Cellular Therapy in Asia

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Medical Tourism

Patients from USA, Europe and Middle East are visiting Asian countries for cellular therapy. Even from patients in Asia are visiting China or Japan to receive cellular therapy.

Many Asian people are visiting Germany, Switzerland for cosmetic cellular treatment.

Some German doctors are giving cellular therapy in Thailand.
Patients’ Rights

1. **Right to Seek Treatments**
2. **Right to Information**
   - Accurate representation to regarding safety and efficacy record of treatment
   - Likely side effects
   - Need for centralized repository of therapies
3. **Right to Informed Consent**
   - Clinical trials
   - Unproven therapies
   - And of course proven therapies too
Regulations for Cellular Therapies in Asia

Korea and Japan have effective regulation. Japan is planning new regulations. Korean FDA (KFDA) approved both allo and auto cellular therapy products. Japan (PMDA) approved only autologous cultured cellular products yet.

China proposed new regulations for cellular therapy but no approved cellular product yet.

Singapore issued regulations but not approved any product yet.

Taiwan issued guideline but not approved any product yet.
Differences in Regulation

• Some autologous cellular therapy is regulated as part of medical practice, not by drug law in China and Japan. Korea, Singapore and Taiwan regulation are regulating as drug following USA and EU.

• Recently, China and Japan proposed new regulation for cellular therapy which try to regulate autologous cellular therapy but not by drug law. New regulation in both country will require manufacturing license for cellular products. Japanese new regulation require clinical benefit data within few years after manufacturing license.

• Temporary conditional approval followed by Phase III/IV study by KFDA will accelerate development and help small company...
Cell Therapy Medical Tourism

• Medical tourism for terminal diseases: a long and inglorious tradition

• Significant risks to
  – Patients
  – The field of Cellular Therapy

• Mainstream medicine has not responded to protect patients nor to the needs of terminal stage patients and patients family
What’s on the Web?

**Stem Cell Research Forges Ahead in Latin America:** Positive results have been noted in a variety of medical conditions utilizing stem cell therapies, including Parkinson’s, multiple sclerosis, diabetes, vision problems, and other neurological disease.....

**StemCellsChina.Com:** If you are interested in receiving stem cell therapy, please fill out this short form. A qualified stem cell doctor will be glad to contact you with helpful treatment information....

**Cell Medicine** arranges stem cell therapy for patients with the following conditions: Autoimmune diseases, cerebral palsy, critical limb ischemia, degenerative joint disease, diabetes, heart failure, multiple sclerosis, osteoarthritis, rheumatoid arthritis & spinal injury... *Treatment is only available outside the US and Canada and is not covered by most insurance.....*
Korean Company in Japan (1)

Therapy is regulated as drug in Korea and is difficult for the company to run the study. In Japan, autologous cell therapy can be regulated as part of medical practice under doctor’s own decision with patient agreement and can make business. Japan is thought to be an easy country to run clinical application without regulatory control. Some Korean patients are receiving cellular therapy in Japan and one of them died because of complications. Cells were processed in Korea and shipped to Japan.
Korean Company in Japan (2)

KFDA stopped shipping not approved cellular products to other country. Then Korean company established CPC in Japan for Korean patients. Over 500 patients/month are visiting Japan for therapy.

There is no effective regulation for autologous cellular therapy in Japan yet if the treatment is based on IRB approval with patient agreement (informed consent)
What ACTO Can Do?

• Ensure
  – Mitigation of patient risks
  – Promotion of scientific development
  – Compassionate and early access to promising therapy
  – Promotion of full financial disclosure
  – Activation of cooperative activities among industry, academy and regulatory agent

• *Simple warnings are not enough!*
How to speed up regulatory process

The best solution is to make it possible for patient to receive wished therapy in home country.

What we can do?

• In some country, need speedy approval of already approved drug/device/therapy in other country
• Conditioned approval for new therapy
Specific to cellular therapy

In general, cellular therapy is developed by small company and/or academy and financially very weak. Cannot conduct large clinical trials. Conditional approval will help small company and accelerate development.

