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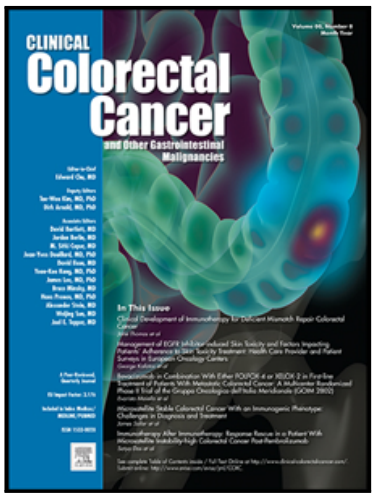

Value-based analysis of therapies in refractory metastatic colorectal cancer in US

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TITLE PAGE

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ABSTRACT

Background: Recent phase 2 trials have provided data supporting regorafenib dose optimization (ReDO) and trifluridine/tipiracil (TAS-102) with bevacizumab (TAS-BEV) as treatment options in refractory metastatic colorectal cancer (mCRC). Historically, regorafenib standard dose (RSD) and TAS-102 have been utilized as third-line options in mCRC. Given the incorporation of ReDO and TAS-BEV as treatment options, we sought to evaluate relative cost-effectiveness of ReDO vs RSD, TAS-102, and TAS-BEV for mCRC from a payer perspective.

Methods: A Markov model was constructed to estimate total costs and quality-adjusted life-years (QALYs) for ReDO, RSD, TAS-102, and TAS-BEV. Clinical parameters were obtained from phase 2 and 3 trials for comparators. Health state utility values were from the RSD phase 3 clinical trial. Incremental cost-effectiveness ratios (ICERs) were utilized to compare treatments. Model robustness was checked with one-way and probabilistic sensitivity analyses.

Results: In the base case, ReDO was dominant over TAS-BEV (ie, provided a higher QALY at a lower cost). ReDO produced an ICER of $104,308 per QALY relative to RSD and $37,966 relative to TAS-102. In one-way sensitivity analyses, monthly drug cost of TAS-BEV was the most influential parameter determining relative cost-effectiveness between TAS-BEV and ReDO. When TAS-102 and RSD were independently compared to ReDO, the most influential parameters were related to duration of OS and PFS and costs of managing AEs.

Conclusions: The optimum dosing strategy for regorafenib has improved its benefit-to-toxicity ratio and relative cost-effectiveness compared to RSD, TAS-102, and TAS-BEV.

MICROABSTRACT

New data support regorafenib dose optimization (ReDO) and trifluridine/tipiracil (TAS-102) with bevacizumab (TAS-BEV) as subsequent treatment options for metastatic CRC. We evaluated the cost-effectiveness of ReDO vs regorafenib standard dose (RSD), TAS-102, and TAS-BEV from a United

States (US) payer perspective. ReDO provided a higher QALY at a lower cost than TAS-BEV; ReDO was cost-effective relative to TAS-102 and RSD.

KEYWORDS: Colorectal cancer; cost-effectiveness analysis; TAS-102; regorafenib; ReDOS

INTRODUCTION

Colorectal cancer (CRC) is the fourth most diagnosed cancer and the third-leading cause of cancer-related mortality in the United States (US).[1-3] While the 5-year survival rate for localized CRC is 90.6%, 5-year survival is drastically lower for metastatic colorectal cancer (mCRC): 14.7%.[3] Approximately 25% of patients with CRC present with mCRC at initial diagnosis.[3,4] Additionally, among patients initially presenting with localized or locally advanced CRC, the likelihood of developing metastases by stage at diagnosis is <10% for stage I, 10% to 20% for stage II, and 25% to 50% for stage III.[4]

The standard treatment for patients with mCRC in the first- and second-line setting is generally fluoropyrimidine-based chemotherapy, often combined with vascular endothelial growth factor (VEGF)-targeted therapies or, for patients with *KRAS* wild-type status, epidermal growth factor receptor (EGFR)-targeted therapies.[5,6] However, nearly all patients progress and require later lines of therapy.[7] When patients with mCRC progress on treatment, selecting a subsequent regimen requires consideration of prior chemotherapy exposure, molecular testing results, tolerance of previous chemotherapy, and patient preferences.[6]

