Internship training

at

ZS Associates India Pvt. Ltd.

Gurgaon

On

Expert opinion on Gene Therapy for Cancer treatment in India

By

Dr. Savarnee Gangopadhyay

PG/16/065

Under the guidance of

Dr Nishikant Bele

Post- Graduate Diploma in Hospital and Health Management

2016-2018

International Institute of Health Management Research, New Delhi

ACKNOWLEDGMENT

On the very outset of this report, I would like to extend my sincere and heartfelt obligation towards all the personages who have helped me in this endeavor. The internship opportunity I had with ZS Associates was a great chance for learning and development.

I am also grateful for having a chance to meet so many wonderful people and professionals who led me through this internship period.

First and foremost, I would like to express my sincere gratitude to **Mr. Nitin Aggarwal**, Principal, KM team

At this juncture I feel deeply honoured in expressing my sincere thanks to **Mr. Vikas Verma, PhD**(Associate consultant) who in spite of being extra ordinarily busy with his duties, took time out to hear, guide and keep me on correct path and providing valuable insights leading to the successful completion of my project.

I would also like to thank all my teammates for their critical advice and guidance without which this project would not have been possible.

I express my gratitude to my college International Institute of Health Management and Research, New Delhi for arranging summer training in good schedule. I also extend my gratitude to my project guide **Dr. Nishikant Bele**, Assistant Professor, IIHMR Delhi for his cooperation, help and encouragement.

I perceive this opportunity as a big milestone in my career development. I will strive to use gained skills and knowledge in best possible way and I will continue to work on their improvement in order to attain desired career objectives.

Sincerely

Dr. Savarnee Gangopadhyay

18/05/2018

DECLARATION

I, **Dr Savarnee Gangopadhyay**, student of International Institute of Health Management Research, New Delhi, hereby declare that I have completed my project titled **Expert opinion on Gene therapy for Cancer treatment in India** from February to May 2018. The information submitted herein is entirely true and original work.

The projects were undertaken and carried out by me, under the guidance of **Dr. Nishikant Bele**, Assistant Professor, IIHMR Delhi, and it has not been submitted to any other university or institute or published earlier.

Place- New Delhi

Date- 18/05/2018

Table of Contents

Table of Graphs

Table of figures

SECTION 1

Organization Profile

ZS Associates is a sales and marketing outsourcing, staff augmentation, and technology firm headquartered in Evanston, Illinois that provides services for clients primarily in the pharmaceutical industry. Andris Zoltners and Prabha Sinha, who worked together as professors of marketing at the Kellogg School of Management at Northwestern University, founded ZS in 1983.

Figure 1: ZS Associates Gurgaon

The firm employs approximately 3,400 employees in 20 offices in North America, Asia and Europe. Most of the workforce is located in large outsourcing hubs in Pune and New Delhi, India. ZS works with 49 of the 50 largest drug-makers and 17 of the 20 largest medical device makers and also serves consumer products, financial services, industrial products, telecommunications, and transportation and logistics industries.

ZS Associates offers integrated sales and marketing services ranging from customer insights and strategy to companies that need specialized expertise in areas ranging from analytics, operations and technology.

The firm serves clients in the consumer products, energy, financial services, high tech, industrial products, telecommunications, transportation and logistics sectors, although a large number of the firm's clients work in the pharmaceuticals, biotechnology, and medical products and services space.

ZS Associates developed the first personal computer-aided sales territory mapping system in 1985. In 2008, ZS created 12 software products focused on incentives, call planning, promotion, strategy, forecasting and account management, and integrated them as one unified sales and marketing software platform: the Javelin™ software suite.

ZS in Sales:

For nearly 30 years, ZS's sales consulting services have helped companies around the world excel at critical sales activities such as: designing sales channels that leverage both direct and indirect paths to market; creating the best sales force structure, territory plan, size, allocation and incentive approach; and integrating sales and marketing programs with extraordinary results and levels of efficiency. ZS Associates offers the following solutions:

- **Business Intelligence and Technology**

- Maximize profit at a fraction of current costs

ZS delivers superior business intelligence solutions that transform data into insight. Business Intelligence practice gives a specialized analytical monitoring and diagnostic solutions that improve sales and marketing and help cut costs.

- **Business Process Improvement**

- Streamline sales and marketing operations

When struggling to uncover operational roadblocks and inefficiencies in sales and marketing departments, ZS helps to reengineer sales and marketing processes and facilitate successful change management within organization. The unique mix of analytics, operations and technology identify and implement the right solutions to improve your organization's commercial operations.

- **Customer Targeting and Activity Planning**

- Increase Sales Success and ROI on Field Force Investment

The sales field force remains one of the most effective channels to engage the customer. But it is also one of the most expensive. And in a market in which one has to achieve more with less, companies must maximize the return on their sales force. ZS helps sales organization identify the best opportunities and field force tactics.

