Encore presentation at NCODA Fall Summit | October 25-27 | Orlando, FL
This poster was previously presented at the ESMO World Congress on Gastrointestinal Cancer 2023 | June 28-Jul 1 | Barcelona, Spain

Health-related quality of life associated with trifluridine/tipiracil in combination with bevacizumab in refractory metastatic colorectal cancer: an analysis of the phase III SUNLIGHT trial

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Background

- The SUNLIGHT trial is a large, international, open-label, randomised, phase 3 study comparing trifluridine/tipiracil (FTD/TPI) plus bevacizumab (bev) to FTD/TPI monotherapy in patients with refractory metastatic colorectal cancer (mCRC)[1,2]
- This trial demonstrated that FTD/TPI + bev significantly improved overall survival (OS) and progression-free survival (PFS) vs. FTD/TPI monotherapy, along with a predictable and manageable safety profile[1]
- Median OS was improved by 3.3 months with FTD/TPI + bev vs. FTD/TPI monotherapy: 10.8 months vs. 7.5 months, respectively; hazard ratio (HR): 0.61 (95% CI: 0.49, 0.77; p<0.001)
- Median PFS was improved by 3.2 months in the FTD/TPI + bev arm vs. FTD/TPI monotherapy: 5.6 months vs. 2.4 months, respectively; HR: 0.44 (95% CI: 0.36, 0.54; p<0.001)

Objective

- To report health-related quality of life (HRQoL) outcomes from the SUNLIGHT trial

Methods

- In SUNLIGHT (NCT04737187), patients were randomised (1:1) to receive FTD/TPI (35 mg/m^2 twice daily on days 1-5 and 8-12 of each 28-day cycle) alone, or combined with bev (5 mg/kg on days 1 and 15)
- Data presented are from a HRQoL sub-analysis, evaluating EORTC QLQ-C30 (a cancer-specific QoL measure composed of functional, symptom and global health status [GHS] scales) and EuroQol EQ-5D-5L (a more general QoL measure, assessing mobility, self-care, usual activities, pain/discomfort and anxiety/depression, and patient's self-rated health [visual analogue score/VAS])
- HRQoL was evaluated at baseline, at each cycle, and at withdrawal visit using EORTC QLQ-C30 and EuroQol EQ-5D-5L questionnaires
- QoL outcomes analysis included change from baseline and time until definitive deterioration of ≥10 points in GHS and sub-scale scores for the QLQ-C30; and change from baseline in VAS and health utility index for the EQ-5D-5L

Results

- Among 492 randomised patients, 239 and 241 (i.e., a total of >97.6%) had QoL data at baseline in the FTD/TPI + bev and FTD/TPI arms, respectively
- HRQoL data are presented for the first 6 cycles, as questionnaire completion rates dropped to less than 10% after this time-point, which did not allow for a meaningful interpretation of the results
- Cancer-related (QLQ-C30) and general (EQ-5D-5L) HRQoL were maintained from baseline to cycle 6, and no clinically relevant changes in mean scores were observed in any sub-domains (Figures 1 and 2)
- QLQ-C30 GHS scores also showed no deterioration in either arm
- Patients receiving FTD/TPI + bev had a reduced risk of GHS definitive worsening of more than 10 points (median time to worsening in GHS was 8.5 months in the FTD/TPI + bev arm vs. 4.7 months in the FTD/TPI arm [HR: 0.50; 95% CI: 0.38, 0.65]; Figure 3A) and in all scales and subscales (Figure 3B)
- In a sensitivity analysis considering disease progression as a definitive deterioration measured by QLQ-C30, HRQoL deteriorated significantly later: median time to deterioration in the FTD/TPI + bev arm was 4.5 months vs. 2.07 months in the FTD/TPI monotherapy arm (HR: 0.49; 95% CI: 0.40, 0.60), consistently favouring the FTD/TPI + bev arm
- A similar result was observed with the EQ-5D-5L utility score and VAS, showing that HRQoL deteriorated later in patients treated with FTD/TPI + bev compared to those treated with FTD/TPI monotherapy

Results

EORTC QLQ-C30

Figure 1A: Change of score from baseline (functional scales and GHS)