The US Food and Drug Administration (FDA) approvals of regorafenib standard dose (RSD) (160 mg/day for 21 days of a 28-day cycle) in 2012 and trifluridine/tipiracil (TAS-102) in 2015 provided additional treatment options that prolong survival for patients with mCRC with a good performance status following progression on fluoropyrimidine, oxaliplatin, and irinotecan. In the CORRECT trial, an international, randomized, placebo-controlled, phase 3 study, the median overall survival (OS) was 6.4 months in the RSD group compared to 5.0 months in the placebo plus best supportive care (BSC) group.[8] In the RECOURSE trial, a randomized, placebo-controlled, phase 3 study conducted in East Asia, the median OS was 7.1 months in the TAS-102 group compared to 5.3 months in the placebo plus BSC group.[9] Before the development of these agents, patients with mCRC had limited treatment options beyond BSC after exhausting standard chemotherapy regimens.[8] Although regorafenib (ie, RSD) has been shown to improve survival in multiple studies in patients with refractory mCRC, the adverse event (AE) profile (eg, hand-foot syndrome) can limit its use.[8,9] However, using a dose-escalating strategy for regorafenib may lower the incidence of AEs and could optimize dosing.[5,10,11]

Regorafenib Dose-Optimisation (ReDOS), a multicenter, open-label, phase 2 study, investigated an alternative regorafenib dose schedule based on dose escalation (ReDO; regorafenib initiated at 80 mg/day and escalated weekly in 40 mg increments up to 160 mg/day if no significant drug-related AEs occurred). The objective was to test the hypothesis of weekly dose titration to increase the chance of retaining patients without progression on therapy via reducing treatment-related toxicities.[5] Rates of several of the most common AEs were lower in the ReDO group compared to the RSD group.[5] The proportion of patients who initiated cycle 3 was significantly higher in the ReDO group (43%) than in the RSD group (26%).[5] Median OS was 9.8 months and 6.0 months for the ReDO group and RSD group, respectively.[5] The ReDO strategy may avoid significant toxicities and enable more patients to remain on therapy and thus potentially lead to increased survival.[5]

TAS-102 has recently been studied in combination with bevacizumab in an effort to improve outcomes in this population. The phase 2 trial, C-TASKFORCE, has provided data to support TAS-102 in combination with bevacizumab (TAS-BEV) as a treatment option for patients with chemotherapy-refractory mCRC.[12] Based on benefits of TAS-BEV in the C-TASKFORCE study, Pfeiffer et al conducted an open-label randomized phase 2 trial to compare TAS-BEV vs TAS-102 alone in patients with chemotherapy-refractory mCRC at 4 cancer centers in Denmark.[12] The median OS was 9.4 months in patients who received TAS-BEV and 6.7 months in patients who received TAS-102 alone; however, the incidence of grade ≥3 neutropenia was higher in patients treated with TAS-BEV.[12] The authors concluded that TAS-BEV may be a viable treatment option for patients with chemotherapy-refractory mCRC.[12] Note: There are FDA-approved biosimilars available for bevacizumab; biosimilars are adopted as a standard practice in the US.

A previous study by Cho et al evaluated the cost-effectiveness of RSD and TAS-102 from a US payer perspective and concluded that neither treatment was cost-effective relative to BSC at standard willingness-to-pay (WTP) threshold of $150,000 per quality-adjusted life-year (QALY).[13,14] However, as cost-effectiveness models allow for a comprehensive assessment of benefits, toxicities, and costs of care under best current estimates, it is prudent to re-evaluate cost-effectiveness as new regimens or new dosing strategies that have the potential to improve upon survival, toxicity, or both become available. In view of the availability of new data showing benefits of ReDO and TAS-BEV and their subsequent new

place in therapy, we sought to evaluate the relative cost-effectiveness of ReDO vs RSD, TAS-102, and TAS-BEV for treatment of mCRC from a US payer perspective.

