Nanoparticles for Cancer Treatment: A Review

Presenters: Amna Rizvi-Toner, Chase Kooyman, Ahamed Ahamed, Agassi Mila

Mentor: Jose Assouline, Ph.D.
Introduction

- **Objective**
  - Literature review of clinical trials investigating nanoparticle-mediated drug delivery (NMDD) for cancer
  - Published within the last five years

- **Why?**
  - Cancer is the second leading cause of death in the U.S.\(^1\)
  - NMDD limits adverse effects from traditional chemotherapy\(^2\)
  - NMDD is becoming more common and will be encountered more frequently by pharmacists

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\(^1\) https://static1.squarespace.com/static/538bab6ce4b0bc9029ed37ba/t/53c1cb6be4b0fe63e4f5c9fd/1405209454360/

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T. Phamduy, 2014
Background

- Nanoparticles\(^2\):
  - \(\sim 1-200\) nm in at least one dimension
  - High surface area to volume ratios
  - Inorganic, organic, and combination
    - Inorganic easy to produce, biocompatible, and modifiable surfaces
      - Suitable for treatment of cancer
      - Examples: metallic, mesoporous silica, and magnetic nanoparticles

[Image: https://www.azonano.com/images/Article_Images/ImageForArticle_3012(2).jpg]
Methods & Results Overview

- Methods
  - PubMed search
    - ("Neoplasms"[Mesh]) AND "Nanoparticles"[Mesh]
    - Filters: clinical trial, past 5 years, humans
- Results
  - Out of 53 articles, 23 were relevant to objective
  - More than half the trials studied paclitaxel (n= 17)
  - Other agents:
    - Camptotheclin
    - Irinotecan
    - Doxorubicin
    - Annamycin
    - 2-Methoxyestradiol
    - Epirubicin
<table>
<thead>
<tr>
<th>Cancer</th>
<th>Drug</th>
<th>Dose</th>
<th>Response</th>
<th>Adverse Effects</th>
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<tbody>
<tr>
<td>Breast Cancer</td>
<td>Nanoparticle Paclitaxel(^3)</td>
<td>300 mg/m(^2) or 220 mg/m(^2)</td>
<td>4% and 2% complete response</td>
<td>Neutropenia – 39%</td>
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<td>Neuropathy – 17% (high dose only)</td>
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<td>Anemia – 20% and 14%</td>
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<td>38% and 36% partial response</td>
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<td>Cremophor Paclitaxel(^3)</td>
<td>175 mg/m(^2)</td>
<td>5% complete response</td>
<td>Neutropenia – 50%</td>
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<td>Nab-PTX plus trastuzumab with</td>
<td>Regimen-dependent</td>
<td>EC/FEC - 78% clinical response, 27% complete</td>
<td>Neutropenia – 36% vs 47% EC/FEC alone</td>
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<td>epirubicin/cyclophosphamide</td>
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<td>response in patients with no response to</td>
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<td>or 5-fluorouracil/epirubicin/</td>
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<td>EC/FEC alone</td>
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<td>cyclophosphamide(^4)</td>
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<td>EC/FEC+nabPTX-tmab – 93% clinical response, 27%</td>
<td>Anemia – 34% vs 42% EC/FEC alone</td>
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<td>complete response in patients with no response to EC/FEC alone</td>
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Results - Paclitaxel Formulations

Nanoparticle Paclitaxel vs Cremophor Paclitaxel
- Nanoparticle formulations associated with significant neuropathy
- Cremophor formulation associated with more significant anemia and neutropenia

Albumin-Bound Paclitaxel (nabPTX) Regimens
- Improved partial response rates when added to an existing regimen
- Improved complete response rates when added to an existing regimen
- Maximum tolerated dose of 260 mg/m$^2$
  - Given once per cycle, weekly
- Frequent Hematologic Toxicities
  - Neutropenia
  - Leukopenia
- Frequent Non-Hematologic Toxicities
  - Sensory Neuropathy
  - Myalgia
  - Arthralgia
Results - Camptothecin Conjugated vs Unconjugated

![Graphs showing concentration vs time for Camptothecin Conjugated and Unconjugated with different dose levels.](image)

- **Graph a** shows the concentration over time for Conjugated and Unconjugated forms at various dose levels.
- **Graph b** illustrates the mean AUC (h·mg/L) for both conjugated and unconjugated forms at different doses.

Dose (mg/m²) vs Mean AUC (h·mg/L)
Conclusion

Provide healthcare professionals with a resource

Take home points?

Future research

- Review on cancer treatment as time progresses
- Review on other disease states that could benefit from nanoparticle treatment
- Medical opportunities
  - Drug delivery (vaccine)
  - Diagnostic techniques (early detection)
  - Anti-microbial techniques
Implications

Healthcare system implication
  ● Healthcare cost?

Medical practice implications
  ● Change scope of practice
  ● Up-to-date

Patient implication
  ● What does this mean for the patient?
References


Thank you!