- **Go-to-Market Strategy and Transformation**

- Achieving Step-Function Increase in Sales and Profitability

ZS helps sales and marketing executives identify critical growth opportunities, determine sales and marketing strategy, and implement the necessary changes – changes that regularly boost the clients' revenue 2-10% or more. ZS knows how to transform sales and marketing strategies and capabilities while minimizing transition risks and driving sustained adoption of new approaches.

- **Sales Channel Strategy and Management**

- Develop and Manage Channel Partner Programs to Meet Evolving Customer Needs

ZS creates winning channel strategies. It aligns go-to-market strategy with overall business strategy by helping clients develop and manage a channel program with the right mix of direct and indirect (partner) channels to meet business goals and customer engagement requirements.

- **Sales Compensation**

- Compensation that boosts sales force retention and market share

An effective sales compensation plan helps retain the top sales people, increase market share, make selling costs predictable and reduce the cost of plan administration. An inferior plan does the opposite. ZS helps to create plans and quotas that support your strategy and streamline administration.

- **Sales Force Design**

- Design a customer-centric sales Force

The sales force is one of an organization's most valuable and expensive marketing resources. Unlike other marketing tactics, building or reshaping a sales force can take considerable time, money, and attention. ZS has designed sales forces for organizations across more than 25 industries and in over 70 countries.

- **Sales Force Effectiveness**

- Maximize the return on your sales force

Over the past 30 years, ZS has conducted thousands of sales force effectiveness engagements with over 700 companies in more than 70 countries and 25 industries. ZS has helped clients' salespeople achieve: longer face time with their customers, more topics discussed during customer visits, significantly improved customer satisfaction ratings—and most important, up to 30% higher sales performance

ZS in Marketing

Leading companies turn to ZS marketing consulting services because they excel at helping them accomplish marketing mandates such as: creating tailored and practical strategies to capitalize on their market opportunities; sorting through myriad options for creating demand to determine the optimal marketing mix; and evaluating marketing programs to dramatically improve their performance.

- **Customer Insights**

- Increase Customer Insight to Make Better Sales and Marketing Decisions

A clear understanding of customer needs, buying processes, buying preferences, perceptions, and potential is essential to sales and marketing success. ZS uses qualitative and quantitative methods spanning both primary and secondary data-based approaches to provide clients with customer insights.

- **Customer Segmentation**

- Enable Sales and Marketing Strategy and Execution through Actionable Customer Segmentation

ZS combines marketing science expertise with decades of experience to help companies around the world develop highly actionable segmentation strategies that drive brand strategy through to tactical execution.

- **Forecasting**

- Create Robust and Transparent Forecasts for Your Products

Understanding fundamental market drivers and their influence in shaping product demand is integral to good business planning and full utilization of company resources. ZS has developed customized forecasting processes to serve the clients. It merges forecasting knowledge and experience with the industry expertise of clients to produce collaborative results

- **Marketing Mix**

- Maximize the Return on Sales and Marketing Investments

Sales and marketing organizations face unrelenting cost pressures. ZS helps sales, marketing and brand executives substantially increase the return on their investments and gives them confidence that they are making the optimal promotional spending decisions.

- **Marketing Performance Measurement and Optimization**

- Improve In-Market Effectiveness Through Timely Insight Into Marketing Performance

Accurate and timely feedback on marketing program performance is critical to the real-time fine tuning and course corrections necessary to maximize marketing results and return on investment. ZS has extensive experience helping clients maximize the value realized from their investments in marketing programs.

- **Pipeline Strategy**

- Optimize Return on New Pharmaceutical and Medical Products

Pharmaceutical brands and medical products may not be generating returns that maximize your company's substantial R&D and marketing investments. With market conditions creating higher barriers to commercial success, the pressures on R&D and marketing executives are becoming only more acute. ZS helps life science companies increase the commercial success of their product pipelines.

RESPONSIBILITIES AS A KNOWLEDGE MANAGEMENT ASSOCIATE

- Assess the knowledge needs and requirements (short-term or long-term) of the firm
- Deliver targeted insights using internal knowledge and external sources
- Help the firm prepare materials for Summits and Conferences
- Support the creation and update of knowledge assets including: client updates, competitive intelligence, industry research etc.
- Maintain, manage and develop the firm's knowledge infrastructure

- Share best practices and tactical knowledge across offices, practice areas and teams