METHODS

Model Structure

A Markov model with 3 health states was used to estimate total costs and QALYs for each comparator (RSD, ReDO, TAS-102, and TAS-BEV). Patients started in the progression-free state (stable disease) and gradually moved to the disease progression state over time. Death could occur in either of the other 2 states. The model had a monthly cycle and a 3-year time horizon. All outcomes were captured from a US payer perspective with an annual discounting rate of 5% applied to both costs and QALYs.[15]

Clinical Parameters

Clinical parameters are listed in the appendix (Table A.1). Clinical parameters included the duration of progression-free survival (PFS) and OS, incidence rates of AEs, and health state utility. Efficacy outcomes for RSD and TAS-102 were acquired from the CORRECT and RECOURSE phase 3 trials, respectively.[8,9] Efficacy outcomes for ReDO and TAS-BEV were acquired from the 2019 ReDOS (NCT02368886) and 2020 Pfeiffer et al phase 2 clinical trials.[5,12] Using the declining exponential approximation of life expectancy (DEALE) method, transition probabilities among the 3 health states for each comparator were estimated from values for median PFS and median OS.[16] For reference, the DEALE method assumes a constant rate of change for disease progression and survival. Different functional forms can be assumed to approximate disease progression and survival. However, in the absence of patient-level data from each clinical trial, the DEALE method was deemed appropriate as it requires only 1 parameter (eg, a median or a mean time to death) for approximation. Uncertainty associated with this assumption and efficacy parameters were evaluated in sensitivity analyses.

AEs occurring at grade ≥3 with incidence rates ≥5% were included in the model. Health state utility values for progression-free (stable) and disease-progression states were obtained from the CORRECT trial of the RSD, which reported EQ-5D scores of 0.73 for the progression-free (stable) state and 0.59 and for the

disease-progression state.[8] These EQ-5D scores were measured during the clinical trial and therefore account for disutility associated with AEs. The clinical trials for the other 3 comparators did not report health state utility values.

Economic Parameters

Economic parameters are listed in Table A.1. Economic parameters included the cost of drug treatment, AE management, and routine medical care. Dosages used in the analysis were obtained from the respective clinical trials.[5,8,9,12] For regorafenib and TAS-102, treatment costs were based on National Drug Codes (NDCs) and wholesale acquisition costs (WACs) from IBM Micromedex Red Book.[17] For bevacizumab, the cost of a biosimilar and its administration were estimated using a Healthcare Common Procedure Coding System (HCPCS) code.[18] For TAS-102 and bevacizumab, monthly costs were estimated using the mean body surface area (1.78 m^2) and body weight (68 kg) in the phase 3 RECOURSE trial of TAS-102.[9] The model assumed that treatments were administered until disease progression and that any unused medications were wasted.

Mean hospital costs for managing grade 3 or higher AEs were calculated using Medicare Severity Diagnosis-Related Groups from the Agency for Healthcare Research and Quality Healthcare Cost and Utilization Project.[19] These costs were applied once during the first cycle. To estimate the costs of routine medical care, patients were presumed to have had biweekly physician visits and to have received complete blood counts with differential and comprehensive metabolic panel tests. The cost of routine medical care was estimated using Current Procedural Terminology (CPT) codes.[18,20] Costs of hospitalizations and routine medical care were inflated to 2020 US dollars using Consumer Price Index for Medical Care.[21] Treatment costs were not inflated as they were obtained from the Red Book in August 2021.[17]

Sensitivity Analyses

Model robustness was checked with one-way sensitivity analyses, probabilistic sensitivity analyses (PSAs), and a scenario analysis in which patients in all 4 comparator arms were assumed to have the same PFS and OS.[7]

Using ReDO as the reference group, the one-way sensitivity analysis evaluated influential parameters determining relative cost-effectiveness among the comparators. Tornado diagrams were constructed to visualize the changes in the net monetary benefit (NMB) at a WTP of $150,000. The cost of treating neutropenia, one of the most prevalent and expensive AEs, can vary widely due to the potential use of broad-spectrum antibiotics, which are often necessary in the setting of febrile neutropenia and the potential, though rare, use of granulocyte-colony stimulating factor to increase neutrophil counts in mCRC. To evaluate the uncertainty associated with the cost of managing neutropenia and its impact of relative cost-effectiveness, the cost of treating neutropenia in the model was varied by 10%, 30%, and 50%. All other parameters were varied by 10%.

PSA results were plotted using cost-effectiveness acceptability curves. For each WTP threshold, the cost-effectiveness acceptability curves show which treatment has the highest probability of being the most cost-effective. All clinical and economic parameters were randomly sampled from assumed distributions, and simultaneous changes in NMBs were recorded in 10,000 Monte-Carlo simulations.

