
Oral Specialty Cancer Medicines: Benefits and Challenges

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The Important Considerations

- The most important question
 - What drug is best for my cancer?
- Drug toxicity
- Dosing
- Compliance
- Reimbursement
- Distribution channels

Toxicity Doesn't Go Away with Orals

Diseases desperate grown
By desperate appliance are relieved,
Or not at all

Shakespeare W. Hamlet, Act 4, Scene 3

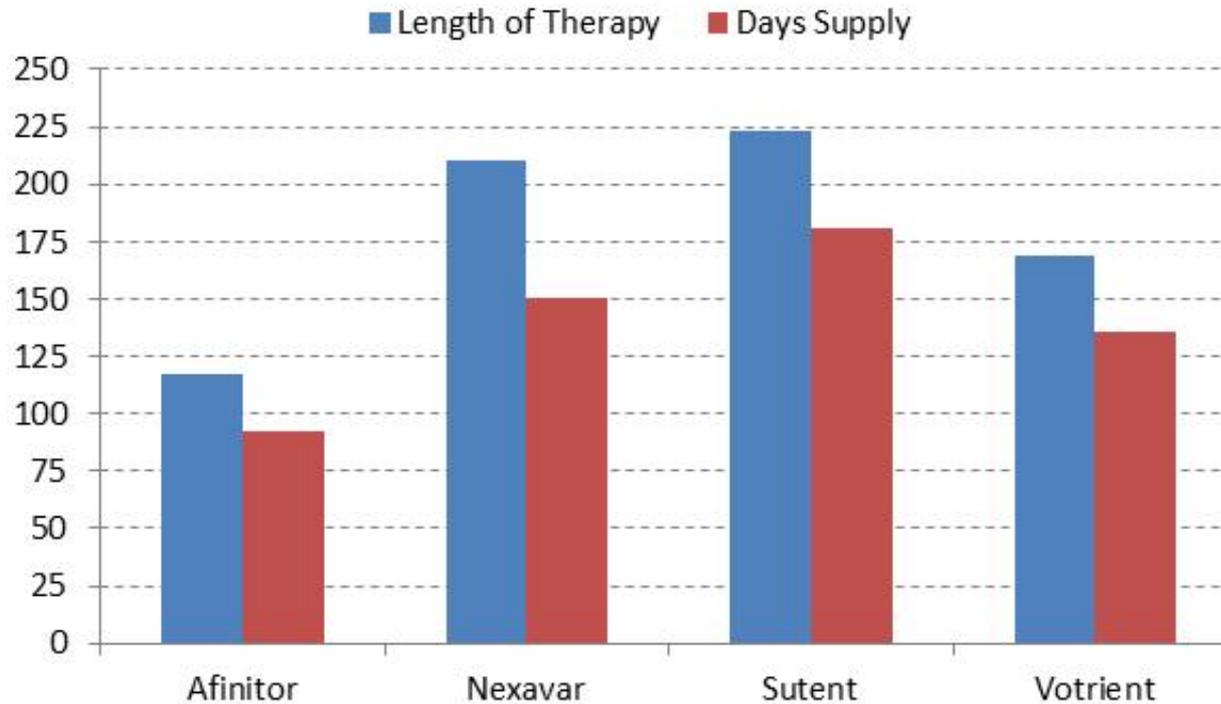
Toxicity Doesn't Go Away with Orals

- Cardiovascular: Hypertension (15% to 34%; grade 3: 4% to 13%), peripheral edema (24%), **decreased left ventricular ejection fraction (11% to 16%; grades 3/4: 1% to 3%)**, heart failure ($\leq 15\%$), chest pain (13%)
- Central nervous system: Fatigue (33% to 62%), headache ($\leq 23\%$), insomnia (15% to 18%), chills (14%), mouth pain (6% to 14%), depression (11%), dizziness (11%), glossalgia (11%)
- Dermatologic: Skin discoloration (25% to 30%), skin rash (14% to 29%), **palmar-plantar erythrodysesthesia (14% to 29%; grades 3/4: 4% to 8%)**, hair discoloration (7% to 29%), xeroderma ($\leq 23\%$), alopecia (5% to 14%), erythema (12%), pruritus (12%)
- Endocrine & metabolic: Hyperglycemia (23% to 71%), hyperuricemia ($\leq 46\%$), hypocalcemia (34% to 42%), hypoalbuminemia (28% to 41%), hypophosphatemia ($\leq 36\%$), hyponatremia ($\leq 29\%$), hypoglycemia (17% to 22%), hypokalemia (12% to 21%), hypomagnesemia ($\leq 19\%$), hyperkalemia ($\leq 18\%$), hypothyroidism (4% to 16%; grades 3/4: $\leq 2\%$), hypercalcemia (13%), hypernatremia (10% to 13%)
- Gastrointestinal: **Diarrhea (40% to 66%)**, **nausea (45% to 58%)**, increased serum lipase (17% to 56%), anorexia (33% to 48%), mucositis (29% to 48%), dysgeusia (21% to 47%), abdominal pain (39%), vomiting (34% to 39%), increased serum amylase (17% to 35%), dyspepsia (15% to 34%), constipation (20% to 23%), weight loss (16%), flatulence (14%), xerostomia (13%), gastroesophageal reflux disease (12%)
- Hematologic & oncologic: **Anemia (26% to 79%; grades 3/4: $\leq 8\%$)**, **leukopenia (78%; grades 3/4: 8%)**, **neutropenia (53% to 77%; grades 3/4: 10% to 17%)**, lymphocytopenia (38% to 68%; grades 3/4: $\leq 18\%$), thrombocytopenia (38% to 68%; grades 3/4: 5% to 9%), hemorrhage (18% to 37%)
- Hepatic: Increased serum AST (39% to 72%; grades 3/4: 2% to 5%), increased serum alkaline phosphatase (24% to 63%; grades 3/4: 2% to 10%), increased serum ALT (39% to 61%; grades 3/4: 2% to 4%), hyperbilirubinemia (10% to 37%; grades 3/4 $\leq 1\%$)
- Neuromuscular & skeletal: Increased creatine kinase (49%), limb pain (14% to 40%), weakness (22% to 34%), arthralgia (15% to 30%), back pain ($\leq 28\%$), myalgia (14%)
- Renal: Increased serum creatinine (12% to 70%)
