The proceedings of the 12th Annual Conference Society Of Regenerative Medicine (SRMTE).

This year the annual conference of SRMTE was held in School of Regenerative Medicine (SORM) and boasts of an impressive clutch of speakers in the space of Stem cell and Regenerative Medicine. The conference started on a positive note with the conveners: Dr. S.G.Ananda.Rao and Dr. Ramesh. Bhonde who went on to set the stage with the content focus matter of the meeting. This year the focus was:

**Way forward for stem cell therapy in India: The present status and the future.**

The conference, as in its tradition saw eminent scientists from the field of stem cells and Tissue Engineering. The opening remarks were by the conveners Dr. S.G. Ananda .Rao, Stem Foundation and Dr. Ramesh Bhonde, Dean, SORM which set the stage for the other eminent speakers to present their views in the conference. Dr. Rao spoke of his association with Dr. Habbibullah and reminisced his strong desire to work in the clinical applications of stem cells especially in liver patients. Dr. Pande also spoke about their association in the past.

The Chief Guest for this year was Dr. Vinod Bhatt , V.C Manipal University. He touched upon the status of research in India and expressed strengthening of our research activities in the field of Stem cells and Regenerative Medicine.

He expressed his wholehearted support to SRMTE by extending his backing through SORM and hosting the conference in SORM every year.

The guest of Honor for the conference was Dr. Raghuram. Bhandary, DCGI, Karnataka state.

This year, Padmashri C.M. Habeebullah symposium was convened instead of the memorial lecture and it began with Dr. Samuel Abraham, Nichi In, Chennai. His presentation was on clinical application of stem
cells. He spoke about Natural Killer Cell activity and their application in Cancer Therapy. He presented clinical data in a study: Corneal endothelial precursor cell transplantation methodology, employing a Nanocomposite gel sheet.

Since the topic of discussion also was to find a suitable middle path for stem cell research in India, he spoke of the differences in policy issues regarding clinical applications using stem cells in India and Japan. The statutory guidelines drafted for cell based therapy, in Japan follows a clear path where regulations are lucid and easy to follow. There are definite timelines for the guidelines to be set into regulations which are implemented by investigators in compliance to the general rules set by them. He expressed his dissatisfaction with the Indian counterpart and pointed out to the vacillations of the ICMR and DCGI and said that without clear regulations and timelines, India may be left behind in this field, especially since developed nations like Japan are already in the forefront in cell based therapies.

Dr. Ramesh Bhonde, SORM presented pre clinical data using mesenchymal stem cell in obese mouse models. Preliminary results demonstrated a decrease in glyceimic index when compared to control. Dr. Aejaz Habeeb, CLRD, presented clinical data in their trial with chronic liver cirrhotic patients using mesenchymal stem cells. Dr. Deepa Bharthiya, NIRRH, spoke about Very Small Embryonic Like Stem Cells (VSELs) and showed promising data about these cells in azospermic mice, and emphasized the importance of the niche and differentiation of VSELs in a niche restored animal. Dr. Pawan Kumar, Stempeutics, spoke of the phase II trial in Osteo Arthritis Patients using Allogeneic Mesenchymal Stem Cells. Dr. Vivek Tanavade, Bioinformatics Institute, Singapore, presented his work in Imperfecta Ossium (FIO) and gene expression study. His study points to the involvement of immune component in FIO & points to the fact that immune cells may be important in bone resorption and play a role in the pathogenesis of FIO. Dr. Mohan Wani, NCCS spoke about the pre clinical data about MSC and Rheumatoid Arthritis. Dr. Gopal Pande spoke about Early Haematopoietic progenitors in yolk salk. He also spoke of a fibrosis model.
The Panel Discussion was spearheaded by the presentation and discussions of Dr. Gururaj. Rao, International Stem Cell Services, who presented regulatory aspects in clinical use of stem cells and opened the discussion in the forum to discuss the future aspects in this field.