Because the total cost of care may heavily depend upon PFS and OS, a scenario analysis was conducted with an assumption that all 4 treatment arms were equally effective (ie, had the same duration of PFS/OS) in order to explore which treatment yielded the lowest total cost of care. As ReDO had the highest OS among the clinical trials, median OS (9.8 months) and PFS (2.8 months) from ReDOS were assumed for all comparators.[5]

All analyses were performed using Microsoft Excel and Visual Basic for Applications.

RESULTS

Base Case Results

In the base case, ReDO produced an incremental cost-effectiveness ratio (ICER) of $104,308 per QALY relative to RSD and $37,966 relative to TAS-102. ReDO was dominant over TAS-BEV, providing a higher QALY at a lower cost (Table 1).

The total cost of care and QALYs for each comparator are listed in Table 2. RSD and TAS-102 had the lowest costs but also the lowest QALYs. ReDO was dominant over TAS-BEV, meaning ReDO is both less costly and more effective than TAS-BEV.

For all comparators, most of the total cost of care occurred in the first 2 months after treatment initiation. This was primarily due to the cost of medications and managing AEs. During the first 2 months, the total costs were $36,141 for RSD, $36,416 for ReDO, $38,927 for TAS-102, and $49,634 for TAS-BEV; 16% to 39% of these costs were due to AEs.

Sensitivity Analyses

The tornado diagrams in Figure 1 show the range of NMBs at WTP thresholds of $150,000 per QALY between ReDO and RSD (A), ReDO and TAS-102 (B), and ReDO and TAS-BEV (C). In the one-way sensitivity analysis, the monthly drug cost for TAS-BEV was the most influential parameter determining relative cost-effectiveness between TAS-BEV and ReDO. When RSD and TAS-102 were independently compared to ReDO, the most influential parameters were related to the duration of OS and PFS. The cost of managing neutropenia was also an influential parameter determining relative cost-effectiveness between ReDO and TAS-102.

The results of the PSA are presented in Figure 2. The probability of ReDO being the most cost-effective treatment was over 50% at a WTP threshold of $120,000 per QALY, which is below the standard US WTP threshold of $150,000 per QALY.[14] The probability of ReDO being most cost-effective was over 90% at a WTP of $240,000 per QALY. The probability of TAS-BEV being more cost-effective than ReDO was 0% at any WTP threshold.

Scenario Analysis

ReDO was the cost-minimizing treatment strategy in a scenario analysis in which all 4 treatments were assumed to be equally effective (ie, had the same duration of OS and PFS) (Table 3). Medications accounted for the majority of costs (ReDO: 83%; RSD: 88%; TAS-102: 78%; TAS-BEV: 79%). AEs were the second highest contributor to cost (ReDO: 13%; RSD: 8%; TAS-102: 18%; TAS-BEV: 18%), and routine care accounted for 2% to 4% of total costs for all comparators.

DISCUSSION

New dosing strategies for regorafenib (ie, ReDO) and therapeutic combinations (eg, TAS-BEV) in chemotherapy-refractory mCRC have the potential to increase survival over previously utilized treatment strategies.[5,12] ReDO also has the benefit of optimization of medication cost and reduction in waste and lower rates of some of the most common AEs compared with RSD. As such, consideration of these benefits, toxicities, and costs of care with each of these regimens becomes increasingly important due to the significant financial burden in patients with mCRC. With the increasing number of treatment options and lack of meaningful clinical benefit, selection of therapy should be based on enhanced value to patients and payers. The findings of this study can guide providers to optimize treatment for their patients from the perspective of efficacy and toxicity, inclusive of financial toxicity.

In mCRC, the regorafenib dosing strategy, ReDO, has improved the benefit-to-toxicity ratio of regorafenib compared to RSD, with an ICER of $104,308 per QALY, which is below the standard US WTP threshold of $150,000 per QALY.[14] ReDO was also cost-effective compared to TAS-102 and TAS-BEV. ReDO was dominant over TAS-BEV, providing a higher QALY at a lower cost. ReDO was cost-effective relative to TAS-102 and RSD at a standard US WTP threshold of $150,000. Our findings highlight the value of optimizing treatment dosage, which not only lowers the total cost of care and the incidence of AEs, but also improves tolerability and outcomes of treatment.

