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MEETING SUMMARY
WCGIC 2020, VIRTUAL MEETING

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HIGHLIGHTS FROM GI CONNECT
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ANCHOR CRC: A SINGLE-ARM, PHASE 2 STUDY OF ENCORAFENIB, BINIMETINIB PLUS CETUXIMAB IN PREVIOUSLY UNTREATED BRAF V600E–MUTANT METASTATIC COLORECTAL CANCER

Grothey A, et al.

WCGIC 2020. Abstract #LBA-5. Oral presentation

BACKGROUND AND STUDY DESIGN

BRAF^{V600E} mutation occurs in 10–15% of patients with mCRC, with poor prognosis

New effective therapies are needed

ANCHOR CRC: phase 2 study in first line BRAF^{V600E} mCRC patients

Eligibility criteria

- mCRC with BRAF^{V600E} mutation
- Untreated in metastatic setting
- No prior treatment with any RAF/MEK/anti-EGFR inhibitors
- ECOG PS 0-1

STAGE 1 (n=40)
Encorafenib + binimetinib + cetuximab

STAGE 2 (n=50)
Encorafenib + binimetinib + cetuximab

Treatment until

- Disease progression
- Unacceptable toxicity
- Consent withdrawal

Continued follow up for survival every 3 months

Primary objective and endpoint: confirmed ORR (investigator assessed)
Secondary endpoints: PFS, OS, safety, QoL, PK

Cut off date: 6 February 2020. Stage 1: n=41; 9 ongoing (22%), 32 discontinued (78%) due to progressive disease (54%)/AEs (10%)/physician decision (7%)/death (5%)/protocol deviation (2%)

AEs, adverse events; ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, epidermal growth factor receptor; mCRC, metastatic colorectal cancer; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PK, pharmacokinetic; QoL, quality of life

RESULTS FOR STAGE 1

Median time on treatment: 4.9 months

Primary endpoint	Patients (n=40), n (%) [95% CI]
Confirmed ORR	20 (50%) [34–66]
Best overall confirmed response	
Complete response	0
Partial response	20 (50%)
Stable disease	14 (35%)
Progressive disease	4 (10%)
Not evaluable	2 (5%)

DCR = 85%

Secondary endpoint	Patients (n=40)	
Median PFS, months (95% CI)	4.9 (4.4–8.1)	
Overall safety summary for stage 1	**Patients (n=41)**	
	All grades n (%)	**Grade ≥3 n (%)**
Any AE	41 (100%)	28 (68%)
Any SAE	23 (56%)	20 (49%)
Any AE leading to dose interruption or dose reduction	28 (68%)	18 (44%)
Any AE leading to discontinuation	8 (20%)	7 (17%)
Any AE leading to death	3 (7%)	3 (7%)

AE, adverse event; CI, confidence interval; DCR; disease control rate; ORR; objective response rate; PFS, progression-free survival; SAE, serious adverse event

CONCLUSIONS

- **ANCHOR study** = first prospective study using a BRAF inhibitor based therapy in 1L $BRAF^{V600E}$-mutant mCRC

- **High confirmed ORR (50%)** is observed
- Median PFS = 4.9 months
- Triplet combination well **tolerated and manageable safety profile** with no unexpected toxicities
- Stage 1: **minimal number of confirmed responses reached**

  → Stage 2 is ongoing with enrolment of additional patients
- Results with 95 patients expected in 2021

1L, first line; mCRC, metastatic colorectal cancer; ORR, objective response rate; PFS, progression-free survival

FIRST-LINE LIPOSOMAL IRINOTECAN + 5 FLUOROURACIL/LEUCOVORIN + OXALIPLATIN IN PATIENTS WITH PANCREATIC DUCTAL ADENOCARCINOMA: LONG-TERM FOLLOW-UP RESULTS FROM A PHASE 1/2 STUDY

Wainberg ZA, et al.

WCGIC 2020. Abstract #LBA-1. Oral presentation

BACKGROUND & STUDY DESIGN

First line treatment options for mPDAC:

- Gemcitabine + albumin-bound paclitaxel particles
- FOLFIRINOX (non-liposomal irinotecan + 5-FU + leucovorin + oxaliplatin)

Second line treatment option for mPDAC:

- Liposomal irinotecan + 5-FU + leucovorin (after gemcitabine-based therapy)

The abstract presents the **long-term follow-up results** of the open-label, two-part phase 1/2 study assessing **liposomal irinotecan + 5-FU + leucovorin + oxaliplatin (NALIRIFOX) in treatment-naïve patients with locally advanced or metastatic PDAC**

Part 1A
Dose exploration
NALIRIFOX*
(n=31)

