Patient Reported Outcomes in Kidney Cancer
Vision of Hope: A Kidney Cancer Educational Symposium
Friday, October 11, 2019

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Director, Research and Clinical Integration, Cancer Prevention and Control
Wake Forest Baptist Comprehensive Cancer Center

Co-Leader, Cancer Control and Outcomes Program
ECOG-ACRIN Cancer Research Group
Agenda

• What are patient-reported outcomes?
• Unique data obtained using PROs
• What have we learned about kidney cancer and its treatment using PROs?
• Moving from PROs as observational to actionable
Assessment Options

• Observation
• Clinical examination
• Labs
• Imaging
• Clinician-rated toxicities
• Patient-reported outcomes (PROs)
What are patient-reported outcomes?
Patient-Reported Outcomes: PROs

Food and Drug Administration (FDA) defines PROs as “outcomes reported directly by patients without interpretation by clinicians”

• BMJ 2010
PROMIS Adult Self-Reported Health

Physical Health
- Physical Function
- Pain Intensity
- Pain Interference
- Fatigue
- Sleep Disturbance

Mental Health
- Depression
- Anxiety
- Anger
- Cognitive Function
- Alcohol Use, Consequences, & Expectancies
- Smoking
- Substance Use
- Psychosocial Illness Impact
- Self-efficacy

Social Health
- Ability to Participate in Social Roles & Activities
- Satisfaction with Social Roles & Activities
- Social Support
- Social Isolation
- Companionship

Also in Spanish
# PROMIS Pain Interference Short Form

**In the past 7 days...**

<table>
<thead>
<tr>
<th></th>
<th>Not at all</th>
<th>A little bit</th>
<th>Somewhat</th>
<th>Quite a bit</th>
<th>Very much</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>How much did pain interfere with your day to day activities?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>2</td>
<td>How much did pain interfere with work around the home?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>3</td>
<td>How much did pain interfere with your ability to participate in social activities?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>4</td>
<td>How much did pain interfere with your household chores?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>5</td>
<td>How much did pain interfere with the things you usually do for fun?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>6</td>
<td>How much did pain interfere with your enjoyment of social activities?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
</tbody>
</table>

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Unique Perspectives Gained from PROs

• PRO measures are the gold standard for assessing subjective concerns
  • Symptoms: pain, fatigue, distress
  • Impact of symptoms on continuing meaningful activities
  • Knowledge, attitudes, behavior

• Same biological value in 2 patients ≠ same impact

• Health-related QOL scores predict survival in many conditions

• PROs signify risk for issues with treatment-related tolerability
Patient-Generated Symptom Data More Accurate than Clinician Ratings

- PROs more accurate than clinician-rated toxicities in assessing symptom burden and quality of life
- Symptom ratings directly from patients provide more precise and reliable symptomatic adverse event detection in clinical trials
- Clinical investigators miss nearly half of symptomatic adverse events

Basch NEJM 2010
Basch et al JNCI 2009
Fromme et al JCO 2004
Velikova et al JCO 2001
Complex Factors Affect Patient-Provider Communication

• Patients face inherent disincentives to reporting symptoms, toxicities
  • Desire to preserve rapport
  • Concerns about dose reductions, dose delays
• Providers assume patients will raise concerns
How can you get high quality information from patients?
PRO Instrument Development Process

What have we learned about kidney cancer and treatment using PROs?
Value Added: PRO Data

• Quantify domains important to the patient
• Facilitate patient-centered care
• Facilitate shared decision-making
• Inform expectations during and following treatment
• Inform role of new agents in treatment
• Enable cost utility analyses to guide health policies
PRO Outcomes: Localized renal cancer

• Laparoscopic nephrectomy vs Open surgery
  > short-term physical function

• Nephron-sparing surgery vs Radical nephrectomy
  > Physical function
    ↓ intrusive thoughts, avoidance behavior, anxiety, worry
  • RN associated with greater worry regarding loss of kidney function

• Partial nephrectomy vs Radical nephrectomy
  > Physical function
    ↓ fatigue, sleep disturbance, pain

• Patient perception of remaining renal function significant and independent predictor of HRQL
PRO Outcomes: Localized renal cancer

• Ablative therapy, active surveillance vs Operative management
  • Comparable psychological outcomes
    • Caveat: sparse data

• HRQL returns to baseline following surgical management
  • 50% by 4 weeks
  • 80% by 12 weeks
PRO Outcomes: Localized renal cancer

Research gaps

• PRO data on robotic surgery, ablation, and active surveillance
  • European Active Surveillance of Renal cancer (EASE) currently underway

