Controversies in CINV - Drug access -

“Are there Strategies to Improve Antiemetic Access?”

June 2019

Mitsue Saito
Dept. of Breast Oncology
Juntendo University Hospital
Tokyo, Japan
My talk

1) SDGs (Sustainable Development Goals) proposed by UN (United Nations)

2) Literature review

3) Questionnaire study
My talk

1) SDGs (Sustainable Development Goals) proposed by UN (United Nations)

2) Literature review

3) Questionnaire study
SUSTAINABLE DEVELOPMENT GOALS
17 GOALS TO TRANSFORM OUR WORLD

1. NO POVERTY
2. ZERO HUNGER
3. GOOD HEALTH AND WELL-BEING
4. QUALITY EDUCATION
5. GENDER EQUALITY
6. CLEAN WATER AND SANITATION
7. AFFORDABLE AND CLEAN ENERGY
8. DECENT WORK AND ECONOMIC GROWTH
9. INDUSTRY, INNOVATION AND INFRASTRUCTURE
10. REDUCED INEQUALITIES
11. SUSTAINABLE CITIES AND COMMUNITIES
12. RESPONSIBLE CONSUMPTION AND PRODUCTION
13. CLIMATE ACTION
14. LIFE BELOW WATER
15. LIFE ON LAND
16. PEACE, JUSTICE AND STRONG INSTITUTIONS
17. PARTNERSHIPS FOR THE GOALS
BACKGROUND

• The 17 Sustainable Development Goals (SDGs) addressed by the United Nations (UN) officially came into force in 2016. Over the next fifteen years, with these new universally-applicable goals, nations worldwide can mobilize efforts to end all forms of poverty, fight inequalities and tackle various problems including health and well-being issues, while ensuring that no one is left behind.

• In the field of health promotion, non-communicable diseases such as cancer have become one of the major problems to be solved by collaboration among countries.
1) No poverty
2) Zero hunger
3) **Good health** and well-being
4) Quality **education**
5) Gender equality
6) Clean Water and Sanitation
7) Affordable and clean energy
8) **Decent work and economic growth**
9) Industry, Innovation and Infrastructure

10) **Reduced inequalities**
11) Sustainable Cities and Communities
12) Responsible Consumption and Production
13) Climate Action
14) Life under Water
15) Life on Land
16) Peace, Justice and strong Institutions
17) Partnerships for the goals

Considering “drug access” all over the world, some of the SDGs should be achieved.
If our **VISION** is the achievement of **SDGs**, our **MISSION** in Supportive Care in Cancer should be the promotion of **Guideline Recognition, application & Drug approval, reimbursement**

- **Partnerships for the goals**
- **Good Health well being**
- **Quality Education reduced Inequalities**
- **Economic Growth decent Work**
Number of people with cancer, 2017
Total number of people suffering from any type of cancer at a given time. This is measured across both sexes, and all ages.
Cancer death rates, 2017

Age-standardized death rates from all cancer types, measured as the number of deaths per 100,000 individuals. Age-standardization assumes a constant population age & structure to allow for comparisons between countries and with time without the effects of a changing age distribution within a population (e.g. aging).

Source: IHME, Global Burden of Disease (GBD)
Disease burden rates from cancers, 2017

Age-standardized DALY (Disability-Adjusted Life Year) rates per 100,000 individuals from all cancer types. DALYs measure total burden of disease - both from years of life lost and years lived with a disability. One DALY equals one lost year of healthy life.

Source: IHME, Global Burden of Disease
Health spending per person, 2016

Units are in 2018 US dollars.

But, How can we achieve these Goals?
And, How can we carry out these Missions?
My talk

1) SDGs proposed by UN

2) Literature review

3) Questionnaire study
So, What should we do?

- Worldwide, adherence to guidelines and accessibility to medicines varies markedly among countries, institutions, physicians and patients.

- To provide the best antiemetics to every patient, regardless of individual situations, we must recognize the present status including differences in policy, drug supplies and physician knowledge and preferences all over the world.
Methods

① We aimed to investigate the present situation of CINV globally, to the extent possible. We initially sought information from regulatory agencies, several world-wide trading pharmaceutical companies.

② The next step in our research was reviewing published articles related to drug access and adherence to guideline recommended medicines.

③ Questionnaire study
Results of method ①

I tried very hard, however... The information obtained from regulatory agencies and pharmaceutical companies was very limited due to their rules and territorial restrictions.

