Modernizing Clinical Trial Eligibility Criteria
Organ Dysfunction, Prior Malignancy, Comorbidity

• Oncology clinical trials (OCT) determine recommended care
  – Based on risk:benefit seen in large randomized OCT
• OCT enrollees are younger and healthier
• Similar recommended care is given to patients who:
  – Could not enroll in OCT re: ineligible
  – are under represented in OCT (older, diverse, rural, poor)
• ? Risk:benefit ratio and toxicity in non OCT patients
• Can eligibility criteria be changed to be more inclusive?
ASCO & Friends of Cancer Research
Eligibility Re-Evaluation Process

• Multi-Disciplinary Working Group
  – Trial Design experts
  – Clinical Trialists: Academic, Community, Pharmaceutical
  – FDA
  – Advocates

• Multiple meetings:
  – Literature Review, data analysis, in depth discussion, consensus development
  – Original data collection (Kaiser Permanente)
  – Consensus recommendations
Eligibility Criteria Examined

• Common Exclusions:
  – Renal function  GFR < 60cc/min
  – Liver function tests
  – Cardiac: CHF/Cardiomyopathy/Hx of MI
  – Prior malignancy < 5 years
  – Comorbidities

• Uncommon enrollment
  – Age ≥75
Kaiser Permanente Data Extracted

• Kaiser Permanente Northern California: 2013 & 2014
• 12,881 Consecutive cases of:
  – Breast: 5865
  – Colorectal: 2927
  – Lung: 3319
  – Bladder: 770
• Data Base review of peri-diagnosis common eligibility criteria
  – Hx Invasive cancer, Hx CHF/cardio-myopathy/MI, age ≥ 75, Charlson
  – Labs: ALT, Bili, GFR,
<table>
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<tr>
<th>Cancer Site</th>
<th>Invasive Cancer &lt;5yr %</th>
<th>CHF/Card Myop</th>
<th>MI %</th>
<th>HIV+ %</th>
<th>ALT &gt;2.0 X ULN%</th>
<th>Bilirubin &gt;1.5 %</th>
<th>Anti coag %</th>
<th>GFR &lt;60cc/min %</th>
<th>Age &gt;75yo %</th>
<th>Sum of % Ineligible</th>
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<tr>
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Charlson Comorbidity Score % with 0-1, 2, or 3+ By Ca Type KPNC 2013-14, n=13,000+

- Breast Ca: 80% (8.9% 0-1, 11.5% 2, 11.5% 3+)
- Colon Ca: 62% (12% 0-1, 26% 2, 24% 3+)
- Lung Ca: 50% (13.1% 0-1, 13.1% 2, 23.8% 3+)
- Bladder Ca: 43% (18.2% 0-1, 18.2% 2, 16.6% 3+)
Modifying Eligibility Criteria
Recommendations

• Renal Function:
  – Calculated creatinine clearance is the best measurement
  – Unless renal toxicity or renal drug clearance is a clear problem, CrCl <30cc/min should be eligibility criteria in later phase trials

• Hepatic function:
  – Mild to moderate dysfunction should be acceptable if pk data and early clinical data show safety
  – Better measurements of function are needed
Modifying Eligibility Criteria Recommendations (cont.)

• Cardiac Function:
  – Conservative approach in early phase studies, but broadening criteria as safety becomes evident
  – If QTc prolongation not of concern in early phase I, then criteria should be eliminated in later studies

• Prior Malignancy:
  – If prior cancer treatment is completed, risk of recurrence is low, & no endpoint interference, current criteria (<5 years) should change
  – Suggested: 2 years off treatment and no evidence of disease
Goal of Modernizing Eligibility Criteria

• Increase enrollment:
  – Greater number of patients
  – Larger percentage of older patients
  – Larger percentage of representative “real life” patients

• Assess effect in commonly seen subsets, both:
  – Treatment benefit
  – Treatment toxicity/side effects in subsets
Modernizing Clinical Trial Eligibility Criteria: Recommendations of the American Society of Clinical Oncology–Friends of Cancer Research Organ Dysfunction, Prior or Concurrent Malignancy, and Comorbidities Working Group

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