• Long-term impact of cancer survivorship

• Sexual function

Rossi, Klatte, Stewart World J Urol 2018
ECOG-ACRIN E2805: PRO findings

• Adjuvant sunitinib or sorafenib for high-risk, non-metastatic renal-cell carcinoma
  • Hass et al. Lancet 2016

Figure 1.
Mean score and 95% CI of fatigue score by treatment arm

Zhao et al Supp Care CA 2018
PROs to Inform Treatment Options: mRCC

- Increasing availability of molecular targeted therapies for mRCC
- Efficacy of new agents:
  - Relieve disease-related symptoms
  - Tolerability of treatment-related adverse events
  - Availability of interventions to manage AEs

➢ HRQL
## PRO Outcomes: Metastatic renal cancer

<table>
<thead>
<tr>
<th></th>
<th><strong>Sunitinib</strong></th>
<th><strong>Sorafenib</strong></th>
<th><strong>Pazopanib</strong></th>
<th><strong>Everolimus</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Outcomes</strong></td>
<td>Improvement in disease-related symptoms compared to IFN-alpha</td>
<td>FKSI-10 score comparable to placebo, maintained HRQL comparable to placebo</td>
<td>Maintained HRQL similar to placebo</td>
<td>Maintained HRQL similar to placebo</td>
</tr>
<tr>
<td></td>
<td>Fewer severe disease-related symptoms than with IFN-alpha</td>
<td>Improvement in some symptoms: coughing, loss of breath, fever, enjoyment of life, worry</td>
<td></td>
<td>Prolonged time to deterioration in HRQL and functional status</td>
</tr>
<tr>
<td></td>
<td>Greater toxicity-adjusted PFS rate than with IFN-alpha</td>
<td>No worsening in symptoms: fatigue, sleep quality, pain, weigh loss</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Prolonged median time to health status deterioration</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Baseline FKSI predictive of OS rate</td>
<td></td>
<td></td>
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</tbody>
</table>

*Baseline FKSI predictive of OS rate*

*Cella Oncologist 2011*
PRO Outcomes: Advanced renal cancer

- METEOR phase III RCT: Cabozantinib and everolimus comparable
  - Disease related symptoms
  - Overall HRQL

<table>
<thead>
<tr>
<th>Cabozantinib Superior</th>
<th>Everolimus Superior</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less shortness of breath</td>
<td>Less diarrhea</td>
</tr>
<tr>
<td>Improved Time to deterioration</td>
<td>Less nausea</td>
</tr>
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Moving from PROs as Observational to PROs as Actionable
Basch et al STAR Trial

• 766 patients randomized to Symptom Tracking and Reporting (STAR) or usual care

• Patients initiating chemotherapy at MSK for metastatic breast, genitourinary, gynecologic, or lung cancers
  • Types selected to represent spectrum of symptoms, metastatic for continuous tx/sx burden

• STAR = 12 PRO-CTCAE items, remote access or use of tablet or kiosk in clinic
  • Email alert to nurses ≥ 2 pts or grade ≥ 3

• Report printed for MD, nurse at each clinic visit
ePRO Symptom Monitoring: Survival Benefit

Figure. Overall Survival Among Patients With Metastatic Cancer Assigned to Electronic Patient-Reported Symptom Monitoring During Routine Chemotherapy vs Usual Care

Crosses indicate censored observations. Enrollment in the patient-reported symptom monitoring group was enriched for a preplanned subgroup with low baseline computer experience as part of a feasibility substudy with a 2:1 randomization ratio in that subgroup (N = 227) and a 1:1 ratio in the computer-experienced subgroup (N = 539), yielding 441 patients in the patient-reported symptom monitoring group, and 325 in the usual care group. With a minimum follow-up of 5.4 years, median follow-up was 6.9 years (interquartile range, 6.5-7.7) for the electronic patient-reported symptom monitoring group and 7 years (interquartile range, 6.6-8.1) for the usual care group.

Basch et al. ASCO 2017, JAMA 2017
Levering Informatics to Implement ePRO Symptom Monitoring

Results

<table>
<thead>
<tr>
<th>Question</th>
<th>Option 1</th>
<th>Option 2</th>
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<tbody>
<tr>
<td>Do you have any new symptoms?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Is your pain worse today?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Is your fatigue worse today?</td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>

Fatigue Scale

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>None</td>
</tr>
<tr>
<td>1</td>
<td>Mild</td>
</tr>
<tr>
<td>2</td>
<td>Moderate</td>
</tr>
<tr>
<td>3</td>
<td>Severe</td>
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</table>

Pain Intensity Scale

<table>
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<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
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Screening in Ambulatory Cancer Care

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Thank you!

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