S6 Table. Patient-reported quality of life for phase II and III studies of anti-angiogenic agents

Author	Trial design/ Setting	No. of patients ^{a)}	Treatment	Patient-reported quality-of-life
Ohtsu et al. (AVAGAST) [1]	Phase III, randomized, double-blind, placebo- controlled/ 1st-line	774	Bevacizumab+fluoropyrimidine/cisplatin vs. placebo+fluoropyrimidine/cisplatin	Mean EORTC QLQ-C30 global health status scores, mean EORTC QLQ-STO22 scores, and all functional and symptom scales, including rate of individual patient changes, were similar over time in both treatment groups. The only exception was the pain scale, which decreased significantly more quickly with placebo (0.77/mo) than with bevacizumab (0.22/mo, p=0.0068).
Fuchs et al. (REGARD) [2]	Phase III, randomized, double-blind, placebo- controlled/ 2nd-line	355	Ramucirumab vs. placebo	More patients in the ramucirumab group reported stable or improved global QoL than in the placebo group, although this difference was not significant (p=0.23). The median time to deterioration in ECOG performance status to a score of 2 or worse was 5.1 months (IQR 1.9–16.8) in the ramucirumab group and 2.4 months (1.3 to not reached) in the placebo group.
Al-Batran et al. (RAINBOW) [3]	Phase III, randomized, double-blind, placebo- controlled/ 2nd-line	665	Ramucirumab+ paclitaxel vs. placebo+paclitaxel	Fourteen of the 15 QoL parameters had HRs <1, indicating similar or longer time to deterioration in QoL for the ramucirumab plus paclitaxel group. The HRs were <0.75 for emotional functioning and nausea/vomiting and >1 for diarrhea. More patients in the ramucirumab plus paclitaxel group than the placebo plus paclitaxel group reported improved or stable scores for all QoL parameters at all on-therapy assessment times, although these differences were not significant.
Li et al. [4]	Phase II, randomized, double-blind, placebo- controlled/ 3rd-line	144	Apatinib QD vs. apatinib BID vs. placebo	The three treatment groups were similar with regard to QoL scores for the different parameters of the EORTC QLQ-C30, with the exception of insomnia, which was significantly improved in patients treated with apatinib treatment groups compared to the placebo group (p=0.002). Cognitive function scored higher in the apatinib treatment groups than in the placebo group after two cycles of treatment, although this was not significant (p=0.067).
Bang et al. [5]	Phase II, single-arm/ 2nd-line	78	Sunitinib	HRQoL was reported to be maintained by sunitinib treatment during the first 3 cycles of the study, although diarrhea and reflux symptoms were worse compared to baseline. At last evaluation of patients, deterioration was reported in most scores of the EORTC QLQ-C30 and QLQ-STO22 compared to the baseline. There were no significant changes in perceived financial difficulties, body image, and hair loss.

EORTC QLQ-C30, European Organisation for Research and Treatment of Cancer quality-of-life questionnaire; EORTC QLQ-STO22, European Organisation for Research and Treatment of Cancer stomach cancer specific questionnaire; QoL, quality of life; ECOG, Eastern Cooperative Oncology Group; IQR, interquartile range; HR, hazard ratio; QD, once daily; BID, twice daily; HRQoL, health-related quality of life. ^{a)}Value reported represents the total number of patients enrolled in the study.

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