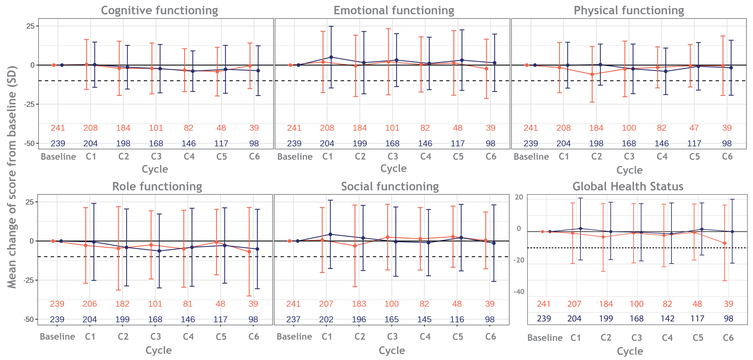
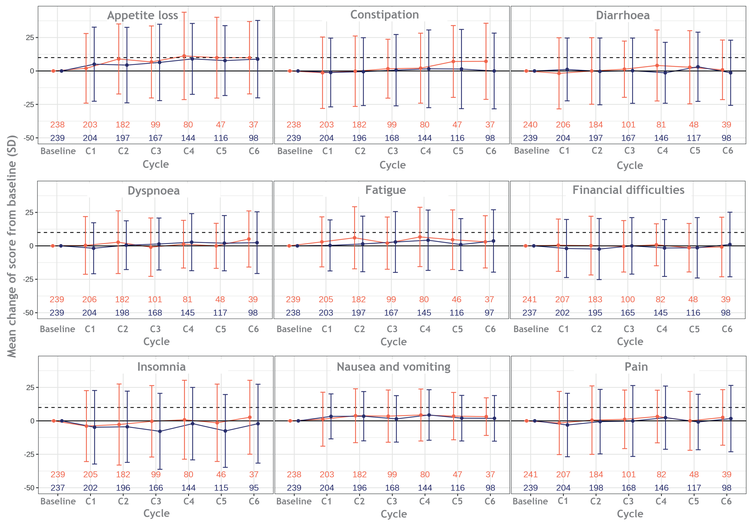
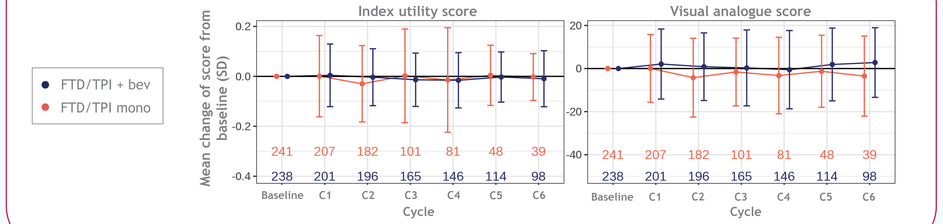


Figure 1B: Change from baseline (symptom scales)



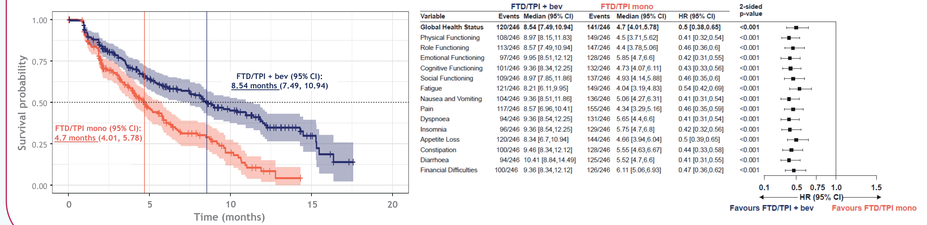
EORTC EQ-5D-5L

Figure 2: Change from baseline



EORTC QLQ-C30

Figure 3: Time to deterioration (A) of GHS; (B) GHS, functional and symptom scores



Conclusions

- The OS/PFS benefits of FTD/TPI + bev as third-line treatment of mCRC are associated with maintenance of QoL
- EQ-5D-5L and QLQ-C30 HRQoL were maintained from baseline to cycle 6 with no clinically relevant changes in mean scores observed in any sub-domains
- There was a trend towards a more prolonged time to definitive deterioration of HRQoL scales and subscales with FTD/TPI + bev than with FTD/TPI monotherapy

References
1. Prager GW, et al. N Engl J Med 2023;388:1657-1667;
2. Tabernero J, et al. Future Oncol 2021;17:1977-1985.

