Health Economical Research for Cell Therapy against Stroke

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\textbf{COI} Financial Disclosure: none
Unlabeled/Unapproved Uses Disclosure: none
Introduction

• Stroke is still a leading cause of death and disability, and despite intensive research, few treatment options exist. A recent breakthrough in cell therapy is expected to reverse the neurological sequelae of stroke.

• We started the clinical trials, Research on advanced intervention using novel bone marrow stem cell (RAINBOW) trials, June 2017. It is a phase 1, open label, uncontrolled, dose response study. The HUNS001-01, autologous bone marrow stromal cell (BMSC) product, is administered to acute ischemic stroke patients.

• However, there are some implications, for examples, Health Technology Assessment (HTA). How much is the cost of cell therapy justified in social economy?
Therapeutic mechanisms

BMSC

Differentiation
- Neural cell
- Endothelial cell
- Pericyte, etc.

Nursing effect
- Growth factors
- Axonal elongation
- Neurogenesis
- Vasculogenesis

Immunomodulation
### Clinical trials in Japan

<table>
<thead>
<tr>
<th>intravenous administration</th>
<th>direct transplantation</th>
</tr>
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<tbody>
<tr>
<td>autologous</td>
<td>STR01</td>
</tr>
<tr>
<td></td>
<td>(Nipro)</td>
</tr>
<tr>
<td>allogeneic</td>
<td>MultiStem / HLCM051</td>
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<tr>
<td></td>
<td>(Athersys / Healios)</td>
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<td></td>
<td>HUNS001-01</td>
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<td>(Hokkaido University)</td>
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<tr>
<td></td>
<td>SB623*</td>
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<td>(SanBio)</td>
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*: The only trial for TBI is on-going in Japan.
**Detailed trial flow in RAINBOW trials**

- **Onset**
  - Standard medication
  - 14 days

- **1st screening**
  - NIHSS ≥6

- **Bone marrow harvest**

- **2nd screening**
  - mRS ≥3
  - Day -7

- **Cell culture**
  - Low dose: $2 \times 10^7$ cells
  - High dose: $5 \times 10^7$ cells

- **Cell administration**

- **Observation**
  - less than 74 days

- **Primary outcome measure**

- **1 year**
Quality-adjusted life year (QALY)

- Cancer treatment
- Cell therapy for stroke

- QALY gained from intervention
QOL score by using EQ-5D-5L

RAINBOW study: Case 1

Perfect health

1.0

Onset

QALY

d14

0.121

d49

0.244

d86

0.437

d147

0.461

d237

0.609

Death

0.0

1st screening

2nd screening

30 days

90 days

180 days

post-transplant
Medical cost in RAINBOW trials

• Manufacturing cost
  – assumption in phase 3
    • 5 years
    • 50 cases/year
  – cell processing isolator
    • initial cost: 400,000USD/booth
    • administration/management cost: 40,000USD/year
  – personnel cost: 120,000USD/year
  – supplies expenses: 5,000USD/case
  – sterility test: 10,000USD/case
  – total cost: 20,000USD/case

• Operation cost
  – bone marrow harvest
  – cell transplantation
  – total cost: 6,000USD/case

Total: 26,000USD/case
Discussion

**Societal Value of Stem Cell Therapy in Stroke – A Modeling Study**

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- Health economical simulation for cell therapy (Svensson et al. 2011).
- Assumptions: 55yo, mRS:2, increase of 1.34 in QALY.
- Reduction of 19,055USD in lifelong medical cost (excluding the cost of cell products).
- 166,500USD in Societal value.

- National Institute for Health and Care Excellence (NICE) in UK proposed that less than £30,000 (about $40,000) per one QALY would be appropriate.
Conclusion

• We showed preliminary data of health economical research in RAINBOW trials.
• Health economical research is critical when the clinical application of cell therapy is justified in social economy.
• In practice, we should aim at increase of 1.0 in QALY (increase of 0.2 in QOL and 5 years in duration) and under 40,000USD in medical cost.