date: 27 May 2021 – minimum follow-up duration 24 months in the NIVO + chemo arm and 35.7 months in the NIVO + IPI arm

	PD-L1 CPS ≥5		All randomised patients	
	NIVO + IPI (N=234)	**Chemo (N=239)**	**NIVO + IPI (N=409)**	**Chemo (N=404)**
Median OS, months (95% CI)	11.2 (9.2-13.4)	11.6 (10.1-12.7)	11.7 (9.6-13.5)	11.8 (11.0-12.7)
HR (95% CI) P value	0.89 (0.71-1.10) 0.2302		0.91 (0.77-1.07) Not tested	
12-month OS rate, %	47	48	49	49
24-month OS rate, %	25	17	23	19
	NIVO + IPI (N=52)	**Chemo (N=86)**	**NIVO + IPI (N=76)**	**Chemo (N=141)**
Median DOR, months (95% CI)	13.2 (8.3-18.3)	6.9 (5.2-7.6)	13.8 (9.4-17.7)	6.8 (5.6-7.2)

chemo, chemotherapy; CI, confidence interval; CPS, combined positive score; DOR; duration of response; HR, hazard ratio; IPI, ipilimumab; NIVO, nivolumab; OS, overall survival; PD-L1, programmed death-ligand 1

RESULTS: TREATMENT-RELATED ADVERSE EVENTS

All treated patients[a], n (%)	NIVO + chemo (N=782)[b]		Chemo (N=767)[b]	
	Any grade	Grade 3-4	Any grade	Grade 3-4
Any TRAEs[c]	739 (95)	471 (60)	682 (89)	344 (45)
Serious TRAEs[c]	175 (22)	133 (17)	94 (12)	77 (10)
TRAEs leading to discontinuation[c]	300 (38)	141 (18)	188 (25)	70 (9)
Treatment-related deaths[d]	16[e] (2)		4[f] (<1)	

- **The most common grade 3-5 TRAEs included:**
  - **NIVO + chemo:** Neutropenia (15%), decreased neutrophil count (11%), anaemia (6%)
  - **NIVO + IPI:** Increased lipase (7%), increased amylase (4%), increased ALT/AST (4% each)
  - **Chemo:** Neutropenia (11-13%), decreased neutrophil count (9-10%), diarrhoea (3-4%)
- **The incidence of TRAEs in patients whose tumours expressed PD-L1 CPS ≥5 was consistent with all treated patients across arms**

[a]Patients who received ≥1 dose of study drug; [b]Assessed in all treated patients during treatment and for up to 30 days after the last dose of study treatment; [c]There were 4 grade 5 events in the NIVO + chemo arm, 1 case each of cerebrovascular accident, febrile neutropenia, gastrointestinal inflammation, and pneumonia. There were no grade 5 events in the chemo arm; [d]Treatment-related deaths were reported regardless of timeframe; [e]One event each of febrile neutropenia, gastrointestinal bleeding, gastrointestinal toxicity, infection, interstitial lung disease, intestinal mucositis, neutropenic fever, pneumonia, pneumonitis, pulmonitis, septic shock (capecitabine-related), and stroke; [f]One event each of diarrhoea-associated toxicity, asthenia and severe hiporexy, pulmonary thromboembolism, and interstitial pneumonia

ALT/AST, alanine aminotransferase/aspartate aminotransferase; chemo, chemotherapy; CPS, combined positive score; IPI, ipilimumab; NIVO, nivolumab; PD-L1, programmed death-ligand 1; TRAEs, treatment-related adverse events

Source: Moehler M, et al. Ann Oncol. 2020;31(suppl_4):abstr LBA6

RESULTS: TREATMENT-RELATED ADVERSE EVENTS

All treated patients[a], n (%)	NIVO + IPI (N=403)[b]		Chemo (N=389)[b]	
	Any grade	Grade 3-4	Any grade	Grade 3-4
Any TRAEs[c]	323 (80)	155 (38)	356 (92)	180 (46)
Serious TRAEs[c]	122 (30)	93 (23)	54 (14)	45 (12)
TRAEs leading to discontinuation[c]	88 (22)	68 (17)	101 (26)	37 (10)
Treatment-related deaths[d]	10[e] (2)		3[f] (<1)	

