

Adjuvant Colon Cancer

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Novel Methodology To Evaluate Drugs for Gastrointestinal Malignancies

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Background: There is no accepted quantitative method to evaluate and compare anti-cancer drugs. The aim was to develop integrated methodology to evaluate anti-cancer drugs and combinations used in the treatment of gastrointestinal (GI) malignancies, and to highlight associations with survival (S), novelty (N), administration (A), adverse events (AEs), and cost (C).

Methodology: Cost in US dollars was calculated to treat a patient weighing 70 kg or with body surface area of 1.7 m², with bevacizumab, chemotherapy (CT), cetuximab, and panitumumab, as indicated. Points (P) were assigned according to the novelty (N) of the treatment, A, AEs and cost/day/survival (C/d/s). “N” was graded from 3 points (imatinib) to 1 (“me too” drug), depending on meeting unmet medical need (eg, sorafenib in advanced HCC), originality of class (eg, cetuximab) for individual drugs and for combinations. “A” was graded from 3 points (oral) to 0 depending on frequency and duration of infusions. “AEs” that were considered grades 1 to 5 according to the Cancer Therapy Evaluation Program Common Terminology Criteria for Adverse Events, Version 3.0, were assigned 4 points (CTC grade 1) to 0 points (fatality) in 0.5-point increments. AEs of tyrosine kinase inhibitors were assigned 2.5 points; panitumumab, 2.5 points; cetuximab, 2 points; panitumumab or cetuximab ± CT (first-line), 2 points; panitumumab or cetuximab ± CT in heavily treated patients, 1.5 points; and bevacizumab, 1 point. Reported data on survival (S) were used. A and AEs of combinations were graded as that of all drugs.

Results: TPn (Total P, novelty) = S in added days over control divided by 360 x 100 x sum of all P assigned to A, AEs, and N (Table 1).

Table 1.

Drugs	S/360 X 100	A	AEs	N	TPn
Cetuximab, wild KRAS vs. mutated KRAS, mCRC	25	2	2	3	175 (TTP)
Panitumumab vs. BSC, wild vs. mutated KRAS, mCRC	10	2	2.5	2	65 (PFS)

Abbreviations: BSC = best supportive care; mCRC = metastatic colorectal cancer; PFS = progression-free survival; TTP = time to progression.

Table 2 shows the cost model (TPc), based on overall survival (OS) and replacing N by C/d/OS. Points were assigned on a scale decreasing from 18 to 0 corresponding to C/d/OS of < \$50 to \$1,600. TPc of C/d/OS, A, and AEs were added and expressed as cost score (%).

Table 2.

Drugs & Combinations	OS (d)	C/d/OS (\$)	Assigned P	A	AEs	C Score (%)
Imatinib x 1 year, advanced GIST	360	57	17	3	2.5	90
Sunitinib x 1 year, resistant GIST	360	101	16	3	2.5	86
Sorafenib x 4 Cy, advanced HCC	84	154	15	3	2.5	82

Gemcitabine ± erlotinib x 4 Cy, advanced PC	10	934	4.5	2	2	34
Cetuximab x 10 Cy vs. BSC, heavily treated pts, no selection, mCRC	45	303	12	2	2	64
Bevacizumab 5 mg/kg/70 kg q2wk x 40 wk (20 Cy) + FOLFOX, 1 st -line mCRC	141	454	9	1	1	44
Bevacizumab 5 mg/m ² q2wk x 40 wk + FU+LV, 1 st -line, mCRC	99	293	13	1	1	60
Bevacizumab 10 mg/kg q2wk x 40 wk + FOLFOX, 2 nd -line, mCRC	66	1391	1.25	1	1	14

Abbreviations: BSC = best supportive care; mCRC = metastatic colorectal cancer; Cy = cycles; FOLFOX = 5-fluorouracil, leucovorin, oxaliplatin; FU+LV = 5-fluorouracil + leucovorin; GIST = gastrointestinal stromal tumor; HCC = hepatocellular carcinoma; PC= pancreatic carcinoma.

Discussion: TPn for cetuximab was 175 (TTP) and panitumumab 65 (PFS) as compared with a TPn for imatinib of 850. Using the cost model, imatinib scored 90% in GISTs, sorafenib 82% in advanced HCC, and gemcitabine with erlotinib 34% in advanced pancreatic cancer. Bevacizumab at higher doses in second-line mCRC scored lower than use of lower doses in the first-line setting.

Conclusion: Higher TPn reflects longer survival while higher cost score suggests cost effectiveness.