Cohort	liposomal irinotecan	5-FU	leucovorin	oxaliplatin
A (n=7)	**70**	2400	400	**60**
B (n=7)	**50**	2400	400	**60**
C (n=10)	**50**	2400	400	**85**
D (n=7)	**55**	2400	400	**70**

Part 1B
Dose expansion
NALIRIFOX*
(50/2400/400/60)
(n=25)

Pooled population
50/60**
NALIRIFOX*
(50/2400/400/60)
(n=32)

Primary objectives: safety and tolerability of NALIRIFOX and characterize DLTs with NALIRIFOX
Secondary objectives: PFS, OS (RECIST V1.1) + other clinical responses: BOR, ORR, DCR at Week 16, DoR

*Regimen: NALIRIFOX on days 1 and 15 of each 28-day cycle. **Pooled population 50/60 = all patients who received liposomal irinotecan 50 mg/m^2 (free base), 5-FU 2440 mg/m^2, leucovorin 400 mg/m^2 and oxaliplatin 60 mg/m^2.
5-FU, fluorouracil; BOR; best overall response; DCR, disease control rate; DLT, dose-limiting toxicity; DoR, duration of response; mPDAC, metastatic pancreatic ductal adenocarcinoma; ORR, overall response rate; OS; overall survival; PFS, progression-free survival; RECIST, response evaluation criteria in solid tumours

RESULTS

Data cut-off date: 26 February 2020

Primary endpoint	Cohort A (n=7)	Cohort B (n=7)	Cohort C (n=10)	Cohort D (n=7)
Tolerability assessment during dose exploration (reason) and details of DLTs	Not tolerable (DLTs) DLTs in 2 patients: neutropenia infection (1), neutropaenic sepsis (1)	Tolerable (DLTs and cumulative safety data) DLTs in 1 patient: febrile neutropenia (1)	Not tolerable (DLTs) DLTs in 2 patients: diarrhoea (2), vomiting (1), anal fissure (1), anal inflammation (1), proctalgia (1)	Not tolerable (cumulative safety data: TEAEs of grade ≥3) No DLTs

Secondary endpoints	Pooled population 50/60* (n=32)
Median PFS, months (95% CI)	9.2 (7.69–11.96)
Median OS, months (95% CI)	12.6 (8.74–18.69)
ORR, % (95% CI)	34.4 (18.6–53.2)
DCR 16 weeks, % (95% CI)	71.9 (53.3–86.3)
Median DoR, months (95% CI)	9.4 (3.52–NE)

***Pooled population 50/60** = all patients who received liposomal irinotecan 50 mg/m^2 (free base), 5-FU 2440 mg/m^2, leucovorin 400 mg/m^2 and oxaliplatin 60 mg/m^2

5-FU, fluorouracil; CI, confidence interval; DCR, disease control rate; DLT, dose-limiting toxicity; DoR, duration of response; NE, not estimated; ORR; overall response rate; OS, overall survival; PFS, progression-free survival; TEAE, treatment-emergent adverse event

CONCLUSIONS

RESULTS FROM PHASE 1/2 SUGGEST THAT NALIRIFOX (50/60)[1] IS TOLERABLE FOR PATIENTS WITH PREVIOUSLY UNTREATED LOCALLY ADVANCED MPDAC

- Primary objective: **no new safety signals** were identified
- Secondary objective on **antitumour activity was promising**
  - Median PFS = 9.2 months
  - Median OS = 12.6 months
- A phase 3 study (NAPOLI-3, NCT04083235) is ongoing to assess efficacy in adults with previously untreated mPDAC

[1] 50/60 regimen = liposomal irinotecan: 50 mg/m^2, 5-fluorouracil: 2400 mg/m^2, leucovorin: 400 mg/m^2, oxaliplatin: 60 mg/m^2 on days 1 and 15 of each 28-day cycle
NALIRIFOX, liposomal irinotecan + 5-fluorouracil + leucovorin + oxaliplatin; mPDAC, metastatic pancreatic ductal adenocarcinoma; OS, overall survival; PFS, progression-free survival