- **The most common grade 3-5 TRAEs included:**
  - **NIVO + chemo:** Neutropenia (15%), decreased neutrophil count (11%), anaemia (6%)
  - **NIVO + IPI:** Increased lipase (7%), increased amylase (4%), increased ALT/AST (4% each)
  - **Chemo:** Neutropenia (11-13%), decreased neutrophil count (9-10%), diarrhoea (3-4%)
- **The incidence of TRAEs in patients whose tumours expressed PD-L1 CPS ≥5 was consistent with all treated patients across arms**

[a]Patients who received ≥1 dose of study drug; [b]Assessed in all treated patients during treatment and for up to 30 days after the last dose of study treatment; [d]Treatment-related deaths were reported regardless of timeframe; [e]One event each of febrile neutropenia, gastrointestinal bleeding, gastrointestinal toxicity, infection, interstitial lung disease, intestinal mucositis, neutropenic fever, pneumonia, pneumonitis, pulmonitis, septic shock (capecitabine-related), and stroke; [f]One event each of diarrhoea-associated toxicity, asthenia and severe hiporexy, pulmonary thromboembolism, and interstitial pneumonia

ALT/AST, alanine aminotransferase/aspartate aminotransferase; chemo, chemotherapy; CPS, combined positive score; IPI, ipilimumab; NIVO, nivolumab; PD-L1, programmed death-ligand 1; TRAEs, treatment-related adverse events

Source: Moehler M, et al. Ann Oncol. 2020;31(suppl_4):abstr LBA6

TAKE-HOME MESSAGE

- NIVO + CHEMO = 1L standard of care in advanced GC/GEJC/EAC
  - CheckMate-649 with 24 months follow-up showed
    - Long-term OS and PFS benefit
    - Higher ORR and more durable responses
- NIVO + IPI did not significantly improve OS vs chemo in patients with PD-L1 CPS ≥5
- NIVO + IPI was stopped early
- No new safety signals identified with NIVO + chemo

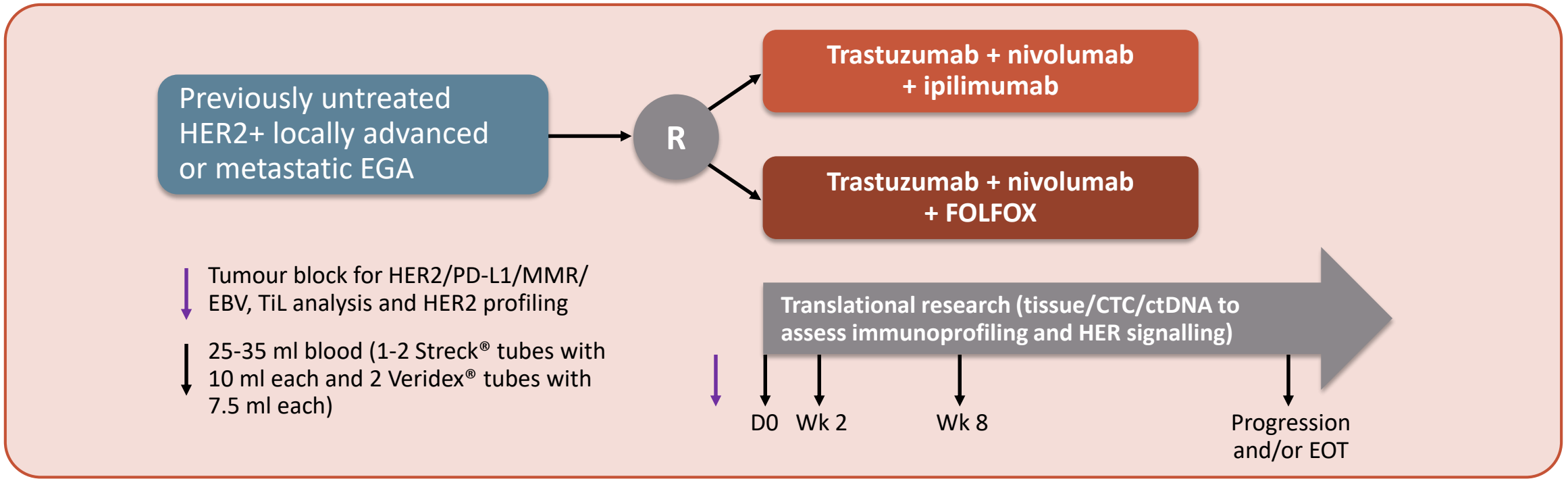
1L, first-line; chemo, chemotherapy; CPS, combined positive score; EAC, oesophageal adenocarcinoma; GC, gastric cancer; GEJC, gastro-oesophageal junction cancer; IPI, ipilimumab; NIVO, nivolumab; ORR, objective response rate; OS; overall survival; PFS, progression-free survival; PD-L1, programmed death-ligand 1