- Respiratory: Cough (27%), dyspnea (26%), epistaxis (21%), nasopharyngitis (14%), upper respiratory tract infection (11%)
- Miscellaneous: Fever ($\leq 22\%$)

Toxicity Doesn't Go Away with Orals

- Cardiovascular: Edema (25% to 27%), hypertension (9% to 22%; grades 3/4: 1% to 4%)
- Central nervous system: Fatigue (39%), insomnia (14%)
- Dermatologic: Bruise (13%)
- Endocrine & metabolic: Increased serum triglycerides (63%), hyperglycemia (57%), hypernatremia (33%), **hypokalemia (17% to 28%; grades 3/4: 3% to 5%), hypophosphatemia (24%; grades 3/4: 7%),** hot flash (19% to 22%)
- Gastrointestinal: Constipation (23%), diarrhea (18% to 22%), dyspepsia (6% to 11%)
- Genitourinary: Urinary tract infection (12%)
- Hematologic: **Lymphocytopenia (38%; grades 3/4: 9%)**
- Hepatic: **Increased serum ALT (11% to 42%; grades 3/4: 1% to 6%), increased serum AST (31% to 37%; grades 3/4: 2% to 3%)**
- Neuromuscular & skeletal: Joint swelling (30%, including joint discomfort), myalgia (26%)
- Respiratory: Cough (11% to 17%), upper respiratory infection (5% to 13%), dyspnea (12%), nasopharyngitis (11%)

Length of Therapy



UnitedHealthcare data, 2012. Renal cell carcinoma patient analysis

Compliance for all oral specialty medications is 58%

Dosing

- Poor tolerability
- Fixed, arbitrary adjustments due to pill size
- Unbalanced clinical trials

Prasad V et al. J Clin Oncol 2014;32: 1620-1629.

Benefit Differentials

- Pharmacy benefit is different than the medical benefit
- Parity laws passed in 30 states
 - 12 states considering
- Operational issues
 - Different systems
 - Costs
- Medicare does NOT have parity provision

Distribution Systems

- Specialty pharmacy
- Retail pharmacy
- Physician distribution
- Compliance studies
 - Improved patient compliance with specialty pharmacy.
 - Possession ratios of 0.66 versus 0.58
 - Copayment was \$50 per month
 - Lower medical costs with specialty pharmacy
 - \$84,000 versus \$97,000

Tschida SJ. Am J Pharm Benefits 2012;4: 165-174

When Do Preferences Count?

A comparison between a equivalent oral and intravenous regimens

FOLFOX4

5-Fluorouracil
Leucovorin

\$846.72 +
\$3600.00 infusion

XELOX

Capecitabine branded
\$28,8451.20

Capecitabine generic
\$25,233.60

Consumers Look at Their Checkbooks

- Consumers buy the plan; patients use the plan
 - The Oregon farmer
 - The Town Car driver in Houston
- Oral specialty drugs*
 - Mean compliance 58% with \$50 monthly co-payment

* Tschida SJ. Am J Pharm Benefits 2012;4: 165-174

Summary

- Orals are neither superior or inferior to intravenous medications
 - What's best for the cancer?
 - What are the trade-offs for equal therapies?
- Dosing change effects are still unknown
- Specialty pharmacies are preferred distribution
- Cost is an issue regardless of administration method