Southeastern Multidisciplinary Approaches to Cancer Symposium

Ovarian Cancer: A Critical Need for Decision-Support as a Result of a Remarkable Expansion of Therapeutic Options

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Disclosures

- Consultant for GSK

This presentation and/or comments will be free of any bias toward or promotion of the above referenced companies or their product(s) and/or other business interests.

This presentation and/or comments will provide a balanced, non-promotional, and evidence-based approach to all diagnostic, therapeutic and/or research related content.

This presentation has been peer-reviewed and no conflicts were noted.

Cultural Linguistic Competency (CLC) & Implicit Bias (IB)

STATE LAW:
The California legislature has passed Assembly Bill (AB) 1195, which states that as of July 1, 2006, all Category 1 CME activities that relate to patient care must include a cultural diversity/linguistics component. It has also passed AB 241, which states that as of January 1, 2022, all continuing education courses for a physician and surgeon **must** contain curriculum that includes specified instruction in the understanding of implicit bias in medical treatment.

The cultural and linguistic competency (CLC) and implicit bias (IB) definitions reiterate how patients' diverse backgrounds may impact their access to care.

EXEMPTION:
Business and Professions Code 2190.1 exempts activities which are dedicated solely to research or other issues that do not contain a direct patient care component.

The following CLC & IB components will be addressed in this presentation:

- *Discuss concerns with the provision of optimal care in ovarian cancer and potential solutions, including insuring data related to patient diversity*
- *Discuss concerns that clinical trial data may not adequately address relevant data related to specific patient populations.*

“A Tale of Two Eras”

Pre and Post bevacizumab in ovarian cancer

“…….It was the worst of times ……..
(limited treatment options for patients)

…….It was the best of times ……
(limited treatment options required to consider)

(Pre) Primary chemotherapy for ovarian cancer

Platinum agents (cisplatin replaced by carboplatin)

Cisplatin + paclitaxel (cisplatin replaced by carboplatin)
5-6 cycles (unchanged today)

Examined in randomized trials:
No value maintenance (> 6 cycles)
No value dose intensification or high dose chemotherapy
No value adding a third drug
No value substituting another cytotoxic for paclitaxel
Negative impact associated with removing platinum agent

(Pre) Platinum-sensitive recurrent ovarian cancer

(Definition: Disease recurrence ≥ 6 months following completion of primary platinum-based chemotherapy)

Carboplatin + second clinically active agent (paclitaxel, PLD, gemcitabine)

- **Combination regimen superior to single agent platinum**
- **Continued until progression or excessive toxicity**
- **Duration of response always < prior response duration**
- **Potential for multiple responses in "platinum-sensitive setting"**
- **No curative potential**

(Pre) Platinum-resistant ovarian cancer

Multiple single agents (weekly paclitaxel; PLD; gemcitabine; topotecan; altretamine; etoposide; docetaxel; ifosfamide; irinotecan; pemetrexed; vinorelbine; 5-FU; tamoxifen)

- **Single agents generally administered in sequence**
- **No evidence for superiority of any single agent compared to another**
- **No evidence for benefit of combinations of cytotoxic drugs**
- **No evidence for benefits of dose intensification or high-dose therapy**
- **No evidence for superiority of specific drug sequencing or schedules**
- **No evidence for clinical utility of immunotherapeutic strategies**
- **Uncertain impact on overall survival or quality-of-life**

And along comes bevacizumab ….

Randomized phase 3 trial evidence of improved survival outcomes (PFS) in ovarian cancer:

Primary chemotherapy (2 studies - GOG, Europe)
chemotherapy + maintenance
Platinum-sensitive recurrent disease (2 studies - GOG, OCEANS)
chemotherapy + maintenance
Platinum-resistant disease (AURELIA)
with paclitaxel, PLD, or topotecan

Phase 3 trial evidence a "bevacizumab containing regimen" followed by another "bevacizumab containing regimen" improves outcomes (PFS)

Followed by PARP inhibitor maintenance therapy of ovarian cancer ……..

Randomized phase 3 trial evidence of improved survival outcomes (PFS) in ovarian cancer:

2 drugs currently routinely employed (olaparib, niraparib) as "maintenance following response to chemotherapy"

Primary chemotherapy maintenance
Platinum sensitive recurrent disease maintenance

BRCA 1, BRCA 2 mutations
HRD (based on several molecular testing platforms)

(Post) Primary chemotherapy of ovarian cancer

Carboplatin + paclitaxel

with or without bevacizumab (+ maintenance)

with or without PARP inhibitor maintenance

<u>Unanswered systemic therapy questions</u>:

Which patient populations should receive bevacizumab?

Which patient populations should receive a PARP inhibitor?

Which PARP inhibitor to administer and optimal duration of maintenance?

Clinical value of combination maintenance bevacizumab + PARP inhibitor?

(Post) Platinum-sensitive recurrent ovarian cancer

Carboplatin + second cytotoxic agent (paclitaxel, PLD, gemcitabine)
with or without bevacizumab (+ maintenance)
with or without PARP inhibitor maintenance

<u>Unanswered systemic therapy questions</u>:
Is the existing definition of this population still appropriate with current standard-of-care primary "maintenance strategies"?
Should bevacizumab be added if administered in the primary setting?
Is there a role for combining bevacizumab and a PARP inhibitor?
What is the optimal duration of therapy?

(Post) Platinum-resistant ovarian cancer

A plethora of options with little direction (listing in alphabetical order ……)

- **AURELIA - bevacizumab + paclitaxel / PLD / topotecan**
- **Mirvetuximab (FRa-positive ovarian cancer)**
- **Pembrolizumab + paclitaxel**
- **Relacorilant + nab-paclitaxel**
- **Single agents (including bevacizumb)**
- **Tumor agnostic agents (including several ADCs)**

<u>Unanswered systemic therapy questions:</u>

- **Is the definition of platinum-resistant disease appropriate”**
- **What is the most effective option for an *individual patient*?**
- **What is the optimal drug sequencing for an *individual patient*?**
- **Impact existing co-morbidities and non-oncologic medications?**

A proposed radical solution to the expanding decision-support dilemma

The answers to many of the questions can be rationally addressed by interrogating real-world data hidden within large electronic medical record databases

Measurable outcomes, both *positive* (overall survival; duration of treatment with a regimen) and *negative* (discontinuation of therapy; dose modifications; hospitalizations; emergency room visits; *evolving strategy of patient-reported outcomes*) ……..

following specific treatments (considering documented co-morbidities/non-cancer related pharmaceuticals) and sequencing

utilizing evolving AI technology ……