SECTION 2

Dissertation report

On

Expert opinion on Gene Therapy for Cancer treatment in India

Expert opinion on Gene therapy for Cancer treatment in India

Abstract

Cancer is becoming one of the most widespread and dreadful diseases globally. India, among many countries is also affected by cancer, which is one of major reasons for mortality in the country. Genetic mutation is one of the many causes of this disease, which can be treated by Gene Therapy. But developing Gene Therapy requires the necessary infrastructure to manufacture it followed by clinical trials to prove its efficacy and safety. The first Gene Therapy to be approved was in China, in the year 2003. Since then although many laboratories have come up in India, specifically for Gene Therapy, we still do not have one in the country. Hence this study is conducted to get an in-depth idea about the research, manufacturing and commercialization trends in Gene Therapy. Interviews were held with experts working in a Global Business Consulting Firm, which included physicians, researchers, consultants and marketing experts with sufficient experience and knowledge. Questions regarding Gene Therapy for Cancer in India were asked and their experienced opinions were noted. The prospect demands Gene Therapy for specific cancers with high incidence and mortality rates in India. Other factors, which play an important role in bringing a new product to the market, were also identified. These included targeting the right patient population, requirement of specialized sales team to market such a product and others. Challenges with respect to awareness and cost of therapy for stakeholders such as doctors and patients, were observed to be of major concern. Overall it was realized that it will take at least 5 -10 years for India to have its own Gene Therapy for Cancer.

Introduction

According to the World Health Organization, the second leading cause of death around the world is cancer. Globally it is responsible for 8.8 million deaths in 2015 and nearly 1 in 6 deaths is due to cancer

In 2015, reported incidence of cancer in India was 1.1 million with an estimated prevalence of 3.9 million. Breast and cervical cancers among women, and head and neck, lung and gastrointestinal cancers among men represent more than 60% of the incidence burden. India has nearly three times the incidence of US and China for head and neck and cervical cancers

Although the understanding, prevention, and treatment of cancer, has seen great advancement but the disease continues to affect millions of people worldwide. The rate of progress being made against cancer has slowed down due to the complexity of the disease compounded with financial, policy and regulatory roadblocks. The already available treatment modalities for cancer include radiotherapy, chemotherapy and surgery. Among these, the most common treatment, chemotherapy, lacks selectivity and can cause non-specific toxicity. Gene therapy on the other hand, is a potentially beneficial cancer treatment approach particularly over chemotherapy.

According to a research report, gene therapy researches are mostly focused on finding the treatment for cancer, followed by genetic diseases and neurological disorders, respectively.

Various funding, grants, and investment from government bodies and venture capitalist firms are aiding companies operating in the gene therapy market to develop new products. Maximum number of clinical trials in the gene therapy segment is in North America, which gives it a dominant position in the gene therapy market.

United States Food and Drug administration (U.S.FDA) defines human gene therapy as the administration of genetic material to modify or manipulate the expression of a gene product or to alter the biological properties of living cells for therapeutic use.

FDA's Center for Biologics Evaluation and Research (CBER) regulates the gene therapy products. Investigational new drug application (IND) is required in the United States prior to initiating clinical studies for humans. Submission and approval of a biologics license application (BLA) is required for marketing a gene therapy product. Similarly, European Medicines Agency approves Gene therapies for the European countries. In India it is the Central Drugs Standard Control Organization that is responsible for the commercialization of gene therapy.

China, in 2003, brought the first commercial gene therapy medicine, Gendicine, to the market for the treatment of head and neck cancers. It is a recombinant, human adenovirus of serotype 5 engineered to contain the human wild-type p53 tumor-suppressor gene. It is stored in a single-use vial at -20°C.

Glybera by UniQure and Strimvelis by GlaxoSmithKline were approved in Europe by the European Commission in 2012 and 2016 respectively. Glybera was approved for lipoprotein lipase deficiency which can cause acute pancreatitis and Strimvelis for Severe Combined Immunodeficiency due to Adenosine Deaminase deficiency in children.

The U.S. Food and Drug Administration approved the first gene therapy available in the United States on 30 Aug 2017 for **Kymriah,** that is used in certain pediatric and young adult patients with a form of acute lymphoblastic leukemia (ALL)

Kymriah is a genetically-modified autologous T-cell immunotherapy. The T-cells are collected from the patient and sent to a manufacturing center where they are genetically modified to include a new gene that containing a specific protein (a chimeric antigen receptor or CAR) that directs the T-cells to target and kill leukemia cells that have a specific antigen (CD19) on the surface. The modified cells are infused back into the patient to kill the cancer cells.

On 18 Oct 2017, the U.S. Food and Drug Administration approved the second gene therapy called Yescarta. It is a cell-based gene therapy used for the treatment of certain types of large B-cell lymphoma in adult patients with who have either not responded to or who have relapsed after at least two other kinds of treatment. It is a type of chimeric antigen receptor (CAR) T cell therapy that is the second gene therapy approved by the FDA and the first for certain types of non-Hodgkin lymphoma (NHL).

Until the late 1990s, India did not have a single laboratory dedicated to gene therapy research. However after 2000, there has been an increase in the number of gene therapy research laboratories owing to generous financial support from the Indian government, in particular the Department of Biotechnology, with the aim to develop gene therapies for various diseases

The first centre dedicated to gene therapy research in India (1998) was the Advanced Centre for Treatment, Research and Education for Cancer (ACTREC, Mumbai). Since then a lot many research laboratories, dedicated entirely to gene therapy treatment, have come up, even then we do not have any commercialized gene therapy treatment for cancer available in India.