IPILIMUMAB OR FOLFOX IN COMBINATION WITH NIVOLUMAB AND TRASTUZUMAB IN PREVIOUSLY UNTREATED HER2 POSITIVE LOCALLY ADVANCED OR METASTASTIC ESOPHAGOGASTRIC ADENOCARCINOMA (EGA) – RESULTS OF THE RANDOMIZED PHASE 2 INTEGA TRIAL (AIO STO 0217)

Alexander Stein. ESMO 2021, Abstract #LBA54

DESIGN OF THE STUDY

INTEGA study (NCT03409848): randomised exploratory Phase 2 investigator-initiated trial with two experimental arms to assess therapy options for advanced or metastatic oesophagogastric adenocarcinoma in patients overexpressing human epidermal receptor type 2 (HER2 positive patients)



Between March 2018 and May 2020 a total of 97 patients were enrolled and 88 randomised (44 per arm)

CTC, circulating tumour cells; ctDNA, circulating tumour DNA; EBV, Epstein-Barr virus; EGA, oesophagogastric adenocarcinoma; EOT, end of treatment; FOLFOX, folinic acid + fluorouracil + oxaliplatin; HER2, human epidermal growth factor receptor 2; MMR, mismatch repair; PD-L1, programmed death-ligand 1; R, randomisation; TiL, tumour infiltrating T-lymphocytes

RESULTS

	All (N=88) ITT		CPS ≥1 (N=59)		CPS ≥5 (N=46)	
	Trast/NIVO /IPI (N=44)	Trast/NIVO /FOLFOX (N=44)	Trast/NIVO /IPI (N=31)	Trast/NIVO /FOLFOX (N=28)	Trast/NIVO /IPI (N=24)	Trast/NIVO /FOLFOX (N=22)
ORR	**32%**	**56%**	36%	**63%**	33%	**67%**
mPFS, months	**3.2**	**10.7**	2.2	**10.7**	2.2	**11**
12-months PFS rate	**15%**	**37%**	14%	**33%**	7%	**38%**
mDOR, months	**5.8**	**9.2**	–	**–**	–	**–**
mOS, months	**16.4**	**21.8**	16.4	**21.6**	12.5	**21.6**
12-months OS rate	**57%**	**70%**	54%	**71%**	53%	**72%**

CPS, combined positive score; DOR, duration of response; FOLFOX, folinic acid + fluorouracil + oxaliplatin; IPI, ipilimumab; ITT, intention to treat; NIVO, nivolumab; m, median; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; Trast, trastuzumab

TAKE-HOME MESSAGE

- Trast/NIVO/FOLFOX showed increased efficacy compared with the historical control from the ToGA[1] regimen
- Trast/NIVO/IPI did not improve 12-months OS rate over Trast/chemo
- Improvement of global health scale (EORTC QLQ C30) with Trast/Nivo/FOLFOX (within 8 weeks)

[1]Bang YJ et al, Lancet. 2010;376(9742):687-97

chemo, chemotherapy; EORTC QLQ C30, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Cancer 30; FOLFOX, folinic acid + fluorouracil + oxaliplatin; IPI, ipilimumab; NIVO, nivolumab; Trast, trastuzumab

