Seamless and efficient cancer drug development

- One size does not fit all
  - Risk:Benefit ratio
- More than one way to adapt
- Breadth of statistical designs
  - FDA is open minded
- Real world data/evidence
  - What patients care about
- It takes a village
  - A Role of Patient Advocacy Groups

**THE DEADLIEST CANCERS COALITION**

THE DEADLIEST, OR RECALCITRANT, CANCERS HAVE A 5-YEAR RELATIVE SURVIVAL RATE OF LESS THAN 50%

- Pancreas: 8%
- Liver: 18%
- Lung: 18%
- Esophagus: 20%
- Stomach: 30%
- Brain: 35%
- Ovary: 46%
- Myeloma: 49%
### Initial Precision Promise

**trial for metastatic pancreatic cancer**

**Coming to 12 US sites**

**Spring 2017**

<table>
<thead>
<tr>
<th>Sub-studies</th>
<th>Master Protocol</th>
<th>Stromal Disruption</th>
<th>DNA Damage Repair</th>
<th>Immunotherapy</th>
<th>Supportive Care</th>
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<tbody>
<tr>
<td></td>
<td>• Initial biopsy, at progression</td>
<td>• HA Hi to PEGPH20, 4 mos</td>
<td>• Platinum 4 mos</td>
<td>• Gem/Abx backbone</td>
<td>• Standardize throughout sites</td>
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<tr>
<td></td>
<td>• DNA panel, WGS/WES</td>
<td>• With platinum OR Gem/Abx</td>
<td>• Parpi if platinum responsive</td>
<td>• FAKi or CCR2i plus anti PD-1</td>
<td>• Learn and modify</td>
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<td></td>
<td>• RNA seq</td>
<td>• Determine persistence</td>
<td>• Parpi if BrCa mutant</td>
<td>• Determine response &amp; biomarkers</td>
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<tr>
<td></td>
<td>• IHC: HA, IO</td>
<td></td>
<td>• Determine biomarkers of response</td>
<td>• CD40 agonist 2 mos in some</td>
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</tbody>
</table>

**3 Sub-studies**
• 2 biomarkers with good hypotheses to test
• 2 standard of care backbones
• Move through multiple lines of therapy – try all three approaches if can
• Biomarker discovery/validation