Our findings contrast with prior cost-effectiveness analyses that evaluated RSD in the chemotherapy-refractory mCRC setting. Becker et al utilized American Society of Clinical Oncology (ASCO) and European Society for Medical Oncology (ESMO) value frameworks to evaluate overall benefit scores and costs of oncology therapies and found that TAS-102 ranked higher in most metrics compared to RSD.[22] It

should be noted that ASCO and ESMO value frameworks are not necessarily built to capture downstream toxicities, including the cost of growth factors, which are included in this study. Both Bullement et al (evaluated in England and Whales) and Kimura et al (evaluated in Japan) concluded TAS-102 was more cost-effective than RSD.[23,24] Bullement and colleagues utilized a different method than this study: the cost of growth factor support was not included and costs were based on a United Kingdom (UK) model, which may differ from a US perspective. For instance, total costs of RSD and TAS-102 were £24,112 and £17,978, respectively, in the UK model vs $45,461 and $49,018 in this model.[23] Bullement and colleagues did state that survival is similar between TAS and RSD.[23] A cost-effectiveness analysis by Cho et al in 2018 found neither RSD nor TAS-102 cost-effective at a US standard WTP threshold of $150,000.[13] In light of emerging clinical evidence, our study is the first cost-effectiveness analysis to assess the relative value of ReDO and TAS-BEV.

The findings from our sensitivity analyses suggest that management of AEs is particularly important, as this relates to both total cost of care and relative cost-effectiveness. Our findings are in line with previous studies reporting a significant economic impact of AEs in mCRC patients, with hematologic toxicity being the most costly AE.[25,26] Further, proactive management of AEs has the potential to improve health state utility values and other patient-reported outcomes, thereby improving the relative cost-effectiveness.[27] While the ReDOS study did not report health state utility values, the study showed that mean quality of life scores were significantly better with the dose-optimization strategy in mCRC patients taking regorafenib for current fatigue, general activity interference, mood interference, walking ability interference, and normal work interference as measured by the Brief Fatigue Inventory questionnaire. Patients in the dose-optimization group also had higher quality of life scores as measured with Hand-Foot Syndrome 14 and Linear Analogue Self-Assessment questionnaires, although the difference was not significant, possibly due to the small sample size in the study.

Further, ReDO may reduce costs to patients and financial toxicity, as additional drug is a waste and ReDO reduces the risk of additional drugs in patient possession. Given that payment structures for oral vs intravenous drugs are different and patients are responsible for upfront payment of their copay, this

reduced waste can translate to a significant reduction in financial toxicity with a potential positive impact on QoL that currently does not have a direct measurement structure.

There are limitations to our study. We applied the DEALE method in our analysis, which utilized median PFS and median OS to estimate transition probabilities between the 3 health states for each comparator; however, if patient-level clinical data were available for each trial, other distribution forms could have been considered to approximate transition probabilities related to PFS and OS. Nonetheless, because base-case results remained robust in sensitivity analyses, a different approximation method would have been unlikely to change the study's conclusion; derived hazard ratios utilizing the Bucher method of indirect comparison for TAS vs regorafenib were 0.88 (95% confidence interval [CI]: 0.68-1.14) for OS and 0.98 (95% CI: 0.78-1.23) for PFS.[23] Clinical (eg, PFS, OS, and AEs) and economic parameters (eg, drug dosages) were obtained from 4 different trials, 1 for each of the comparators.[5,8,9,12] The ReDOS trial evaluated the safety and efficacy of ReDO compared to RSD; however, data from both ReDOS and CORRECT trials were utilized, as CORRECT was an international, placebo-controlled phase 3 study.[5,8] No head-to-head trials exist for ReDO, TAS-102, or TAS-BEV. In the absence of head-to-head data, obtaining inputs from the corresponding phase 2 or phase 3 trials was deemed reasonable. In order to address uncertainty in efficacy and safety of the comparators and evaluate which comparator would yield the lowest cost, a scenario analysis was performed assuming that all 4 comparators were equally efficacious (ie, had the same PFS and OS). The results of the scenario analysis were consistent with base case results: ReDO was the lowest-cost comparator. Moreover, while we utilized published drug costs, the actual price of the treatments may vary across health plans. Yet, these were the most reasonable estimates for drug costs, as rebates and discounts between manufacturers and health plans are confidential. Finally, the incidence of AEs and their costs may vary considerably, depending on patient health status and the use of prophylactic treatments to manage AEs. The actual incidence rates of AEs in the real world may be higher or lower than the numbers reported in the clinical trial, given considerable heterogeneity in the case-mix and practice patterns across regions and institutions. We explored the potential impact of lower or higher AE management costs in the one-way sensitivity analysis;

it did not have a large impact on the overall cost-effectiveness of ReDO, as it makes up only 13% of the total cost of care, even with an assumption that AEs require hospitalization

CONCLUSION

Our study evaluated relative cost-effectiveness of 4 comparators in mCRC patients from a US payer perspective. The optimum dosing strategy for ReDO has improved the benefit-to-toxicity ratio and its relative cost-effectiveness. The dose optimization strategy, ReDO, was more cost-effective than TAS-102 and RSD at the standard WTP threshold in the US. ReDO was dominant over TAS-BEV, providing a higher QALY at a lower cost.