Then...
2 Literature review (1)

• Search engine; PubMed

• Keywords

1) Supportive Care & developing country

⇒ However, most of them are not related to cancer
Literature review (2)

• Key words; CINV & developing country

1) Evaluation of anti-emetic use in chemotherapy-induced nausea and vomiting in a third-world country (Lebanon)

Abeer A. Zeitoun Pharm D¹ and Jeanette G. Nassif Pharm D²
¹Clinical Assistant Professor, ²Clinical Assistant Professor, Pharmacy Practice Department, School of Pharmacy, Lebanese American University, Byblos, Lebanon


2) Baseline patient characteristics, incidence of CINV, and physician perception of CINV incidence following moderately and highly emetogenic chemotherapy in Asia Pacific countries

Ruey Kuen Hsieh · Alexandre Chan · Hoon-Kyo Kim · Shiying Yu · Jong Gwang Kim · Myung-Ah Lee · Johan Dalén · Hun Jung · Yan Ping Liu · Thomas A. Burke · Dorothy M. K. Keefe

DOI 10.1007/s00520-014-2373-2

This is the only literature which has met our needs in my view.
The article related to drug access and adherence to guideline in daily practice in a developing country

<table>
<thead>
<tr>
<th></th>
<th>Minimal</th>
<th></th>
<th>Low</th>
<th></th>
<th>Moderate</th>
<th></th>
<th>High</th>
<th></th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
<td>n</td>
<td>%</td>
<td>n</td>
<td>%</td>
<td>n</td>
<td>%</td>
<td></td>
</tr>
<tr>
<td>Appropriate regimen</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>3</td>
<td>5.9</td>
<td>1</td>
<td>0.8</td>
<td>253</td>
<td>88.5</td>
<td>25</td>
<td>83.3</td>
<td>0.0001*</td>
</tr>
<tr>
<td>No</td>
<td>48</td>
<td>94.1</td>
<td>125</td>
<td>99.2</td>
<td>33</td>
<td>11.5</td>
<td>5</td>
<td>16.7</td>
<td></td>
</tr>
<tr>
<td>Appropriate dose</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>1</td>
<td>100</td>
<td>0</td>
<td>0</td>
<td>13</td>
<td>5.1</td>
<td>3</td>
<td>12</td>
<td>0.003*</td>
</tr>
<tr>
<td>Low</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>100</td>
<td>107</td>
<td>42.3</td>
<td>7</td>
<td>28</td>
<td></td>
</tr>
<tr>
<td>High</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>133</td>
<td>52.6</td>
<td>15</td>
<td>60</td>
<td></td>
</tr>
<tr>
<td>Appropriate duration</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>3</td>
<td>100</td>
<td>1</td>
<td>100</td>
<td>51</td>
<td>20.2</td>
<td>0</td>
<td>0</td>
<td>0.0001*</td>
</tr>
<tr>
<td>No</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>202</td>
<td>79.8</td>
<td>25</td>
<td>100</td>
<td></td>
</tr>
</tbody>
</table>

*Statistically significant results ($P < 0.05$).
Results of method ② from the Literature review

• To alert health care professionals of the adverse consequences resulting from non-adherence to guidelines is crucial.

• Drug selection, combination, dosing, route of administration and duration of treatment should be properly recognized, if the regimen is based on guidelines.

• The role of clinical pharmacist should be reinforced.
My talk

1) SDGs proposed by UN

2) Literature review

3) Questionnaire study
   • method ③
A Questionnaire study

Web research, asking questions regarding supportive care for cancer patients, such as

• drug approval by governments,
• application of guidelines,
• treatment reimbursement and drug availability in daily practice,

was planned.

• Oncologists, pharmacists and nurses in Asian & African countries were the respondents.
Democratic Republic of the Congo

Republic of Nepal

Republic of Korea

People's Republic of China

Kingdom of Thailand

Kingdom of Cambodia

Republic of the Philippines

Mongolia

Japan
1) Is each chemotherapy performed based on any guidelines? *
① Yes
② No

2) Which guideline do you mainly follow for chemotherapy? *
① ASCO
② NCCN
③ ESMO
Other:

3) Which guideline do you mainly follow for supportive care in cancer? *
① ASCO
② NCCN
③ ESMO
④ MASCC
Other:

Web questionnaire https://forms.gle/nsMKj7UFVekowuRM9
4) Which **antiemetics** are approved by your government?
   ① aprepitant
   ② granisetron
   ③ ondansetron
   ④ palonosetron
   ⑤ olanzapine

