Assessing Japan’s Three Early Access Programs Based on Recent Discussions: Scope And Financial Aid

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OBJECTIVE
Access to medicines is usually given under the regulatory approvals and subsequent coverage decisions, after efficacy and safety have been proven by clinical trials. Recently, systems to enable exceptional early access have been explored to meet significant, unmet, and urgent medical needs for frontier medicines. In Japan, the Advanced Medical Care B (AMC-B) system is already in operation. Two other systems, the Japanese version of Compassionate Use system (CU) and the Patient-Initiated Mixed-Care system (PIMC), are planned to start. The objective of this study is to understand the design and institutional positioning of these three systems, identifying opportunities for further improvements.

METHOD
A documentary research was conducted by analyzing government documents and the Diet Record.

RESULTS
As a result of the documentary search, three systems were identified to serve for the aim of early access in Japan: Advanced Medical Care B (AMC-B), Patient-Initiated Mixed-Care system (PIMC), Compassionate Use (CU). Each system is described in detail below.

Advanced Medical Care B (AMC-B)
- The present form of Advanced Medical Care (AMC) started in 2012. AMC consists of AMC-A and AMC-B. AMC-A is for approved technologies and unapproved drugs are not made available under this system. AMC-B is for unapproved/off-label drugs.
- Researchers at Health Insurance-Covered Medical Institution plan a clinical study to evaluate the unapproved/off-label technologies and apply to the review board (“Committee for Advanced Medical Care”).
- The review board designates technologies that include the use of unapproved medicines or off-label indications, after requests from researchers.
- The cost of unapproved/off-label drug is not reimbursed in AMC-B system, but in many cases part of the cost is paid by involving companies or with research budget. The cost of the concomitant approved treatments are reimbursed.

Patient-Initiated Mixed-Care system (PIMC)
- The Patient-Initiated Mixed-Care system (PIMC) is planned to start in 2016.
- Patients and the attending doctors consult Core Clinical Research Hospitals to find an opportunity to use unapproved/off-label drugs.
- The cost of unapproved/off-label drug is not reimbursed in AMC-B system, but in many cases part of the cost is paid by involving companies or with research budget. The cost of the concomitant approved treatments are reimbursed.

Japanese version of Compassionate Use system (CU)
- The Compassionate Use (CU) or Expanded Clinical Trial system is to be fully introduced in 2016 and larger medicines at later stages of clinical development, opening up opportunities for patients who are not eligible for the clinical trials.
- A (In figure 3): When a clinical trial/CU is ongoing, patients are expected to participate in it.
- B: If no clinical trial/CU is ongoing, they have an option to develop a PIMC clinical research and ask for approval. In figure 3: Basically, Clinical study.

RESULTS (CONTD)

Table 1. Comparison of the three systems for early access

<table>
<thead>
<tr>
<th>System</th>
<th>Patients</th>
<th>Design</th>
<th>Efficacy</th>
<th>Safety</th>
</tr>
</thead>
<tbody>
<tr>
<td>AMC-B</td>
<td>Limited to patients in designated hospitals.</td>
<td>Mainly safety</td>
<td>Need for safety</td>
<td>Need for safety</td>
</tr>
<tr>
<td>AMC-C</td>
<td>Limited to patients in designated hospitals.</td>
<td>Mainly efficacy</td>
<td>Need for efficacy</td>
<td>Need for efficacy</td>
</tr>
<tr>
<td>CU</td>
<td>Open to all patients, regardless of hospital.</td>
<td>Both</td>
<td>Both</td>
<td>Both</td>
</tr>
</tbody>
</table>

Additional information - Table 1
- For AMC-B and CU, sites are restricted to large central hospitals. Under PIMC, patients can be treated in nearby hospitals.
- CU extends target patients of clinical trials. AMC-B is for patients and drugs for which clinical trial is not being conducted. PIMC further extends target patients and drugs.

CONCLUSIONS
- The scopes of the three systems were found to be complementary to one another, covering both approved medicines and patients excluded from clinical studies.
- All the three systems aim for regulatory approval of the medicine or reimbursement, but not for patients’ treatments. Due to this, the accessibility to investigational drugs are restricted compared with other countries such as U.S.
- The new systems for early access are expected to expand the existing opportunities for investigational drugs for only a limited part of the patients.

References
1) MHLW Chu-i-kyo, 30 Sept. 2015, meeting material
2) MHLW-PMDC, 17 Sept. 2015, meeting material
3) MHLW notice by Health Policy Bureau (OT1-2. 31 July 2012)