INTEGRATE IIB: A RANDOMISED PHASE III OPEN LABEL STUDY OF REGORAFENIB + NIVOLUMAB VS STANDARD CHEMOTHERAPY IN REFRACTORY ADVANCED GASTRO-OESOPHAGEAL CANCER (AGOC)

Nick Pavlakis. ESMO 2021, 1438TiP

RATIONALE

- **Refractory AGOC:** No standard treatment after failure of 2L therapy

- **2L option:**
  - **Ramicirumab:** in patients unsuitable for chemotherapy
  - **Apatinib:** evidence for benefit beyond 2L but only in Chinese patients

- **There is strong need for more treatment options in patients with AGOC**

- **INTEGRATE IIb:**
  - **Will compare the effectiveness of regorafenib + nivolumab vs current standard chemotherapy in pre-treated patients with AGOC**
  - **Investigator-initiated study sponsored by the AGITG**

2L, second line; AGITG, Australasian Gastrointestinal Trials Group; AGOC, advanced gastro-oesophageal cancer

DESIGN OF THE STUDY

INTEGRATE IIb study (NCT04879368): randomised, open-label, phase 3 study of regorafenib + nivolumab vs chemotherapy in refractory AGOC

Key eligibility criteria

- Metastatic or locally recurrent gastro-oesophageal cancer
- Adenocarcinoma or undifferentiated carcinoma
- Evaluable according to RECIST v1.1 by CT scan performed within 21 days prior to randomisation
- Failed or intolerant to at least 2 lines of prior anti-cancer therapy (at least a platinum agent and a fluoropyrimidine analogue as single agents or in combination) for recurrent/metastatic disease
- HER2+ patients must have received prior treatment with trastuzumab
- ECOG PS 0 or 1

Stratification factors

- Geographic (Asia vs rest of world)
- Prior VEGF inhibitors (Yes vs No)
- Prior immunotherapy (Yes vs No)

N=450
R
2:1

n=300

REGONIVO
Regorafenib: 90 mg orally, once daily on days 1–21 of each 28 day cycle
Nivolumab: 240 mg IV every 2 weeks

n=150

CONTROL
Investigator choice chemotherapy: paclitaxel, docetaxel, irinotecan, or oral trifluridine/tipiracil (TAS102)

Primary endpoint

- OS

Secondary endpoints

- PFS
- OTRR
- DCR
- QoL
- Safety
- PK
- Biomarkers
- Immune therapy predictors: IHC, PD-L1, CPS, tissue TMB, and blood

Status: As of 30 August 2021, 29 patients enrolled globally

AGOC, advanced gastro-oesophageal cancer; CPS, combined positive score; DCR, disease control rate; ECOG PS, Eastern Cooperative Oncology Group performance status; IHC, immunohistochemistry; IV, intravenous; OS; overall survival; OTRR, objective tumour response rate; PD-L1, programmed death ligand-1; PFS; progression-free survival; PK, pharmacokinetics; QoL, quality of life; R, randomisation; REGONIVO, regorafenib in combination with nivolumab; TMB, tumour mutational burden; VEGF, vascular endothelial growth factor