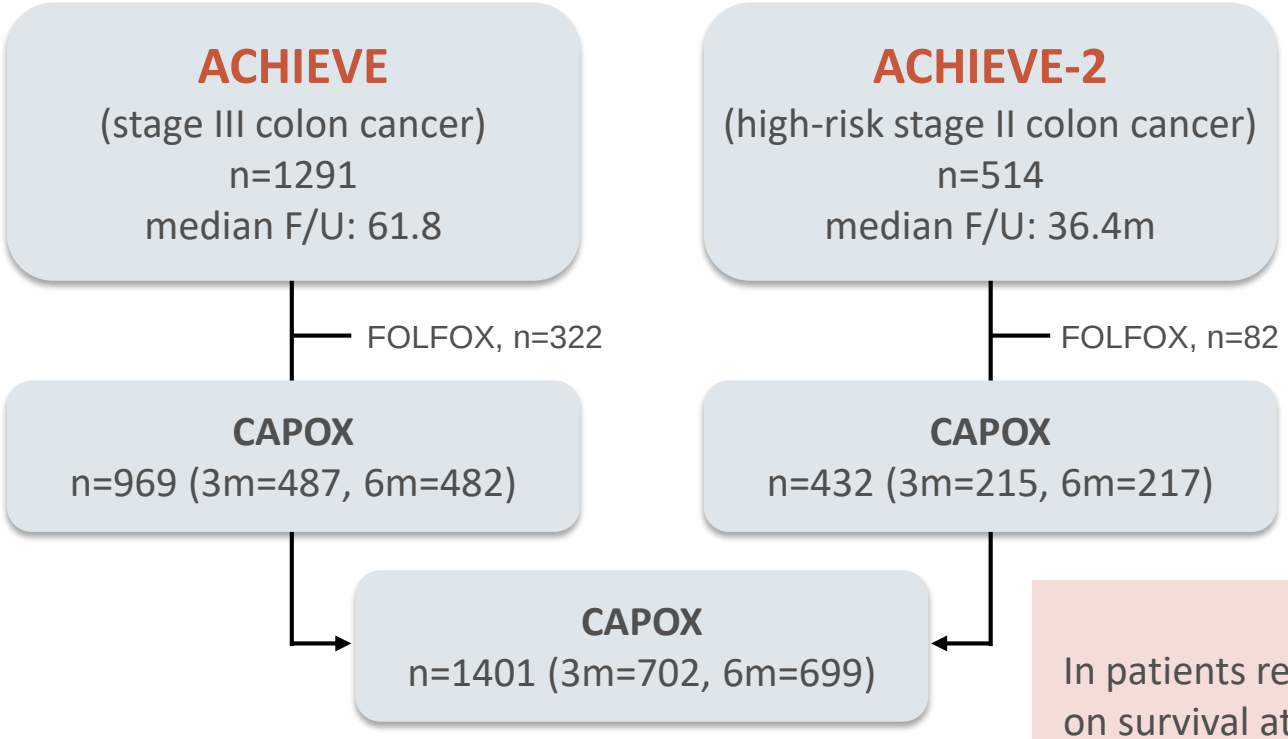
RELATIVE IMPACT OF T4 AND N2 ON THE EFFICACY OF 3 VERSUS 6 MONTHS OF ADJUVANT CAPOX FOR HIGH-RISK STAGE II AND STAGE III COLON CANCER: ACHIEVE AND ACHIEVE-2 TRIALS

Yamanaka T, et al.

WCGIC 2020. Abstract #O-16. Oral presentation

BACKGROUND AND STUDY DESIGN

- Based on **results of IDEA** collaboration: **early colon cancer treatment recommendations are based on T and N** in clinical practice guidelines



Distribution of 1401 patients by T and N

	N0	N1	N2
T1		56	**5**
T2		84	**12**
T3	273	414	**134**
T4	**159**	**172**	**92**

Purpose of the study

In patients receiving CAPOX, which has a stronger impact on survival at 3 and 6 months: T4 or N2?

- The abstract presents the results from patients receiving 3m and 6m CAPOX

3m, 3 months; 6m, 6 months; CAPOX, capecitabine + oxaliplatin; F/U, follow up; FOLFOX, folinic acid (leucovorin) + fluorouracil (5-FU) + oxaliplatin; m, months

RESULTS: 3M AND 6M CAPOX BY T AND N

Duration	3-yr DFS	HR (95% CI)
3m	95.8%	0.82 (0.32–2.08)
6m	92.9%	1.00

Duration	3-yr DFS	HR (95% CI)
3m	75.8%	0.88 (0.50–1.56)
6m	71.0%	1.00

Distribution of 1401 patients by T and N

	N0	N1	N2
T1		56	5
T2		84	12
T3	273	414	134
T4	159	172	92

Duration	3-yr DFS	HR (95% CI)
3m	89.1%	0.77 (0.54–1.11)
6m	84.3%	1.00

Duration	3-yr DFS	HR (95% CI)
3m	75.7%	1.32 (0.66–2.63)
6m	80.6%	1.00

Duration	3-yr DFS	HR (95% CI)
3m	61.9%	1.15 (0.79–1.70)
6m	68.1%	1.00

3m, 3 months; 3-yr DFS, 3-year disease-free survival; 6m, 6 months; CAPOX, capecitabine + oxaliplatin; CI, confidence interval; HR, hazard ratio