The panelists comprising of distinguished scientists, including Dr. S.G. Ananda Rao and Dr. Gopal Pande expressed concern over the lack of clarity in regulations. The general consensus was that guidelines to ensure quality assurance and quality control of stem cell processing must be implemented. Recommendations from the panel members in the SRMTE meeting was to create a referendum comprising of all stake holders in the stem cell space including clinical scientists, doctors and hospitals and representing this to the government for further deliberations with definite time frame, not withstanding the support of social media to accelerate the process. (This coming from a powerhouse panel comprising of Dr. S.G. Ananda Rao, Dr. Gopal Pande, Dr. Ramesh Bhonde and similar stalwarts in the area should be taken up seriously.)

The panelists agreed that DCGI should come with a proper frame work based on the inputs given by the Draft guidelines and make Stem cell clinical studies in India more viable. They must include more stake holders from the private sectors as they will take this field further and create more jobs in this field, rather than creating ambiguity in this space of stem cell clinical applications.

The conference ended on a positive note to continue the tradition of research and learning. On the promotisssory note and support of Vice Chancellor Dr. Vinod Bhatt, Manipal University, we hope to promote 5 students in the stem cell area and provide platform for exchanging their research experience with the delegates and also invite an international delegate to participate in the next years’ conference.

The 12th meeting SRMTE heralded a new step in the direction of public policy in the area of stem cell clinical applications. Based on the recommendations of our panelists and a cumulative policy decision deliberated for 12 years SRMTE has come up with a referendum to the government for a change in public policy regarding stem cell therapy and would like to fast track the process in the government to accelerate
clinical trials which will in turn make them more acceptable in our medical community to be put to practice.

Abstracts:

Fibrogenesis Imperfecta Ossium (FIO): Can understanding a bone disorder teach us how bone is formed?
Vivek Tanavde, Candida Vaz, Vandana Dhiman & Sanjay Bhadada

Abstract: FIO is an extremely rare metabolic bone disorder. Since 1956 only 16 cases have been reported in literature. Dr. Bhadada at PGI, Chandigarh identified two cases from the same family. These patients responded well to growth hormone treatment. In this study we compared the transcriptional profile of bone tissue from each patient before and treatment with growth hormone. 723 genes were differentially expressed in patient NL whereas 3964 genes were differentially expressed in patient BL before and after treatment. This variation in the number of differentially expressed genes could be due to biological variation between patients or disease stage specific differences in the patients when the samples were harvested. 267 genes were differentially expressed in common in both patients. These genes are robust enough to be differentially expressed in both patients over and above the biological or sampling variation. Pathway analysis of these genes using Ingenuity Pathways Analysis (IPA) showed that immune related pathways like antigen presentation pathway, allograft rejection signaling were significantly over represented in these patients. Immunological disease was the top disease associated with differential gene expression. This study points to the involvement of immune component in FIO & points to the fact that immune cells may be important in bone resorption and play a role in the pathogenesis of FIO.

A Randomized, Double Blind, Placebo Controlled, Phase 2 Study Assessing The Safety & Efficacy Of Stempeucel® In Patients With Osteoarthritis Of Knee

Dr Pawan Kumar Gupta
Senior Director – Medical Services
Stempeutics Research

Background: Osteoarthritis is the most common disease of aged population, approximately 30% of population above 60 years suffer from this disease. Several important characteristics of multipotent mesenchymal stromal cells (MSC) suggest that these cells may offer therapeutic benefit to these patients. Bone marrow derived MSC (BMMSC) are known to possess strong immunomodulatory and anti-inflammatory properties, and promote tissue regeneration through paracrine activity. Stempeucel® is manufactured from BMMSC obtained from healthy volunteers and the product is comprised of pooled allogeneic BMMSCs obtained from multiple donors. Stempeucel® express MSC-associated surface markers, differentiate into bone, cartilage and adipose cells, possess potent immunosuppressive activity and secrete various paracrine factors including TGF beta, PGE amongst others.