Acknowledgements: On behalf of all SUNLIGHT investigators, we thank and acknowledge all the patients, their families, and site personnel for participating in the study. SUNLIGHT was funded by Servier and Taiho Oncology Inc. GWP: Consulting/advisory, Amgen, Daiichi Sanyo Europe GmbH, Incyte, Merck Serono, Pierre Fabre, Roche/Genetech, Servier, Lilly O., Bayer US LLC. JT: Consultancy/advisory, Roche, Merck KGaA, Amgen, Servier, MSD, Pierre Fabre, Novartis, AstraZeneca, BMS: Speaker's Bureau, Servier, Amgen, Merck, MSD, Pierre Fabre. MF: Consultancy/advisory, Amgen, Taiho Pharm., Bayer, Pfizer, Seagen, GSK, Incyte, Nouscom, Roche/Genentech, Mirati Ther. BMS, Eisai, Merck; Speaker's bureau, Guardant Health: Honoraria, Amgen: Research Funding, Amgen, Verastem. FC: Consulting/advisory, Amgen, Merck KGaA, Pfizer, Roche/Genentech, Bayer US, LLC; Research funding, Amgen, BMS, Ipsen, Merck KGaA, Merck Sharp & Dome, Roche/Genetech, Servier, Symphogen; Bayer US, LLC. EVC: Consulting/advisory, Bayer, Lilly, Roche, Servier, BMS, MSD, Merck KGaA, Novartis, AstraZeneca, Array BioPharm, Daiichi Sankyo, Pierre Fabre, Taiho Pharm., Incyte, Astellas, GSK, Nordic Gp, Pfizer, Takeda, ALX Oncol. Abbvie, BeiGene, BI, Mirati Ther., Seagen, Terumo, Zymeworks, Ipsen; Research funding Amgen, Bayer, BI, Lilly, Novartis, Roche, Ipsen, Merck., Merck KGaA, Servier, BMS, EE: Consulting/advisory, Amgen, Roche, Merck Serono, Sanofi, Servier, Bayer, BMS, Array BioPharm, Pierre Farbe, MSD; Travel/accommodation/expenses, Roche, Merck Serono, Sanofi, Amgen, Array BioPharm, Servier, BMS; Honoraria, Roche, BMS, Servier, Amgen, Merck Serono, Array BioPharm., Sanofi, Merck, Novartis, Seagen; Research funding, Roche, BMS, Servier, Amgen, Array BioPharm., Medimmune, Pierre Farbe, Sanofi, Merck, BeiGene, Celgene, Dobsiopharm, Genetech, HalioDx, Hutchison MedPharm, Janessen-Cilag, Merck/mi, MSD, Merus NV, Mirati Ther., Novartis, Pfizer, Pharmamar, Taiho Pharm., AstraZeneca, BI. FMC: Travel/accommodation/expenses, Janssen Oncology, Novartis. LW: Consulting/advisory, GSK, Servier; Speaker's bureau, BMS; Travel/accommodation/expenses, Servier; Honoraria, BeiGene, BMS, MSD. DS: None. ZP: None. PGP: Travel/accommodation/expenses, Servier, Ipsen; Honoraria, Merck, Pierre Fabre, Ipsen; Research funding, Servier. GL: Travel/accommodation/expenses: Nutricia; Honoraria, Nutricia, Servier. CC: Consulting/advisory, Roche, Bayer, Amgen, MSD, Pierre Fabre. Nordic BioScience; Speaker's bureau, Servier, Merck, Pierre Fabre; Honoraria, Roche, Amgen, Bayer, Servier, MSD, Merck, Pierre Fabre; Research funding, Merck, LaRoche, Mirati Ther., Pierre Fabre, Tesa Ther., TheraMyc; Daiichi Sankyo, Samsung Bioepsis, Ipsia, Ikena Onc. Merus, Neophore, Orion Biotech. Hutchison MedPharm., Scandion Onc., Oria Therap., Sotio, Inspirna, Scorpion Ther., Tolremo, Cardiff Oncol.; Other relationship, Medscape, MJH Life Sci. Peerview, Phys. Ed. Res, Imedex/HMP; Stock/other ownership interests, Oriria Ther. Editorial assistance was provided by Martin Gilmour and Liz Meredith of Empowering Strategic Performance Ltd, and supported by Servier.