• Cellular therapy is not a simple drug/device but therapy with various elements needed for medical practice

• Who will own product license if you need approval as a drug. ➔ Need new regulation based on new concept.
• **Goals**
  1. Quickly make available medically necessary new drugs and medical devices to the Japanese people
  2. Promote innovation with and practical application of research discovery originating in Japan
  3. Encourage evidence building to find best treatments with combination of marketed drugs, medical devices etc.

  **Improve medical standards in Japan**

  **Spread the Japanese innovation throughout the world**

• **Main subjects**
  1. Further leap and independence of clinical trial sites based on the past 9 years’ activation plan
  2. Measures toward the creation of innovative drugs, medical devices etc. originating in Japan (Innovation)
2. **Measures toward the creation of innovative drugs, medical devices etc. originating in Japan (Innovation)**

(1) Improve the infrastructure for clinical research / trials

- Create “Clinical Trials Core Hospitals” that are able to conduct investigator-initiated clinical research of high quality (ICH-GCP compliant) etc.

(2) Improve the ethics and the quality of clinical research

(3) Strengthen the measures to promote clinical trials in the areas where companies are reluctant to develop drugs and medical devices etc.

(4) Cope swiftly with large-scale natural disasters
干细胞临床试验研究管理办法（试行）
（征求意见稿）

第一章 总则
第一条 为保证干细胞临床试验研究过程规范，结果科学可靠，保护受试者的权益并保障其安全，根据《中华人民共和国药品管理法》、《医疗机构管理条例》和《药物临床试验质量管理规范》等相关法律法规，制定本办法。
第八条

在中华人民共和国境内从事干细胞临床试验研究，包括境外机构以合作或投资等形式在中国开展的干细胞临床试验研究，必须遵守本办法。

本办法不包括已有规定的造血干细胞移植和以产品注册为目的的临床试验。

中国干细胞研究机构或人员在境外以合作或投资形式开展干细胞临床试验研究，应当遵守当地政府制定的相关法律法规。
干细胞临床试验研究基地管理办法（试行）
（征求意见稿）

第一章 总则
第一条 为加强干细胞临床试验研究的监督管理，根据《药物临床试验质量管理规范》、《药物临床试验机构资格认定办法（试行）》和《干细胞临床试验研究管理办法（试行）》，制定本办法。
干细胞制剂质量控制及临床前研究指导原则（试行）
（征求意见稿）

一、前言
二、干细胞制剂的质量控制
（一）干细胞的采集、分离及干细胞（系）的建立
（二）干细胞制剂的制备
（三）干细胞制剂的检验
（四）干细胞制剂的质量研究

三、干细胞制剂的临床前研究
（一）安全性评价
（二）有效性评价
Clinical Trials vs. Experimental Therapies/Medical Innovation

• Field will never progress without well controlled clinical trials

• Patients not eligible for controlled clinical trials should be able to choose unproven but scientifically validated therapies, if truthfully and ethically informed

• Patients’ need to understand the difference between the two paradigms

• It is difficult to find sponsor for the autologous cellular therapy if it is regulated as drug to study such as activated T-cell/NK cell or DC therapy with autologous antigen. Who will own product license if you need approval as a drug.
Role of Local Regulatory Authority

• ACTO acknowledges jurisdiction of local regulatory authorities
• However the degree of regulation and safeguards vary markedly and are often not enforced
• Key roles of independent ethics committees
  Specially autologous cellular therapy in China and Japan which is not directly regulated yet
• Need for international harmonization
  – International Conference on Harmonization (ICH)
  – International industry/professional organizations
Responsibility of Investigators/clinicians

- Must be ethical treatment procedures
- Regulatory compliance
- Publication/dissemination of results
- Following GCPs/clinical standards established by local regulatory authorities
- Responsibility in advertising
- Reporting adverse events
- Patient supportive care and follow up
What we should do

• Legitimate cell therapy opportunities for medical tourists: appropriately regulated by local authorities
• However there are so many unethical and potentially dangerous cell therapies
• Cellular therapy should not be an indulgence for patient and patient family
• Proposals from ACTO
  1. Consumers’ guide
  2. Regulatory convergence and international harmonization
  3. Partnership with patient advocacy groups

Will activate Asian cellular therapy activities in collaboration with academy, industry and regulatory agents.
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