CLINICAL PRACTICE POINTS

Regorafenib and TAS-102 are FDA-approved for refractory mCRC and have comparable OS improvement compared with BSC alone. The new dosing strategy and drug combination, ReDO and TAS-BEV, respectively, are now recommended given recent phase 2 trial data: the ReDO strategy demonstrated a lower incidence of AEs compared to RSD, potentially enabling more patients to initiate a third treatment cycle; TAS-BEV showed an increased median OS of 2.7 months compared to TAS-102.

This cost-effectiveness analysis evaluated ReDO as compared to TAS-BEV, RSD, and TAS-102 in refractory mCRC from a US payer perspective. ReDO was both less costly and more effective than TAS-BEV; ReDO was also cost-effective relative to RSD and TAS-102 at a WTP threshold of $150,000.

Using a dose-escalation strategy for regorafenib (ie, ReDO) may lower the incidence of AEs and could optimize dosing, making it a valuable treatment option for patients with mCRC who have progressed through other lines of therapy.

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TABLES

Table 1. ICERs

Treatment comparison	ICER
ReDO vs RSD	$104,308 per QALY
ReDO vs TAS-102	$37,966 per QALY
ReDO vs TAS-BEV	Dominant[a]

[a] ReDO dominant over TAS-102-BEV, providing a higher QALY at a lower cost.

Key: ICER – incremental cost-effectiveness ratio; ReDO – regorafenib dose optimization; RSD – regorafenib standard dose; TAS-102 – trifluridine/tipiracil; TAS-BEV – TAS-102 with bevacizumab; QALY – quality-adjusted life-year.

Table 2. Total cost of care and QALY by comparator

	RSD	TAS-102	ReDO	TAS-BEV
Drug	$45,461 (85%)	$49,018 (74%)	$59,614 (83%)	$104,902 (84%)
AE	$5,715 (11%)	$15,160 (23%)	$9,008 (13%)	$17,179 (14%)
Routine care	$2,146 (4%)	$2,367 (4%)	$3,078 (4%)	$2,666 (2%)
Total cost	**$53,323 (100%)**	**$66,545 (100%)**	**$71,701 (100%)**	**$124,746 (100%)**
Total QALYs	0.394	0.435	0.571	0.511

Note: Percentage indicates proportion of total cost.

Key: AE – adverse event; ReDO – regorafenib dose optimization; RSD – regorafenib standard dose; TAS-102 – trifluridine/tipiracil; TAS-BEV – TAS-102 with bevacizumab; QALY – quality-adjusted life-year.

Table 3. Total cost of care by comparator if all comparators were equally effective

	RSD	TAS-102	ReDO	TAS-BEV
Total cost	**$73,075 (100%)**	**$83,782 (100%)**	**$71,701 (100%)**	**$97,617 (100%)**
Drug	$64,282 (88%)	$65,544 (78%)	$59,614 (83%)	$77,359 (79%)
AEs	$5,715 (8%)	$15,160 (18%)	$9,008 (13%)	$17,179 (18%)
Routine care	$3,078 (4%)	$3,078 (4%)	$3,078 (4%)	$3,078 (3%)

Note: Estimates are based on 2.8 and 9.8 months for median PFS and OS based on the ReDOS study.

Key: AE – adverse event; OS – overall survival; PFS – progression-free survival; ReDO – regorafenib dose optimization; RSD – regorafenib standard dose; TAS-102 – trifluridine/tipiracil; TAS-BEV – TAS-102 with bevacizumab; QALY – quality-adjusted life-year.

FIGURE LEGENDS

Figure 1. One-way sensitivity analysis: Changes in net monetary benefit at the WTP threshold of $150,000 per QALY

Key: OS – overall survival; PFS – progression-free survival; QALY – quality-adjusted life-year; ReDO – regorafenib dose optimization; RSD – regorafenib standard dose; TAS-102 – trifluridine/tipiracil; TAS-BEV – TAS-102 with bevacizumab; WTP – willingness to pay.