Research Question

1. What is the prospect of Gene Therapy for Cancer in India?
2. Why are there no Gene Therapies in India?
3. What are the challenges in manufacturing and commercialization of Gene Therapy for Cancer in India?

Objectives

General objective: To understand the prospect of Gene Therapy for Cancer in India.

Specific Objectives:

1. To study the impact of Gene Therapy on treatment of Cancer in India
2. To understand the manufacturing and commercialization challenges of Gene Therapies
3. To understand the research trends

Review of Literature

Concepts used in the study

Gene therapy is a procedure used to modify a person's genes to treat or cure disease. The various mechanisms by which gene therapy works are:

- Replacement of disease-causing genes with healthy copies of the genes
- Inactivation of disease-causing genes that do not function properly
- Introduction of new or modified genes into the body to help treat a disease

There are various diseases for which Gene therapy products are being studied, including cancer, genetic diseases, and infectious diseases.

The various types of Gene therapy products are:

Plasmid DNA: These are the circular DNA molecules that can be genetically engineered to carry therapeutic genes into human cells.

Viral vectors: Some gene therapy products are derived from viruses as they have a natural ability to deliver genetic material into cells. Modified viruses can be used as vectors (vehicles) to carry therapeutic genes into human cells once they have been modified to remove their ability to cause infectious disease.

Bacterial vectors: Bacteria can also used as vectors (vehicles) to carry therapeutic genes into human tissues after being modified to prevent them from causing infectious diseases.

Human gene editing technology: It helps in disrupting harmful genes or repairing mutated genes.

Patient-derived cellular gene therapy products: In this case cells are removed from the patient, genetically modified (often using a viral vector) and then returned to the patient.

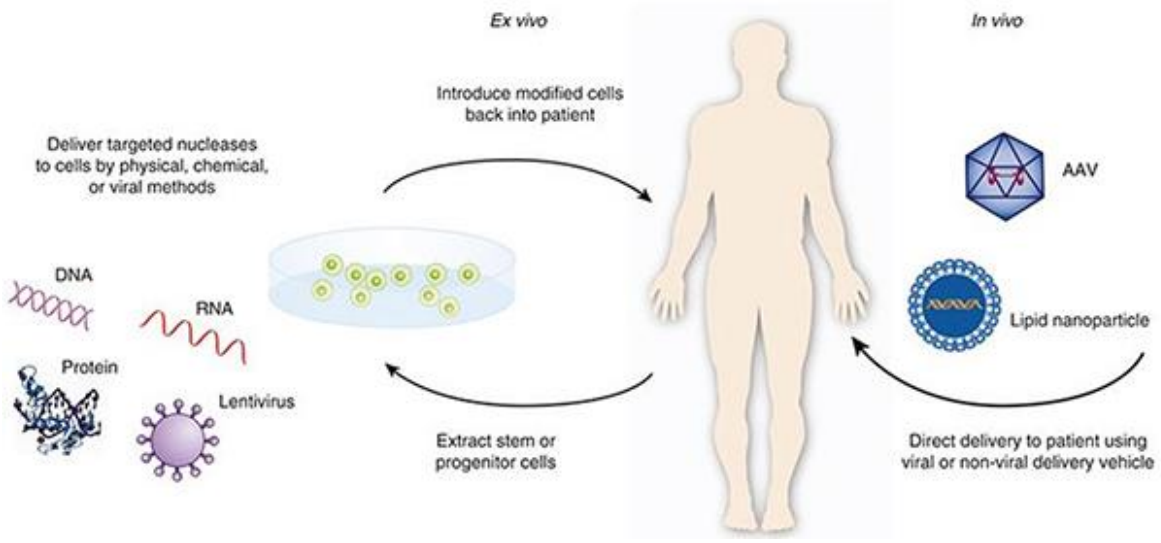
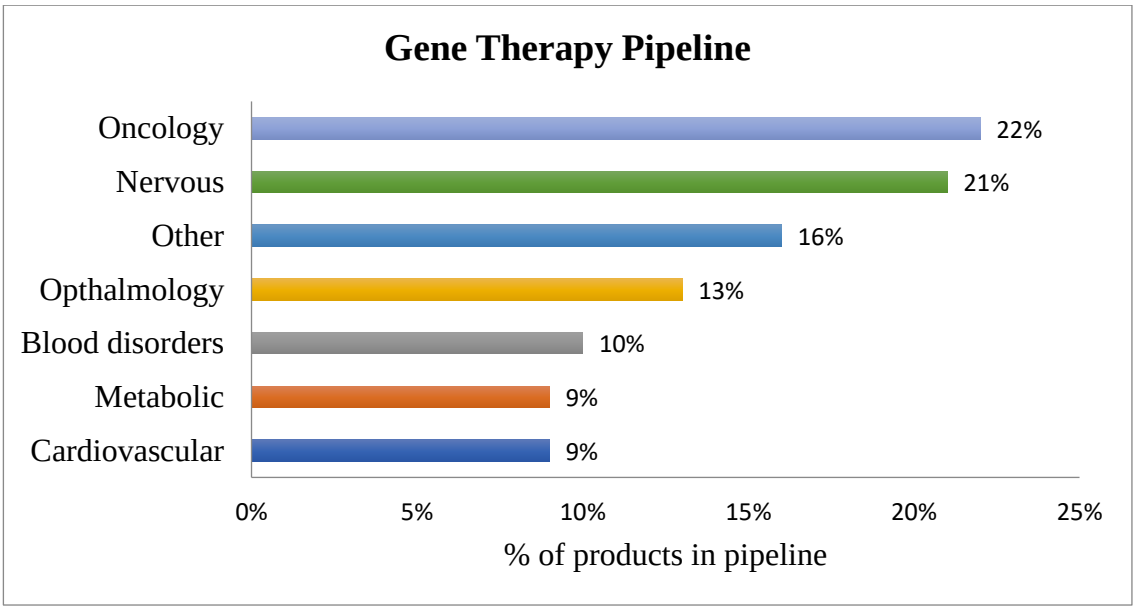


