Abstract PCN49

INDIRECT COMPARISON OF HEALTH-RELATED QUALITY OF LIFE DATA FOR PATIENTS WITH TREATMENT-REFRACTORY METASTATIC COLORECTAL CANCER TREATED WITH TRIFLURIDINE/TIPIRACIL (PRECONNECT TRIAL) COMPARED WITH BEST-SUPPORTIVE CARE AND REGORAFENIB (CORRECT TRIAL)

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KEY TAKE-AWAYS

- **As there are no studies directly comparing the health-related quality of life (HRQoL) of patients with metastatic colorectal cancer (mCRC) receiving trifluridine/tipiracil (FTD/TPI; TAS-102) versus regorafenib, we performed an indirect comparison using individual patient data from the ongoing single-arm PRECONNECT trial and published data from the randomized placebo-controlled CORRECT trial.**
- **Quality of life (QoL) was better in patients treated with FTD/TPI compared with regorafenib (as measured by the EuroQol 5-Dimension questionnaire [EuroQol-5D] visual analog scale [VAS] and the Quality of Life Questionnaire-Core 30 [QLQ-C30] global health status).**
- **Compared with placebo, the QoL for patients treated with FTD/TPI was greater when measured by the EuroQol-5D VAS, and comparable when measured by the QLQ-C30 global health status.**
- **This indirect comparison suggests that, in terms of QoL, FTD/TPI may have an advantage over regorafenib.**

BACKGROUND

- FTD/TPI is registered in over 70 countries worldwide, including the USA, Japan, Australia, and several European countries, for the management of patients with mCRC who have been previously treated with, or are not considered candidates for, standard therapies.
- Regorafenib, a tyrosine kinase inhibitor, is also indicated in the same setting as FTD/TPI.[1]
- Preliminary data using patient-reported outcomes from the international, phase 3b early-access PRECONNECT study (NCT03306394) suggest that patients with pretreated mCRC can maintain their QoL while receiving FTD/TPI treatment.[2]
- To date, there are no studies directly comparing the QoL for mCRC patients being treated with FTD/TPI versus regorafenib and/or best supportive care (BSC).
- Thus, we performed an indirect comparison using QoL data from patients receiving FTD/TPI in the ongoing single-arm PRECONNECT trial (data cut-off, 30 September 2018) and from patients who received regorafenib or placebo in the randomized CORRECT trial (NCT01103323).[3]

METHODS

- Potential studies were reviewed for inclusion based on a range of study and baseline patient characteristics in order to ensure commonality between the studies, including the administration and reporting of a QoL instrument in common with PRECONNECT.
- Two randomized, placebo-controlled trials (CORRECT[3] and CONCUR[4]) were considered for inclusion; however, CONCUR was excluded as it was conducted only in Asian countries, meaning the patient population was not comparable to that of PRECONNECT.
- The chosen study, CORRECT (NCT01103323), compared regorafenib plus best supportive care with placebo plus best supportive care.[3] Only non-Japanese patients from CORRECT were considered comparable to the PRECONNECT population and included in the analysis.
- QoL data from the CORRECT study were reported as the time-adjusted area under the curve (AUC) of QoL scores in patients receiving regorafenib compared with those receiving placebo.[5]
- To generate comparable data from PRECONNECT, time-adjusted AUC values were calculated for the QLQ-C30 global health status scores and the EuroQol-5D VAS scores from patients receiving FTD/TPI in PRECONNECT.
- Match-adjusted indirect comparisons between FTD/TPI and regorafenib or placebo were performed[6,7] using the individual patient AUC data in PRECONNECT and the published summary statistics for AUC from CORRECT.[5]
- Key characteristics for matching were determined based on available data, and were: age, body mass index, gender, Eastern Cooperative Oncology Group Performance Status, number of previous lines of therapy for metastatic disease (≤2; >2), time from diagnosis of metastasis (<18 months; ≥18 months) and KRAS mutation.[8]

RESULTS

- The calculated effective sample sizes[8] were not markedly smaller than the original sample sizes, indicating that the values estimated in this analysis are reliable and that the PRECONNECT and CORRECT trials are comparable **(Table 1).**

Table 1. Estimated FTD/TPI effective sample sizes for comparison with placebo and with regorafenib data from CORRECT[8]

	Effective Sample Size for Comparison with Placebo + BSC in CORRECT	Effective Sample Size for Comparison with Regorafenib + BSC in CORRECT
QLQ-C30 Global Health Status (n=672)	509 (76%)	623 (93%)
EQ-5D VAS (n=654)	494 (75%)	606 (93%)

BSC, best supportive care; EQ-5D, EuroQol 5-Dimension questionnaire; QLQ-C30, QoL Questionnaire-Core 30

- Baseline characteristics of the patients in the two study cohorts are shown in **(Table 2)**.

