

Neoadjuvant Paclitaxel Poliglumex (PPX),
Cisplatin and Radiation (RT) for
Esophageal Cancer:
A Preliminary Analysis Of a Phase II Trial

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PPX as a Radiosensitizer

- A drug conjugate that links paclitaxel to a polyglutamic acid polymer.
- PPX molecular weight of 40,000, as compared to 854 for paclitaxel. This large size underlies PPX radiosensitization.
- Tumors have increased permeability to large molecules. Radiation further increases the vascular permeability of solid tumors.
- Preclinical data by Milas demonstrate a PPX radiosensitization index of 7-8 as compared to 1.5-2 for paclitaxel, cisplatin and 5-FU.

Prior Brown University Phase I Studies of PPX/RT in Esophagogastric Cancer

- Phase I PPX/ RT

MTD of single agent PPX was 70 mg/m²/week x 6 weeks
with 50.4 Gy

- Phase I PPX/ Cisplatin/ RT

MTD of PPX 50 mg/m² + cisplatin 25 mg/m² x 6 weeks
with 50.4 Gy

*Dose Limiting Toxicities: esophagitis, nausea,
dehydration.*

Phase II Study: Objectives

- Determine the pathologic complete response of neoadjuvant PPX/cisplatin/RT
- Determine the toxicities of PPX/cisplatin/RT

Eligibility

- Adenocarcinoma or squamous cell cancer of the esophagus or GE Junction.
- Potentially resectable. Regional adenopathy allowed. Distant organ metastases excluded.
- Adequate hematologic, renal, liver function

Treatment Plan

Radiation

PPX 1 8 15 22 29 36 → Surgery

Cisplatin 1 8 15 22 29 36

Dose:

- Radiation: 50.4 Gy, 1.8 Gy fx x 28 treatments
- PPX: 50 mg/m²/week x 6
- Cisplatin: 25 mg/m²/week x 6

Patient Characteristics (N=40)

Median Age	62
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Histology

Adenocarcinoma	37
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Squamous	3
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All Toxicities

	<u>Grade 3</u>	<u>Grade 4</u>	<u>Grade 5</u>
• Esophagitis	6%	-	-
• Nausea	8%	-	-
• Allergy	6%	-	-
• Fatigue	3%	-	-
• Electrolytes	15%	6%	-
• Platelets	-	-	-
• Neutrophils	6%	-	-

Outcome

Pathologic Complete Response

- 8 of the first 28 patients (28.5%) undergoing surgery.
All of which were adenocarcinomas.

Survival: Too early

Conclusions

- PPX, cisplatin and concurrent radiation is a well tolerated, easily administered regimen for esophageal cancer
- Low incidence of significant esophagitis
- Promising pathologic complete response rate consistent with the preclinical data of PPX and radiation.

Future Phase III Proposal:

5-FU/Cisplatin/RT → Surgery

Versus

PPX/Cisplatin/RT → Surgery

Hypothesis:

- Survival will be equal
- Quality of life will be improved
- Toxicities will be reduced - less esophagitis, no feeding tube, no central venous access
- Pathologic CR will be slightly higher

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