Preclinical studies: Safety studies have demonstrated that stempeucel® is non-toxic and non-tumorigenic. Efficacy studies have demonstrated evidence of regeneration of cartilage and decrease in pain scores after intra-articular administration of stempeucel®.

Methods: Total of 60 patients were randomized to different dose levels of stempeucel®: 25, 50, 75 and 150 million cells or placebo. Stempeucel® was administered intraarticularly to the knee joint followed by 2 ml of hyaluronic acid (20 mg). Subjective evaluations (Visual analogue scale (VAS), Intermittent and Constant Osteoarthritis Pain (ICOP), Western Ontario and McMaster Universities Osteoarthritis (WOMAC-OA) Index) were done at baseline, after 1 week, 1, 3, 6 and 12 months after injection. Magnetic Resonance Imaging (MRI) of knee was done at baseline, 6 and 12 months.

Results: Intraarticular stempeucel® was safe with Adverse Events (AE) predominantly in the higher dose groups. Knee pain and swelling were the most common adverse events. There was no evidence of ectopic tissue or tumor formation till 12 months of follow-up. Clinically relevant improvement in a persistent manner was seen in 25 million dose group in all subjective parameters (VAS, ICOAP, WOMAC). Whole-Organ Magnetic Resonance Imaging Score (WORMS) of MRI knee did not show any deterioration from baseline.

Conclusion: Stempeucel® is safe when administered intraarticularly for OA of knee joint. Indicative efficacy is seen in 25 million dose group. Further large scale studies are required to conclude regarding efficacy of stempeucel® in OA of knee.

12th Annual meeting of SRMTE
1st Feb, 2016
School of Regenerative Medicine, Manipal University, Bangalore.

Regenerative Potential of VSELs
Deepa Bhartiya, Stem Cell Biology Department, National Institute for Research in Reproductive Health, Parel, Mumbai 400 012

ABSTRACT
A lot of hope was bestowed on stem cells to regenerate age-related diseased organs. Few recent publications from the country show that trials using adult stem cells including bone marrow cells as well as mesenchymal cells have not been successful. Similar mixed results have been published from various parts of the world using adult stem cells. As far as pluripotent stem cells including embryonic stem cells and induced pluripotent stem cells are concerned, they have the potential to differentiate into 3 germ layers and give rise to 200 cell types of the body - but whatever beneficial effects observed in preclinical mice studies are short lived and not as spectacular as envisaged. It has been concluded that the field of pluripotent stem cells has not moved as expected. The stem cell trial using autologous iPSC cells has been suspended in Japan and they are instead planning to instead use allogeneic iPSC cells for cell therapy. But in that case – it would be better to use human ES cells which are pluripotent rather than use iPSC cells which have several inherent drawbacks. To conclude, there is still no consensus on what is the best stem cell candidate for regenerative medicine! We recently argued that adult stem cells are indeed progenitors which arise from the endogenous, pluripotent very small embryonic-like stem cells (VSELs) which may be a better alternative compared to ES/iPSC cells which exist only in a Petri dish. As a result we need to develop strategies to target VSELs to achieve regeneration. But what is of greater importance is to ascertain whether a particular disease is stem cell disease or results due to altered niche. We recently realized that azoospermia after busulphan treatment in testis is due to a compromised niche since VSELs persist in azoospermic testis but are unable to differentiate. We could restore spermatogenesis by transplanting niche (Sertoli and mesenchymal) cells. Similarly we are intrigued by the fact that VSELs are greatly increased in numbers in a streptozotocin treated diabetic pancreas. Also we need to recognize that most diseases associated with organ failure are age-related. This thought process will be discussed during my presentation.