REACH GI CONNECT VIA TWITTER, LINKEDIN, VIMEO & EMAIL OR VISIT THE GROUP'S WEBSITE

http://www.giconnect.info

Follow us on Twitter
@giconnectinfo

Follow the
GI CONNECT
group on LinkedIn

Watch us on the
Vimeo Channel
GI CONNECT

Email
antoine.lacombe
@cor2ed.com

GI connect®
POWERED BY COR2ED

GI CONNECT
Bodenackerstrasse 17
4103 Bottmingen
SWITZERLAND

Dr. Froukje Sosef MD

+31 6 2324 3636

froukje.sosef@cor2ed.com

Dr. Antoine Lacombe Pharm D, MBA

+41 79 529 42 79

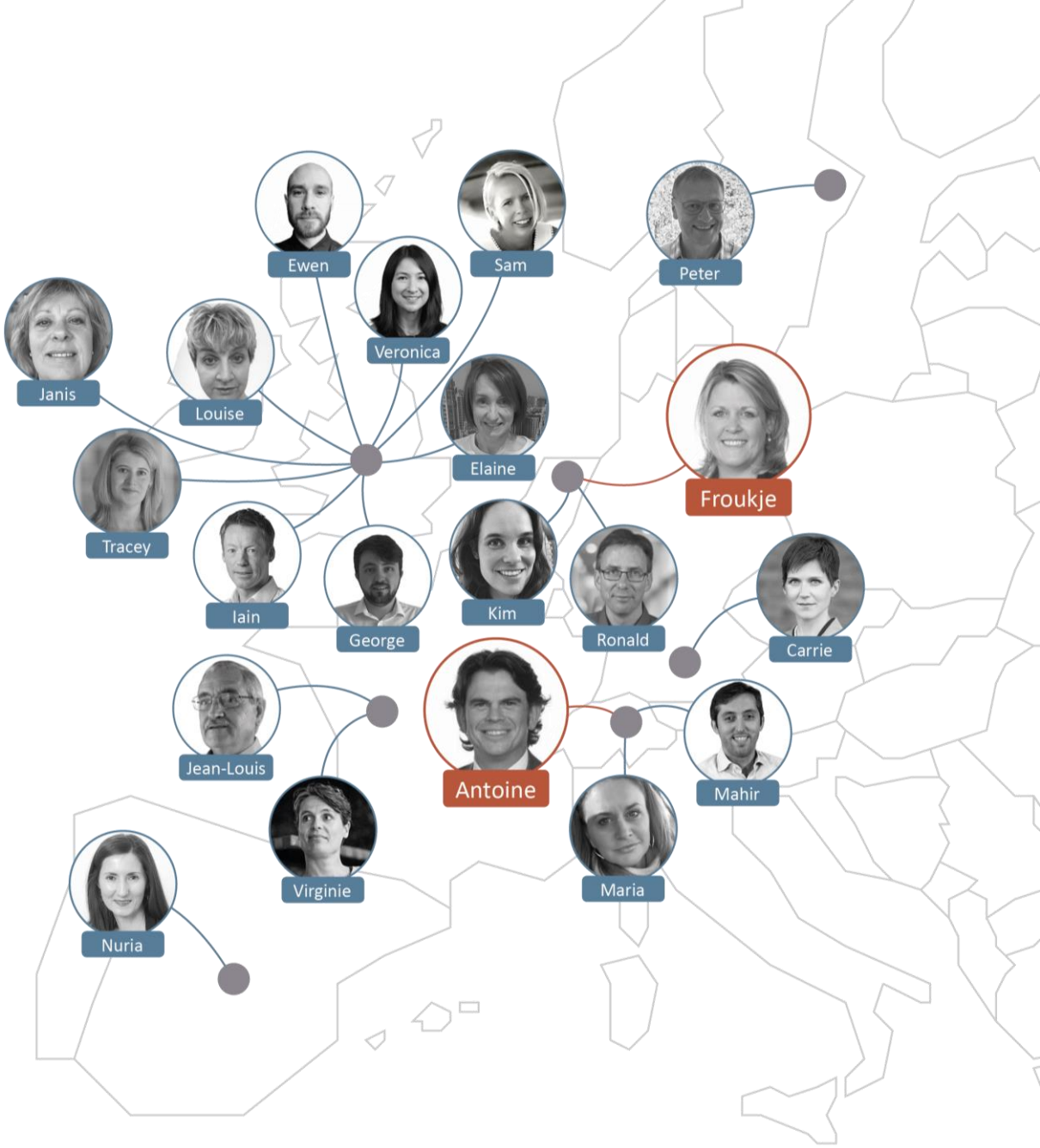
antoine.lacombe@cor2ed.com

Connect on
LinkedIn @GI CONNECT

Watch on
Vimeo @GI CONNECT

Visit us at
giconnect.info

Follow us on
Twitter @giconnectinfo



Heading to the heart of Independent Medical Education Since 2012