Table 2. Baseline characteristics in PRECONNECT and CORRECT (non-Japanese patients)

	PRECONNECT	CORRECT: non-Japanese[8]	
	FTD/TPI (n=793)	Regorafenib + BSC (n=438)	Placebo + BSC (n=222)
Median age, years	62	61	61
Median body mass index, kg/m²	24.9	25.0	26.2
Male, n (%)	475 (59.9)	264 (60.3)	137 (61.7)
ECOG performance status >0, n (%)	383 (48.3)	214 (48.9)	100 (45.0)
>2 previous systemic anti-cancer therapies for metastatic disease, n (%)	503 (63.4)	320 (73.1)	164 (73.9)
Time from diagnosis of metastatic disease to randomization/inclusion ≥18 months, n (%)	653 (82.3)	355 (81.1)	175 (78.8)
KRAS mutation, n (%)*			
Wild type	328 (41.4)	179 (40.9)	76 (34.2)
Mutant type	390 (49.2)	234 (53.4)	143 (64.4)
Unknown	75 (9.5)	25 (5.7)	3 (1.4)

BSC, best supportive care; ECOG, Eastern Cooperative Oncology Group; FTD/TPI, trifluridine/tipiracil
*Percentages may not total 100 due to rounding

- Median baseline QoL values were similar across the three treatment arms in PRECONNECT and CORRECT:
  - The global health status median score was 67 for all three groups.
  - The VAS median score was 70 for trifluridine/tipiracil, 69 for regorafenib, and 70 for placebo.
- When matched either to placebo or regorafenib patient characteristics, the mean QoL AUC values for patients receiving FTD/TPI in PRECONNECT were higher than the published values for patients receiving placebo **(Table 3)** or regorafenib **(Table 4)** in CORRECT **(Figure 1)**.[5]
- The differences between the matched FTD/TPI QLQ-C30 global health status AUC values and the placebo and regorafenib values were 5.3 (63.0 and 57.7, respectively; **Table 3**) and 6.3 (62.6 and 56.3, respectively; **Table 4**); these values are both greater than the established minimally important difference of 5.[9]
- For the EQ-5D VAS AUC values, the difference between FTD/TPI and placebo was 6.3 (65.8 and 59.5, respectively; **Table 3**) and for regorafenib 6.8 (65.3 and 58.5, respectively; **Table 4**); these values are close to the established minimally important difference of 7.[10]
- There was no overlap of the 95% confidence intervals for the EQ-5D VAS AUC values for placebo-matched FTD/TPI and placebo **(Table 3; Figure 1A)**.
- When comparing regorafenib-matched FTD/TPI with regorafenib, there was no overlap of the 95% confidence intervals for the EQ-5D VAS AUC values and the QLQ-C30 global health status AUC values **(Table 4; Figure 1)**.

RESULTS

Table 3. Mean time-adjusted area under the curve (AUC) QoL values for patients receiving FTD/TPI in PRECONNECT compared with those receiving placebo + BSC in CORRECT[5]

Mean time-adjusted AUC (95% CI)	PRECONNECT FTD/TPI		CORRECT: non-Japanese[5]
	Not matched	After matching to CORRECT Placebo	Placebo + BSC
QLQ-C30 Global Health Status	62.9 (61.5, 64.3)	63.0 (61.7, 64.4)	57.7 (53.4, 62.0)
EQ-5D VAS	65.8 (64.5, 67.2)	65.8 (64.4, 67.1)	59.5 (55.4, 63.7)