Unseen face of human adipose derived mesenchymal stem cells in restoration of normoglycemia and lipid profile in Diet Induced Obese (DIO) mice

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Human adipose tissue is a neglected source of stem cells as it is an unwanted and uncontrollable giving rise to obesity whether one likes it or not. However recent research indicates that it is an endocrine organ that plays an important role in controlling metabolic syndrome. Insulin resistance (IR) accompanied by hyperglycemia, hyperinsulinemia and hypertriglyceridemia is a hallmark of type 2 diabetes. Attempts to achieve normoglycemia by employing hypoglycemics have little success in maintaining glucose homeostasis. Hence, there is a need to look for alternative forms of therapy. Mesenchymal stem cells (MSCs) derived from various tissues have been shown to exert beta cell regeneration and thereby control of hyperglycemia. However, the role of MSCs derived from human adipose tissue (ADSCs) in controlling IR and hypertriglyceridemia has not been elucidated. Hence, we injected high fat diet (HFD) induced C57BL/6 mice with ADSC suspension (ADSCs) /ADSC conditioned media(CM) /ADSC cell lysate (CL)/Metformin was used as a positive control. We observed that ADSCs treated mice exhibited 51%, decrease in IR as quantified by HOMA-IR and 40% decrease in Triglyceride Glucose index. This was accompanied by concomitant decrease in oxidized low density lipoprotein and Interleukin 6 as compared to the untreated HFD control. MSC injection showed improvement in glucose tolerance revealed by area under the curve and reduction in fatty infiltration in the liver resulting from HFD as evidenced by histopathological studies. Upregulation of miRNA 206, an indicator for muscle regeneration was observed in skeletal muscle indicating mechanism of action of ADSCs treatment. Taken together our data indicates for the first time the importance of ADSCs therapy in ameliorating IR in DIO mice suggesting its possible therapeutic usage in human subjects.

Adipose-Derived Mesenchymal Stem Cells Prevent Systemic Bone Loss in Collagen-Induced Arthritis.

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Author information

Abstract

Rheumatoid arthritis (RA) is an autoimmune disease characterized by chronic inflammatory synovitis leading to joint destruction and systemic bone loss. The inflammation-induced bone loss is mediated by increased osteoclast formation and function. Current anti rheumatic therapies primarily target suppression of inflammatory cascade with limited or no success in controlling progression of bone destruction. Mesenchymal stem cells (MSCs) by virtue of their tissue repair and immunomodulatory properties have shown promising results in various autoimmune and degenerative diseases. However, the role of MSCs in prevention of bone destruction in RA is not yet understood. In this study, we investigated the effect of adipose-derived MSCs (ASCs) on in vitro formation of bone-resorbing osteoclasts and pathological bone loss in the mouse collagen-induced arthritis (CIA) model of RA. We observed that ASCs significantly inhibited receptor activator of NF-κB ligand (RANKL)-induced osteoclastogenesis in both a contact-dependent and -independent manner. Additionally, ASCs inhibited RANKL-induced osteoclastogenesis in the presence of proinflammatory cytokines such as TNF-α, IL-17, and IL-1β. Furthermore, treatment with ASCs at the onset of CIA significantly reduced clinical symptoms and joint pathology. Interestingly, ASCs protected periarticular and systemic bone loss in CIA mice by maintaining trabecular bone structure. We further observed that treatment with ASCs reduced osteoclast precursors in bone marrow, resulting in decreased osteoclastogenesis. Moreover, ASCs suppressed autoimmune T cell responses and increased the percentages of peripheral regulatory T and B cells. Thus, we provide strong evidence that ASCs ameliorate inflammation-induced systemic bone loss in CIA mice by reducing osteoclast precursors and promoting immune tolerance.

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Repopulation of Cirrhotic Liver by Stem Cells: A Promising Strategy to bridge the Liver Transplantation

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Presenting author: Dr. Md. Aejaz Habeeb

Abstract

Liver cirrhosis is one of the major causes of morbidity and mortality worldwide. Liver transplantation is the only successful and curative option for the management of this disease. However, cost effectiveness, timely availability, operative risks, need of life-long immunosuppressant, and shortage of donor organs are major challenges to fulfill the demand. Stem cells transplantation has emerged as a bridge to liver transplantation for repopulation of cirrhotic liver due to its potential for long-term proliferation. Stem cells are emerging as safe and effective therapeutic option in the management of liver cirrhosis due to their hypo-immunogenicity and high proliferative ability. Combination of MSCs with hepatic progenitor cells could be best option to ameliorate immunomodulation, fibrotic reconstruction and repopulation of lost hepatocytes to replenish the deficient liver functions. Merging of nanotechnology and whole liver bioengineering approaches could provide several unanswered questions of regenerative mechanisms and developing extra-corporeal liver support systems.