Figure 2: Gene Therapy procedure

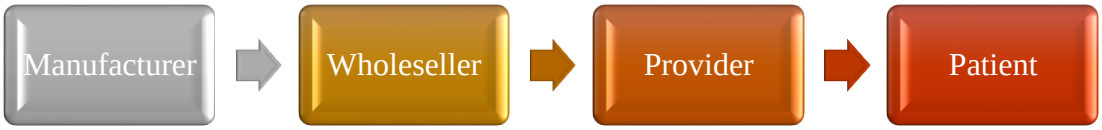
According to a White paper by IMS Health, on Cell & Gene Therapies, the already existing pipeline of gene therapies for various therapeutic areas are as shown in the graph below. Here N = 130 (with therapies in pre clinical to pre registration stages)



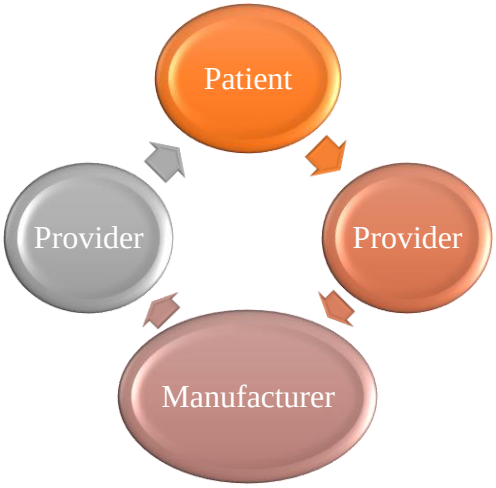
Graph 1: Gene Therapy Pipeline

Difference between traditional logistical chain and Gene Therapy supply chain

Traditional Logistical Chain:



Gene Therapy Supply Chain:



A snapshot of current Gene Therapy prices and usage by the patients

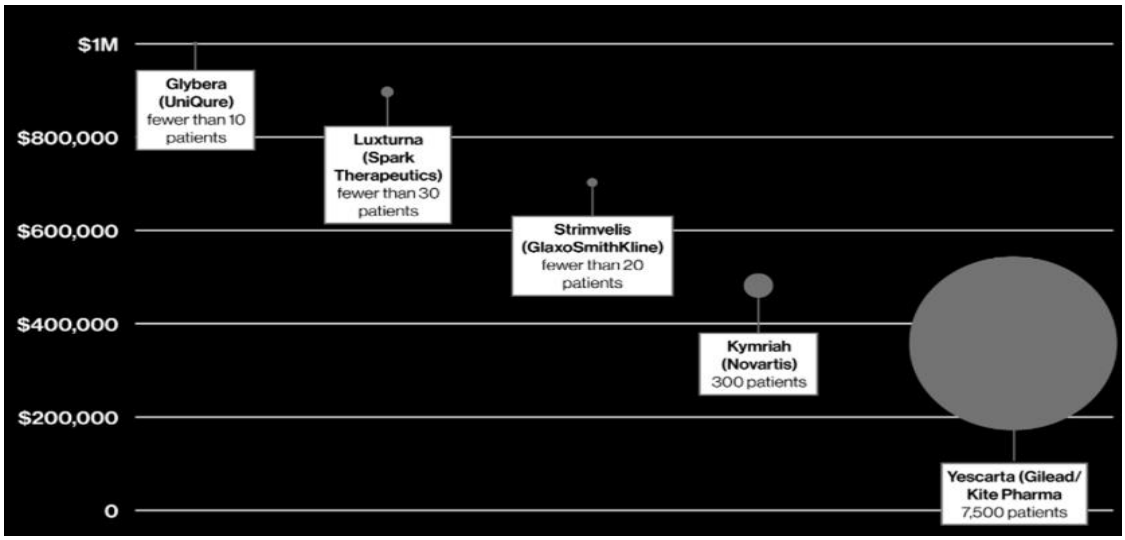


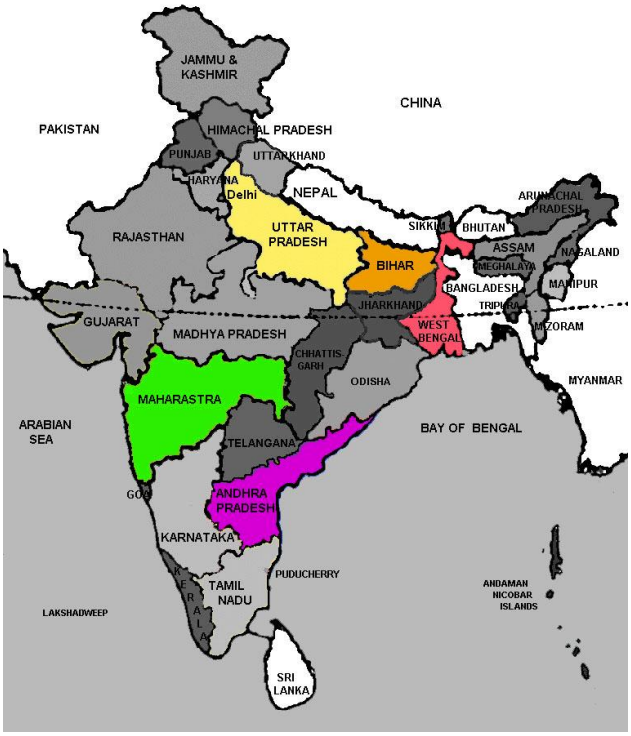
Figure 3: Gene Therapy prices and eligible patients

Cancer Scenario in India

47.2% of all cancers in India are constituted by the top 5 cancers in women and men. They are:

Men	Women
• Lip, Oral Cavity • Lung • Stomach • Colorectum • Pharynx	• Breast • Cervix • Colorectum • Ovary • Lip, Oral cavity

Top five states with highest incidence and mortality rates of Cancer in India (ICMR- 2014)



1. Uttar Pradesh
2. Maharashtra
3. Bihar
4. West Bengal
5. Andhra Pradesh

Figure 4: Cancer in Indian states

Studies/ papers

In a research article by Imran Ali et al. on, ‘Cancer Scenario in India with Future Perspectives’ it is stated that cancer is the second most common cause of death in India and accounts for 0.3 million deaths per year.

An article on ‘Gene therapy in India: A focus’ by Sarvani Chodisetty and Everette Jacob Remington Nelson states that until late 1990s there were no laboratories for research on gene therapy in India. Post the year 2000, there are institutions that are coming up and the Government is playing a significant role by funding scientists and clinicians for conducting research.

A report on , ‘Why commercialization of gene therapy stalled; examining the life cycles of gene therapy technologies’ by Ledley FD et al. concludes that reason for delay in commercialization of gene therapy may be the disharmony between the maturation of gene therapy technologies and capital investment in development-focused business models.

Deanna Cross and James K. Burmester in their research article on, ‘Gene Therapy for Cancer Treatment: Past, Present and Future’ state that apart from the already existing therapies for cancer such as radiotherapies, chemotherapies and surgeries, gene transfer is a new and evolving treatment modality where introduction of new genes into a cancerous cell or the surrounding tissue causes cell death or slows down the growth of the cancer.

A research article on, ‘Gene Therapies for Cancer: Strategies, Challenges and Successes’ by Swadesh K. Das et al. discusses the recent advances in gene therapy and their impact on a pre-clinical and clinical level.

Methodology

Study area: An institution-based study was conducted in a global consulting firm, from February 05, 2018 to May 04, 2018.

Study design:

A combination of qualitative and quantitative study with non-probability convenience sampling with four clusters of experts was carried out. The clusters included physicians, researchers, marketing experts and consulting experts. An in-depth interview was conducted with each of 16 experts. Set of questions were separate for separate clusters with a few overlapping questions. One expert can have more than one opinion.

Questions were based mainly on

i. Background of Gene Therapy
ii. Manufacturing of Gene Therapy for Cancer in India
iii. Clinical trials for Gene Therapy in India
iv. Commercialization of Gene Therapy for Cancer in India

Sample size:

Sample size was 16. It included four groups namely physicians, researchers, marketing experts and consulting experts.

Inclusion criteria:

1) Experts including physicians, researchers, marketing experts and consulting experts.
    a) Physicians  : It includes experts who were involved in active patient treatment and thus understand evolving treatment options.

b) Researchers  : They were actively involved in laboratory research.

c) Marketing experts  : They have past experience in the marketing field and know about the market trends.

d) Consulting experts  : They have past experience in providing decision support to the pharmaceutical clients.

2) Experts who were willing to participate in the study.

Exclusion criteria;

1) Other employees with no experience in the required fields were excluded from the study.