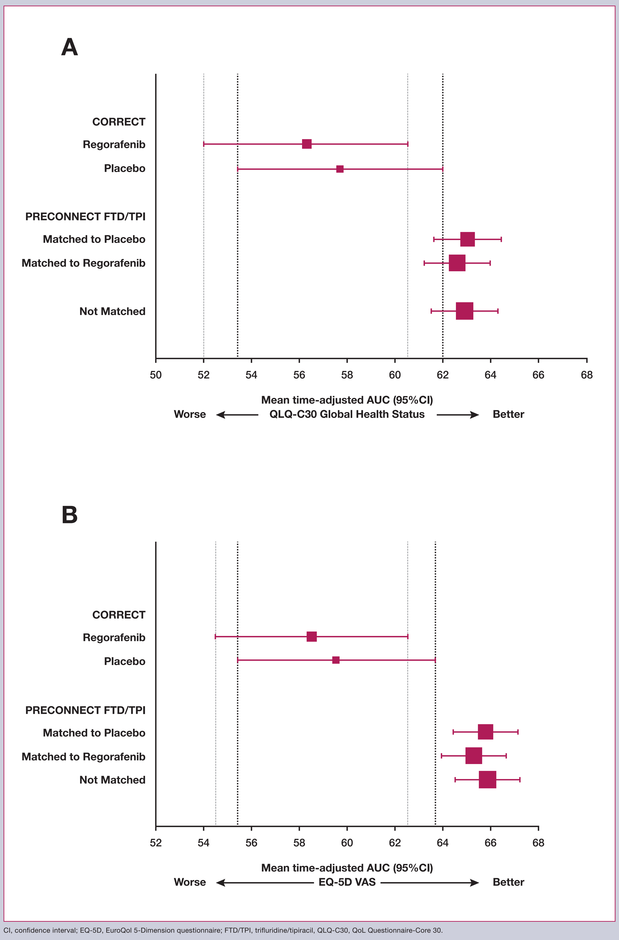
BSC, best supportive care; CI, confidence interval; EQ-5D, EuroQol 5-Dimension questionnaire; FTD/TPI, trifluridine/tipiracil; QLQ-C30, Quality of Life Questionnaire-Core 30

Table 4. Mean time-adjusted area under the curve (AUC) QoL values for patients receiving FTD/TPI in PRECONNECT compared with those receiving regorafenib in CORRECT[5]

Mean time-adjusted AUC (95% CI)	PRECONNECT FTD/TPI		CORRECT: non-Japanese[5]
	Not matched	After matching to CORRECT Regorafenib	Regorafenib + BSC
QLQ-C30 Global Health Status	62.9 (61.5, 64.3)	62.6 (61.2, 64.0)	56.3 (52.0, 60.5)
EQ-5D VAS	65.8 (64.5, 67.2)	65.3 (63.9, 66.6)	58.5 (54.5, 62.5)

BSC, best supportive care; CI, confidence interval; EQ-5D, EuroQol 5-Dimension questionnaire; FTD/TPI, trifluridine/tipiracil; QLQ-C30, Quality of Life Questionnaire-Core 30

Figure 1. Mean time-adjusted (A) QLQ-C30 Global Health Status and (B) EuroQol-5D-3L Visual Analog Scale area under the curve (AUC) values for patients receiving FTD/TPI in PRECONNECT compared with those receiving placebo or regorafenib in CORRECT[5]



CI, confidence interval; EQ-5D, EuroQol 5-Dimension questionnaire; FTD/TPI, trifluridine/tipiracil, QLQ-C30, QoL Questionnaire-Core 30.

LIMITATIONS

- This analysis was conducted using only one eligible study from the published literature to compare with PRECONNECT individual patient data. It is not known how generalizable the results may be across other mCRC trials that are collecting QoL data.
- Matching was limited to those characteristics reported in the CORRECT published data and also collected in PRECONNECT. Any comparison of non-randomized treatment groups may be biased by observed and unobserved cross-trial differences. Although the use of matching-adjusted indirect comparison can remove or reduce these differences, some residual confounding may remain.

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DISCLOSURES

MG, KC and XS are employees of Adelphi Values; SGM, MB, LV, and NM are employees of Servier; JT has received honoraria for speaker/advisory roles from Servier, Roche, Lilly, Celgene, Shire, Amgen, Sanofi, Merck, Lilly, and Sirtex; AF has received compensation for participation to advisory boards and research grants to his institution from Amgen, Bayer, Merck, MSD, Roche, Lilly, Servier, and Bristol; LW has received honoraria for consulting or advisory roles from Servier and Halozyme, has served on a Speakers' Bureau for Amgen, and holds patents, royalties, and intellectual project from Cervico.

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