CONCLUSIONS

TNM STAGING OF COLORECTAL CANCER SHOULD BE RECONSIDERED BY T STAGE WEIGHTING

- T stage affects colon cancer survival more significantly than N stage
- T4 had a negative impact on the efficacy of 3m CAPOX
- N2T1–T3 (and not T4) did not have a negative impact on the efficacy of 3m CAPOX
- T4 tumours showed a different pattern of relapse (results not shown)
- Further confirmation in large sample data are needed

- **If these data are confirmed in IDEA consortium for stage III:**
  - 3 months CAPOX could be a treatment option for N2T1-T3
  - 6 months CAPOX could be a treatment option for N1T4 or N2T4
- **For stage II high risk:** difficult to validate

3m, 3 months; CAPOX, capecitabine + oxaliplatin

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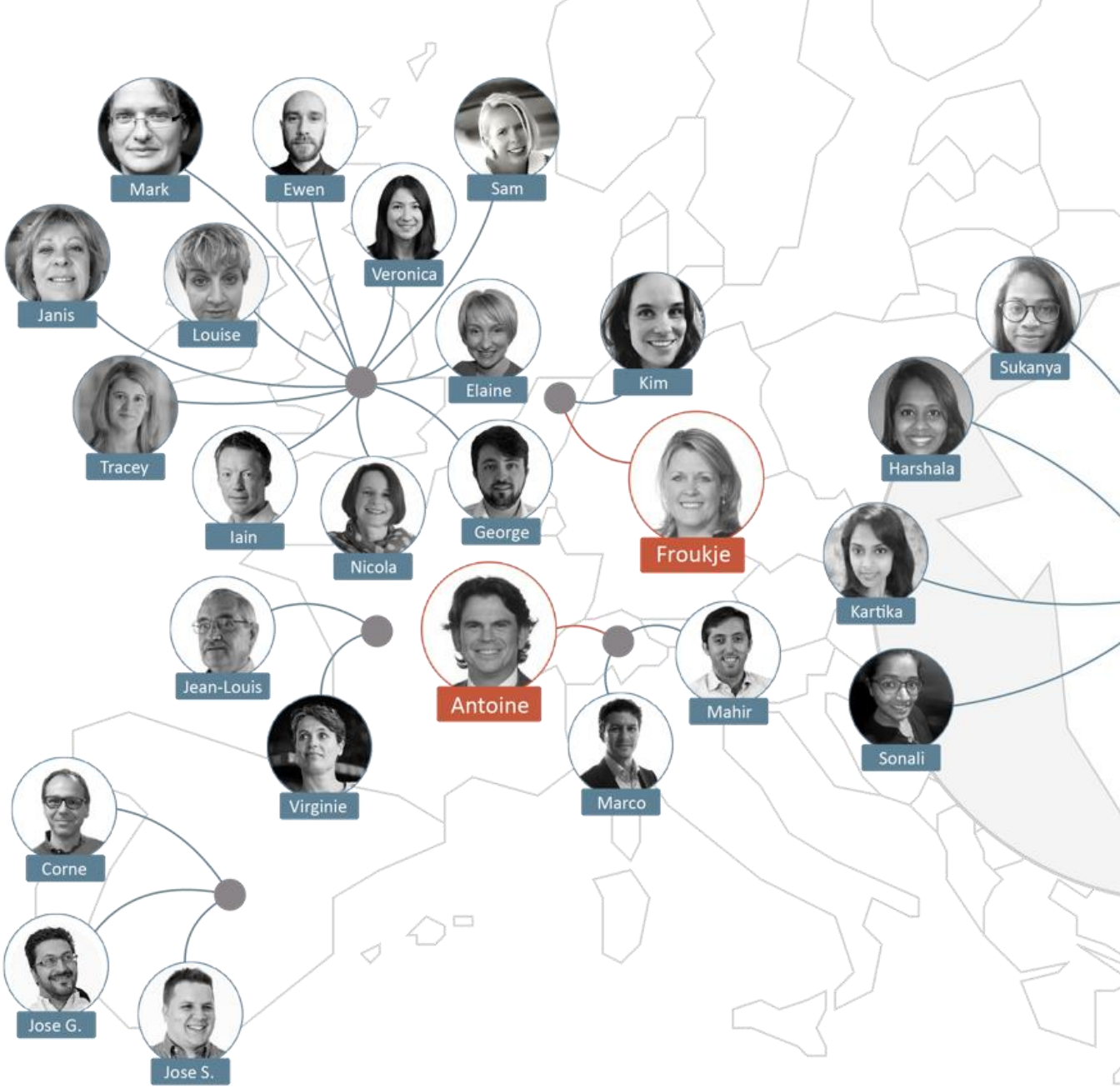

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