Data collection tool and technique:

A self-administered, semi structured in-depth interview was conducted with 16 experts.

Questions

Marketing Expert | Consultants | Physicians | Researchers

1. In your opinion which indication will be most benefited by Gene Therapy?
2. Based on your experience, what proportion of cancer patients will be willing to take Gene Therapy?
3. If Gene Therapy comes with a feature of diagnostic test that can be used for response monitoring, will it increase the willingness of the doctors to prescribe it and how challenging will it be to market such a product?
4. What proportion of cancer patients will be willing to take Gene Therapy?

5. On a scale of 1 - 5, please rate the following as the most preferred route of administration for Gene Therapy?-IV, SC, Tumor site
6. On a scale of 1 - 5, which channel of communication would be most suitable for physician's awareness about Gene Therapy product?-Mail/In-person/Camps
7. If Gene Therapy is launched in India, what percentage of doctors do you think will prescribe it?

8. On a scale of 1 - 5, please rate the following as the most preferred target population for Gene Therapy?-Pediatrics, Adults, Geriatrics
9. Which cancer indication should be taken up for research in India, to bring a Gene Therapy product?
10. Which among the following is the most important factor to determine the value of a Gene Therapy oncology product?- Efficacy, Safety

11.On a scale of 1-5, how important is it for the Gene Therapy marketing and sales team to provide the following, while visiting hospitals for their products?- Manufacturing discounts, payment options/insurance
12. How many times should the sales force teams visit doctors for successful commercialization of Gene Therapy products in India?

13. If you had to recommend India states for conducting a pilot study for Gene Therapy for cancer, which would they be?
14. On a scale of 1-5, What should be the clinical trial endpoints for testing Gene Therapy products?- OS, PFS, ORR, CR
15. On a scale of 1-5, what should be the efficacy of Gene Therapy for it to be successful in India? 0-30%
16. On a scale of 1-5, what should be the level of safety of Gene Therapy for it to be successful in India?- 5-15%

17. If a Gene Therapy product with good efficacy is launched in India, how early can it turn into a success?

18. How challenging will it be to market Gene Therapy oncology product in India?
19. Do you think marketing for Gene Therapy products would need a special team with relevant subject matter experience?
20.What could be the challenges for supply chain management (with respect to specific cold storage needs etc.)?

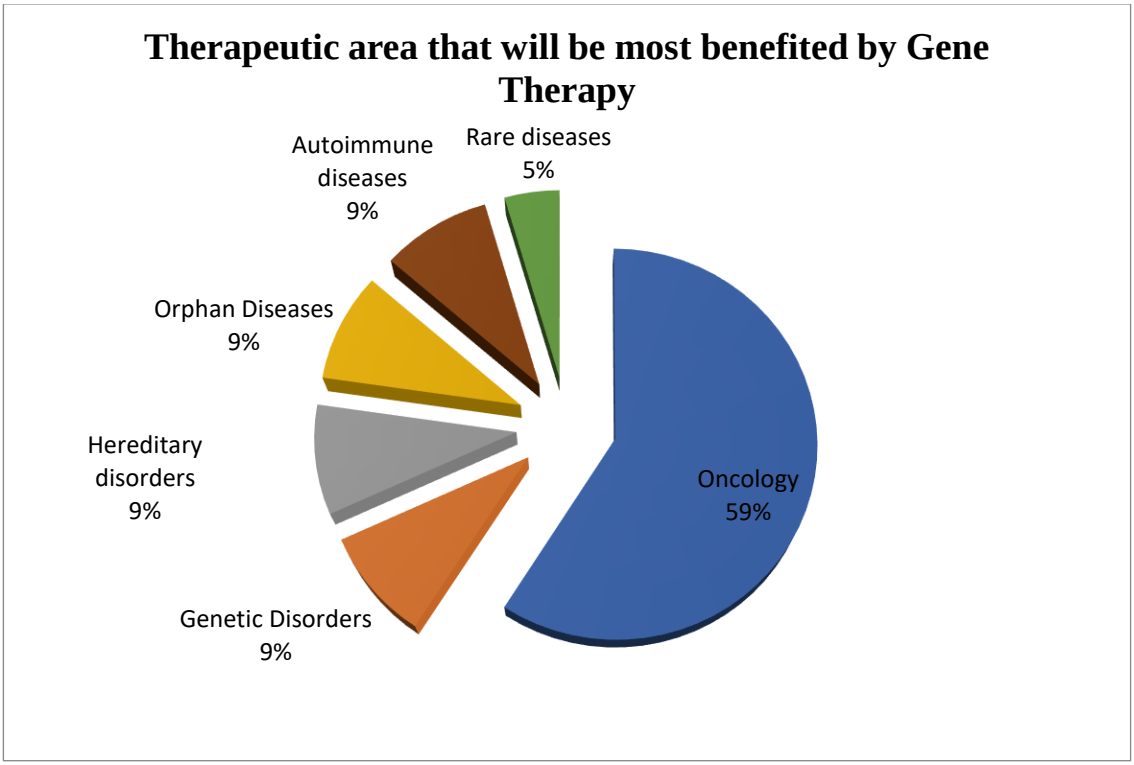
21. On a scale of 1-5, if a clinical trial is held for Gene Therapy Cancer product in India, what will be the level of willingness of patients to participate in the trial?
22. Which setting will be more appropriate to administer Gene Therapy? - IPD/OPD
23.Which specialty will be most suitable to administer this therapy?
24.Which patient segment looks to be best suited for receiving Gene Therapy?

