What is Pancreatic Cancer?

Pancreatic cancer is a deadly disease that occurs when cells in the pancreas grow out of control to form a tumor. The pancreas is responsible for digestion and for regulating blood sugar.

WHO IS AFFECTED?
- Most people diagnosed are over age 55
- More likely to affect men than women
- African Americans and Ashkenazic Jewish communities are at higher risk

WHAT ARE THE RISK FACTORS?
- The cause of most pancreatic cancer cases is unknown, although some risk factors have been identified:
  - Smoking
  - Family history
  - Diabetes
  - Obesity
  - Chronic pancreatitis
  - Inherited mutation in the BRCA-2 gene

WHAT ARE THE SYMPTOMS?
- Pancreatic cancer typically does not have any signs or symptoms until the disease is advanced, when the tumor is likely large and has spread to other organs. Symptoms may include:
  - Jaundice (yellowing skin or eyes)
  - Dark urine
  - Abdominal pain
  - Sudden or unexpected weight loss
  - Changes in appetite
  - Gallbladder or liver enlargement
  - Blood clots
  - Diabetes

HOW IS IT TREATED?
- The only way to cure pancreatic cancer is through surgery. Other treatments may help alleviate symptoms and prevent complications.

Depending on the stage of pancreatic cancer, treatment may include:
- Surgery
- Chemotherapy and radiation
- Immunotherapy
- Pain control
- Treatments being investigated include cancer metabolism-based therapies

For patients with metastatic pancreatic cancer who have already been treated with two previous therapies, there are no FDA-approved 3rd line treatments and no national oncology guideline recommendations.
WHAT IS THE PROGNOSIS?9-11

Over 90% of patients do not survive 5 years. Factors affecting prognosis include:

- **Tumor Size:** Tumors that have spread beyond the pancreas typically cannot be removed by surgery and carry a poorer prognosis.

- **Circulating Tumor Cells (CTCs):** CTCs are cancer cells that slough off tumors into the bloodstream. They may land in a new location to cause metastasis. Higher CTC levels are associated with a lower chance for survival.

Outlooks are especially poor for patients who have failed systemic therapies: an analysis of 19 prospective pancreatic cancer trials demonstrated a median survival time of just 2.0 – 2.5 months after progression from second-line therapy.12

<table>
<thead>
<tr>
<th>TUMOR STAGE</th>
<th>PERCENT OF PATIENTS WHO SURVIVE 5+ YEARS FOLLOWING DIAGNOSIS</th>
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<tbody>
<tr>
<td>Localized to pancreas only</td>
<td>34%</td>
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<tr>
<td>Restricted to pancreas and surrounding tissues</td>
<td>12%</td>
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<tr>
<td>Spread to distant tissues</td>
<td>3%</td>
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TYME-88-PANC Clinical Trial: **SM-88 in Pancreatic Cancer**13,14

**OVERVIEW**

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<tr>
<th>PHASE II</th>
<th>PHASE III</th>
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<tr>
<td>49 heavily pretreated patients with radiographically progressive metastatic pancreatic cancer</td>
<td>Approximately 250 patients who have been previously treated with two systemic therapies</td>
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<tr>
<td>More than 80% of patients had received at least two prior lines of therapy</td>
<td>Randomized 1:1 to SM-88 920 mg or an investigator-chosen therapy</td>
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<tr>
<td>Randomized 1:1 to one of two doses of SM-88: 460 mg or 920 mg</td>
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<td>Average patient age is 66</td>
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**OUTCOMES**

<table>
<thead>
<tr>
<th>PHASE II</th>
<th>PHASE III</th>
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<tr>
<td>Multiple indicators of efficacy and safety</td>
<td>Overall survival</td>
</tr>
<tr>
<td>Change in tumor size as measured by CT scans</td>
<td>Clinical benefit rate (stable disease or better)</td>
</tr>
<tr>
<td>Change in CTC levels as measured through blood tests</td>
<td>Change in CTC levels as measured through blood tests</td>
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<td>Quality of life indicators</td>
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**ABOUT SM-88**

- Investigational oral cancer metabolism-based therapy
- Thought to interrupt the metabolic processes of cancer cells by breaking down their key defenses, leading to cell death through oxidative stress and exposure to the immune system.
- Demonstrated encouraging tumor responses across 15 cancers—including pancreatic, lung, breast, prostate, sarcoma and lymphoma—with minimal serious grade 3 or higher adverse events.

**REFERENCES**