As the secretary of SRMTE, I feel that the Society should take a firm stand on the issue of stem cell and cell based therapy in India. It goes without saying that a decisive course has to be adopted, where hospital based therapies must be initiated in the space of stem cells. As a society we strongly oppose the IND route for stem cells.

Regulating the clinical use of stem cells

Main concerns:

- The two main aspects for any therapeutic modality are safety and efficacy
- Inherent safety of adult stem cells has been clearly demonstrated over several decades in both autologous and allogeneic settings and is well documented by bone marrow transplantation work.
- In this scenario it seems questionable ask for pre-clinical and clinical safety studies for adult tissue-derived stem cells.

Safety aspect #1:

At present, possible inherent safety concerns of adult stem cells are limited to:

- Contamination introduced during collection, handling, processing, storage and/ or administration.
- Infectious agents that could be present in the host (should not be an issue with autologous use)
- Chromosomal changes that might occur during long-term culturing and sub-culturing of cells (mainly applicable to mesenchymal stem cells)
• All these safety aspects can be reliably controlled by following safe procedures guided by cGMP norms and by quality control checks.

• The cell processing facility can be governed by a set of rules that ensures quality.

• Entry of “spurious” cells should be prevented.

Safety aspect #2:

Deployment of stem cells in clinics – how do we use them

• Proper clinical protocols are put in place after review by scientific and ethical committees.

• Strict adherence to protocols can be required to prevent unsafe use of cells in the clinics.

• A well-thought-out, wider approach is needed since unregulated clinics are not linked only to stem cells. Many clinics also provide other so-called miracle cures unrelated to stem cells. In fact, many such clinics also abuse routine norms of medicine and there are many cases related to issues such as drug overdosing and improper medication.

• Proper oversight mechanism is required to prevent such clinics from operating.

• Only because a few clinicians and some spurious clinics are creating trouble, the entire field of regenerative and cell-based therapies cannot be put to the gallows.

• Safety can be ensured by oversight of processing centers as well as clinics.

Efficacy:

Efficacy of adult stem cells has been observed in a number of indications. For many of the indications, large amount of data is available in peer-reviewed published literature. Adult stem cells have been tested and demonstrated to be useful in number of conditions. The data have to be acknowledged and a list of approved conditions can be created.

• A realistic list of indications that can be treated by adult stem cells should be created based on an exhaustive and comprehensive review of all literature available world-wide. Treatment should cover adjunct use of cells as well. Advances in stem cell applications must be continually monitored and the list updated periodically.
• Submission of new indications through prescribed channels should be encouraged.

Compulsion of IND:

To require IND process and phase 1-3 trials as well as RCT before being allowed will create a major barrier for any fruitful advances in this field. In effect, it will sequester this field in the hands of a few companies that will gain a monopoly – which will be definitely in the worst public interests. It will also force us to re-invent the wheel by completely ignoring the vast amount of already accumulated data.

• Instead of pushing all stem cell therapies to the IND route, the move should be to encourage multiple clinical research projects by various organizations.

• Large scale clinical research is the only way possible to ensure a rapid and reliable progress in this field.

• If IND process is forced, then all data being generated by multiple centers around India will stop. Since in essence, use of adult stem cells has already entered into the generic space, there will be minimal interest by companies to spend the vast amount of money needed to take them through the several years required for the IND and NDA route. Patients will be forced to wait longer and finally pay more as this promotes monopolization.