5) What is the standard antiemetic therapy for **cisplatin** in your institution? *
   ① serotonin receptor antagonist (5HT3ra)
   ② 5HT3ra+aprepitant
   ③ 5HT3ra+dezamethasone (DEX)
   ④ 5HT3ra+DEXA+aprepitant
   ⑤ 5HT3ra+DEXA+aprepitant+olanzapine

6) What is the standard antiemetic therapy for **AC** (anthracycline cyclophosphamide-containing) regimen in your institution? *
   ① serotonin receptor antagonist (5HT3ra)
   ② 5HT3ra+aprepitant
   ③ 5HT3ra+dezamethasone (DEX)
   ④ 5HT3ra+DEXA+aprepitant
   ⑤ 5HT3ra+DEXA+aprepitant+olanzapine
7) What do you recommend for prophylaxis or treatment of **neutropenia** during chemotherapy?
①CDK4/6 inhibitors  
②mTOR inhibitor  
③immune checkpoint inhibitors  
④trastuzumab  
⑤lapatinib  
⑥pertuzumab  
⑦TDM-1

8) Is G-CSF (Filgrastim) approved by your government? *
①Yes  
②No

9) Which molecular–targeted therapies are available in your country? *
①Yes  
②No

10) Is a multidisciplinary team approach available for the variety of adverse events induced by recent molecular–targeted therapy? *
①Yes  
②No
11) What kind of multidisciplinary professionals are involved with cancer patients?
① Pharmacist
② Nurse
③ medical oncologist
④ surgical oncologist
⑤ radiation oncologist

12) What are the barriers for providing best supportive care for every patient?
① Delay of drug approval
② economical issues
③ institutional policies
④ Guideline application issues
Which guideline is applied in Cancer treatment most?

- **participants**
- NCCN GL
- ASCO GL
- ESMO GL
- Domestic GL

Legend:
- **people**
- **country**
Which guideline is applied in Supportive Care in Cancer most?

Chart Title

- participants
- NCCN GL
- ASCO GL
- ESMO GL
- MASCC GL
- Domestic GL

Legend:
- people
- country
Drug approval for CINV

- Congo: 1 (aprepitant, granisetron, ondansetron, palonosetron, olanzapine)
- Mongolia: 1 (aprepitant, granisetron, ondansetron, palonosetron, olanzapine)
- Cambodia: 2 (aprepitant, granisetron, ondansetron, palonosetron, olanzapine)
- The Philippines: 3 (aprepitant, granisetron, ondansetron, palonosetron, olanzapine)
- Thailand: 5 (aprepitant, granisetron, ondansetron, palonosetron, olanzapine)
- Nepal: 5 (aprepitant, granisetron, ondansetron, palonosetron, olanzapine)
- China: 4 (aprepitant, granisetron, ondansetron, palonosetron, olanzapine)
- Korea: 4 (aprepitant, granisetron, ondansetron, palonosetron, olanzapine)
- Japan: 5 (aprepitant, granisetron, ondansetron, palonosetron, olanzapine)
## How are the practical antiemetic therapy in each country?

<table>
<thead>
<tr>
<th></th>
<th>Congo</th>
<th>Mongolia</th>
<th>Cambodia</th>
<th>Philippines</th>
<th>Thailand</th>
<th>Nepal</th>
<th>China</th>
<th>Korea</th>
<th>Japan</th>
</tr>
</thead>
<tbody>
<tr>
<td>CDDP</td>
<td>○</td>
<td>, AC</td>
<td>●</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5HT3ra</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>○</td>
<td>●</td>
<td>○</td>
<td>●</td>
<td>●</td>
</tr>
<tr>
<td>5HT3ra+DEX</td>
<td>○</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>○</td>
<td>●</td>
<td>●</td>
<td>●</td>
</tr>
<tr>
<td>5HT3ra+DEX+NK1ra</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>○</td>
<td>●</td>
<td>●</td>
<td>●</td>
</tr>
<tr>
<td>5HT3ra+DEX+NK1ra+OLZ</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>○</td>
<td>●</td>
<td>●</td>
<td>●</td>
</tr>
<tr>
<td>5HT3ra+NK1ra+OLZ</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>○</td>
<td>●</td>
<td>●</td>
<td>●</td>
</tr>
</tbody>
</table>

- **The current guideline based antiemetic therapy**
- **Evidence based antiemetic therapy historically**
In Summary: There are some discrepancies between report and practice