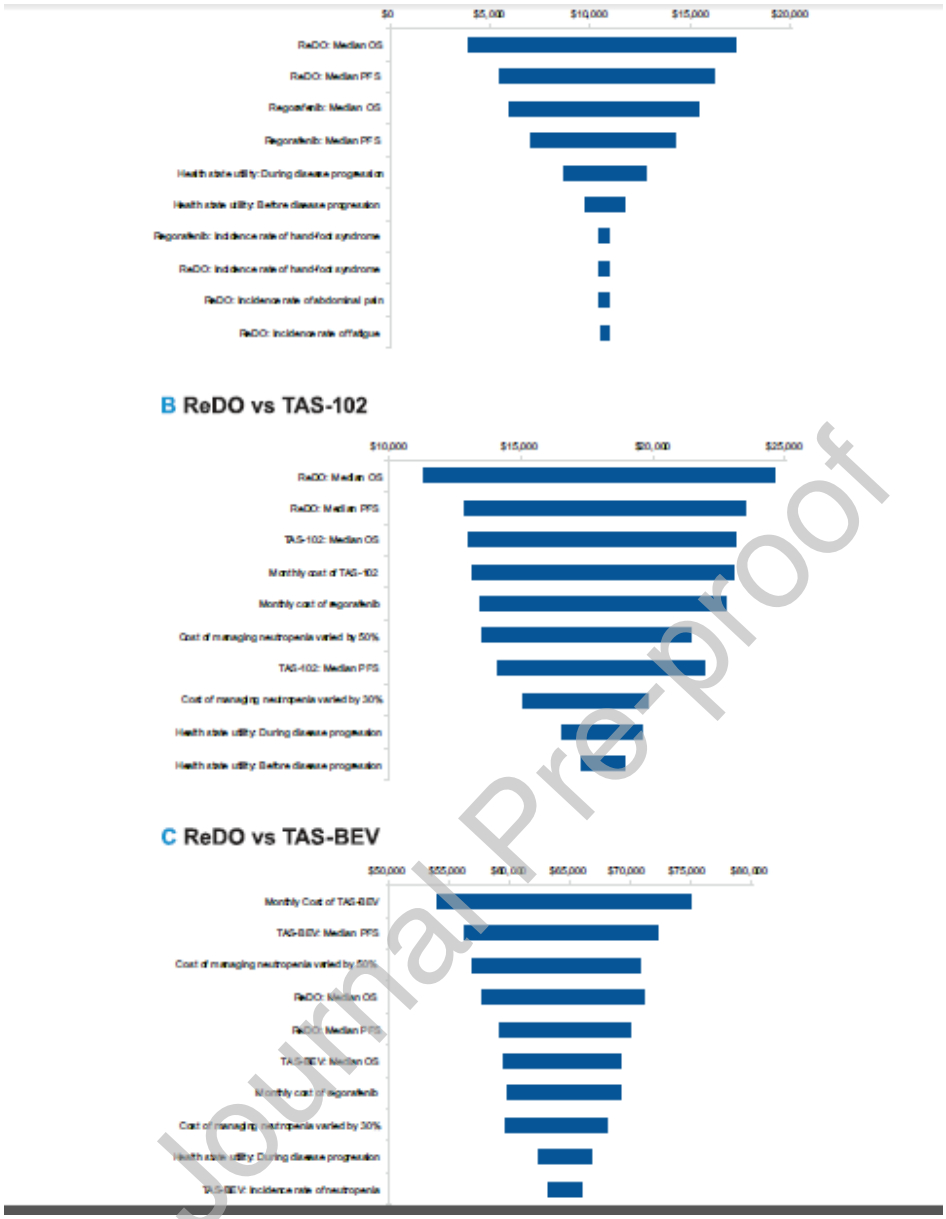

Figure 2. Cost-effectiveness acceptability curves

Key: ReDO – regorafenib dose optimization; RSD – regorafenib standard dose; TAS-102 – trifluridine/tipiracil; TAS-BEV – TAS-102 with bevacizumab; WTP – willingness to pay.

Figure 2

Click here to access/download;Figure;Figure 3. Cost-effectiveness acceptability curves.eps