• Therapeutic use of adult stem cells should be allowed as long as safety is ensured. Patients can be treated in “research mode” where there is oversight of all procedures, protocols and end-points. However, insisting that adult stem cells be treated as investigational new products is not justified. Especially, autologous use of stem cells can definitely not be subjected to the IND process since inherently it is a medical procedure. Oversight of medical procedures can be through a process of institutional review boards, ethical and scientific review boards and careful scrutiny of end-points and outcomes.
Import Allowed?

• Add to this the feature in the guideline that allows import and in only a short while India will be flooded by foreign products.

• Allowing import of stem cells is detrimental to indigenous business especially when the Indian regulatory policies have been unclear, unhelpful, and largely restrictive to enhancement of knowledge and development of the stem cell field in India so far.

• Now just when regulatory framework is being put in place it is imprudent to allow foreign products to enter the Indian market especially if foreign FDA clearances will pave the way for these products to gain market dominance.

Bone marrow Transplantation:

• Been used for more than 50 years

• Essentially is stem cell transplantation

• Is allowed as autologous as well as allogeneic mode

• Is considered and performed as a medical procedure

• No IND process followed for BMT

• Bone marrow processing mainly performed in blood banks – sub-optimal conditions, no QA/QC

Regulation of Bone marrow transplantation

– Appropriate facility for processing bone marrow

– cGMP

– Class 100/Class 10,000

– HEPA/ Positive pressure
• Slow-freezing profiles

• Continuous monitoring of samples

• Technical competence

  – Expertise in stem cell handling (not available in blood banks)

  – Special requirements of stem cells

• Quality checks

  – Colony Forming Assays

  – Post-thaw viability and functional assay

  – Sterility and endotoxin

**Essentially similar to regulations in place for Umbilical cord blood stem cells**

The majority of stem cell use is based on autologous use of stem cells and in a majority of cases involves mainly enrichment of bone marrow – thus not altering the essential composition of bone marrow – and thus can be considered to be akin to an autologous graft – similar to a bone or skin graft which is normally done, considered to be medical practice and not under DCGI purview.

**MSC vs IVF:**

Ex vivo expanded stem cells cannot be considered as manipulated if we can show clearly that the cells do not lose their original identity. It is even less demanding that manipulation of egg and sperm as in case of IVF. If MSCs can be considered manipulated, then certainly manipulation of the egg will qualify to be regulated by DCGI.

**Concerns over Involvement of DCGI:**
• There must be assurance of a fast, fair, transparent application and review process with definite
time-lines.

• Slow processing of applications a major deterrent – fast-tracking of stem cell applications
required.
  • If IND process is followed, the time required to bring any therapy will be very long
  • If DCGI is involved, then transparency, time commitment and clarity is a must.

• **Education of regulatory authority is of paramount importance** and a necessary prerequisite
before they are given the control or else we will have a problem. A division of DCGI must be
dedicated to stem cell and regenerative medicine.

• Prior data (national and international) must be allowed and taken into consideration for all
applications. In most cases, use of enriched bone marrow or cord blood or fat has been already
proven to be safe in autologous and in many cases allogenic use as well. Pre-clinical safety data is
not required for autologous enriched samples.

• Separate regulation of adult stem cells (those obtained from post-natal tissues) from those of iPS,
ES, Fetal stem cells etc.

**Role of Government:**

• The government should promote a strong research environment by providing funding for
clinical trials. In the past, clinical research in regenerative medicine has been limited to a
few government institutions and to a very few number of companies. Over some years
clinical research in this space was even discouraged by funding agencies. Moreover,
data published in peer-reviewed journals from government sponsored clinical trials have
been completely ignored in all regulatory documents brought forth by the government. If
they don’t trust the data, then why have they continued to fund the same organizations? And if they are ignorant of them or worse still deliberately ignoring the data, one wonders what came out of all the public money spent in the effort.

- Aim should be to create a transparent, friendly and progressive atmosphere for development of the regenerative medicine space.