<table>
<thead>
<tr>
<th>country</th>
<th>Congo</th>
<th>Mongolia</th>
<th>Cambodia</th>
<th>Philippines</th>
<th>Thailand</th>
<th>Nepal</th>
<th>China</th>
<th>Korea</th>
<th>Japan</th>
</tr>
</thead>
<tbody>
<tr>
<td>respondents</td>
<td>2</td>
<td>1</td>
<td>2</td>
<td>4</td>
<td>3</td>
<td>2</td>
<td>4</td>
<td>1</td>
<td>10</td>
</tr>
<tr>
<td>GL'Oncology)</td>
<td>NCCN</td>
<td>NCCN</td>
<td>NCCN ASCO</td>
<td>NCCN ESMO</td>
<td>NCCN ESMO</td>
<td>NCCN ASCO</td>
<td>NCCN ASCO</td>
<td>NCCN ASCO</td>
<td>NCCN domestic</td>
</tr>
<tr>
<td>GL(CINV)</td>
<td>NCCN</td>
<td>NCCN</td>
<td>NCCN ASCO</td>
<td>NCCN ESMO</td>
<td>NCCN ESMO</td>
<td>NCCN ASCO</td>
<td>NCCN ASCO</td>
<td>NCCN ASCO</td>
<td>NCCN ASCO</td>
</tr>
<tr>
<td>aprepitant(approved)</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
</tr>
<tr>
<td>granisetron(approved)</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
</tr>
<tr>
<td>ondansetron(approved)</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
</tr>
<tr>
<td>palonosetron(approved)</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
</tr>
<tr>
<td>olanzapine(approved)</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
</tr>
<tr>
<td>5HT3ra</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
</tr>
<tr>
<td>5HT3ra+DEX</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
</tr>
<tr>
<td>5HT3ra+DEX+NK1ra</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
</tr>
<tr>
<td>5HT3ra+DEX+NK1ra+OLZ</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
</tr>
<tr>
<td>5HT3ra+NK1ra+OLZ</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
</tr>
</tbody>
</table>
The delay of applying optimal antiemetics is due to...
Results

• Twenty-nine oncology professionals in various countries including Congo, Mongolia, Cambodia, Thailand, the Philippines, Nepal, Korea, China and Japan answered the questionnaire.

• International guidelines, such as NCCN and ASCO, were reportedly well known and multidisciplinary approaches were reportedly applied in daily clinical practice.

• However, the practical standard treatments differed among countries.

• To access optimal drugs, there are 3 barriers: drug approval, guideline application and financial support.
Conclusions

Clinical Question: Are there Strategies to Improve Antiemetic Access?

• My personal answer: Yes. **Education** such as recognition of Guidelines correctly is the first one.
• The development of own domestic guidelines adjusted by their own environment (if necessary) might be the second one.
• The **awareness** of people including patients, government and regulatory agency personnels should be the next.

How?
• Disseminating “**MASCC activity**” all over the world.
• That is what we have to discuss, create and execute!
• **Education** & Advertisement of **MASCC GL** are in my mind.
• for Education: not only the **current GLs** but also the **past ones** which must be useful for the countries or institutions trying to catch up with the current one.
Considerations

• In order to promote cancer treatment including supportive care, education based on guidelines and multidisciplinary team building are essential.

• Meeting these goals should be basically facilitated by their own motivation.

• For education, collaborative efforts among countries might be helpful.

• The challenges of promoting drug approval and financial support from outside of countries await resolution.

• For future collaboration with UN, WHO or academic associations in developing countries might be helpful.
Acknowledgement to collaborators

- Dr. Jun Noritake (Thailand)
- Dr. Manabu Okawada (Cambodia)
- Dr. Jong-Heun Kim (Korea)
- Dr. Shilin Xia (China)
- Dr. Muchanga Sifa Marie (Congo)
- Dr. Alex Mutombo (Congo)
- Dr. Vivian Enriquez (the Philippines)
- Dr. Angelica Montesa (the Philippines)
- Dr. Anton Villanueva (the Philippines)
- Dr. Bharati Shrestha (Nepal)
- Dr. Bibek Acharya (Nepal)
- Dr. Kotaro Iijima
- Dr. Toru Mukohara
- Dr. Junichiro Watanabe
- Dr. Minoru Nakane
- Dr. Rumiko Okamoto
- Ms. Ms. Uki Saito (Pharmacist)
- Ms. Napat Saigosoom (Med student in Thailand)
- Dr. Bierta Barfod
Please come & join 2021MASCC in YOKOHAMA, Bay city, close to Tokyo(Haneda) airport!