- **Singling out Stem Cells:**

  - Singling out stem cells among the myriad other unproven therapeutic modalities seems to be prejudiced and unfair. Being overly worried about the unethical practices in this field ignores the unethical practices rampant in other medical fields such as ART as well as unproven therapies in the fields of homeopathy, ayurveda, sidda and unani medicines. Moreover, the field of allopathy itself has several examples of non-adherence to principles espoused here.

**Possible Solutions:**

- **Get processing center to get registered/ licensed as cell processing center. For this clear, transparent rules needed. A definite time-line and guaranteed turn-around times is a must. Assurance is required that center will get licensed within a definite time frame otherwise there will be no progress. If the govt. agency does not finish within the time frame then center should get automatically licensed and allowed to start work.**

- Guidelines for processing Cord Blood stem cells are already in place and should be the norm for all processing centers. The same guidelines should be extended to all processing centers instead of creating a new set of rules.

- **Require treatment centers to register. They cannot offer treatment or advertise if they are not registered. They can treat conditions that have data supporting the use of the cells for**
that particular indication. They are allowed to do patient-funded research or trials under oversight – but no need to go for IND. Essentially it is similar to what ICMR guidelines permit for minimally manipulated (permissible) category. Only difference is that a comprehensive list of treatable conditions will be created and regularly updated. Indications can be given different status depending on how close they are to be considered as treatment. For example: Category 1 (treatable; eg. Burger’s disease), 2 (can be patient-funded research; eg. Multiple sclerosis), 3 (clinical trial, needs more clinical data; eg. Ataxia). Also there has to be an option for compassionate use.

**Patient funded Research:**

Patient-funded research is a good option under certain conditions such as:

- clear protocols are present for treatments
- ic-scert and ethical committee clearance is obtained
- patient informed consent is obtained
- safety of process and cells are ascertained
- clear, objective end-points (formation of new blood vessels, maintenance of cartilage) are delineated. Subjective, vague end-points should not be used.

- Advertisement of stem cell use without substantial evidence for that particular indication should be prevented. Clinics that advertise false claims should be reprimanded. However, false claims and advertising are intertwined with each other. It is a bigger issue that must be addressed on a broader level in the health-advertising space.
• Safety trials not needed for autologous use and allogenic mesenchymal stem cells. Encourage multicentre trials by government agencies, non-government organizations, companies, clinics, hospitals.

• Provide large scale funding and transparent funding mechanism with clear goals and accountability.

World over, in countries like Japan, the government is being pro-active in identifying groups involved in clinical applications of stem cells and have accepted their safety data and efficacy data and allowed stem cell therapy.

*NATURE MEDICINE* | NEWS

**Japan to offer fast-track approval path for stem cell therapies**

David Cyranoski

*volume 19 | number 5 | may 2013 nature medicine:*

The proposed amendments to the pharmaceutical law will create a new, separate approval channel for regenerative medicine. Rather than using phased clinical trials, companies will have to demonstrate efficacy in pilot studies of as few as ten patients in one study, if the change is dramatic enough, or a few hundred when improvement is more marginal. According to Toshio Miyata, deputy director of the Evaluation and Licensing Division at the Pharmaceutical and Food Safety Bureau in Tokyo, if efficacy can be “surmised,” the treatment will be approved for marketing. At that stage, the treatment could be approved for commercial use and, crucially for such expensive treatments, for national insurance coverage. Japan to offer fast-track approval path for stem cell therapies Phased out With the bar for regenerative therapies dramatically lowered by requiring only limited safety and efficacy data—and essentially doing away with the need for high-powered phase 3 trials—the amendments’ architects say it will be possible to get a stem cell treatment to the market in just three years, rather than the typical six or more. The law should also give local producers of regenerative medicine an edge even over those selling stem cell therapies in South Korea, where an accelerated system has helped companies get more stem cell treatments on the market than any other country (see *Nat. Med.* 18, 329, 2012). “It’s bold,” says Yoshihide Esaki, director of Bio-Industry Division, a bureau of the Ministry of Economy, Trade and Industry based in Tokyo, which promoted legislation calling for the update.