25. Will industries be willing to conduct clinical trials for Gene Therapy in India? Any specific company in mind?
26. Which can be a major source of funding for Gene Therapy oncology product?
27. What will be the manufacturing challenges with respect to Gene Therapy oncology products?

Result

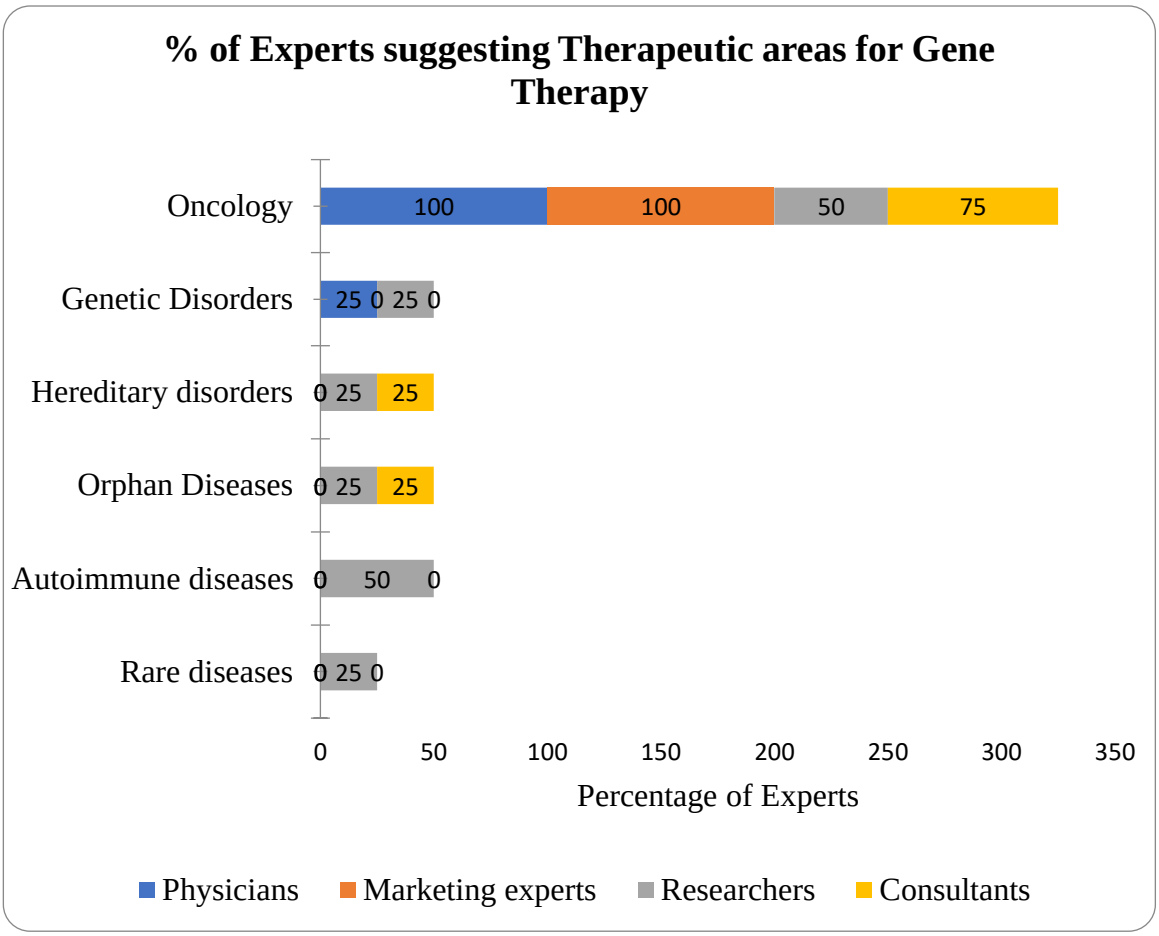
1. Background of Gene Therapy

Question: Gene Therapy seems to have exciting prospects in various indications. In your opinion which indication can be most benefited by this therapy?



Graph 2: Therapeutic area for Gene Therapy

According to the experts, Oncology is the therapeutic area that will be most benefited by Gene Therapy.



Graph 3: Percentage of Experts suggesting Therapeutic areas for Gene Therapy

100% of physicians and marketing experts believe that oncology will be the most benefited indication by Gene Therapy in India. Half of the consultants suggest oncology whereas the other half believe Gene Therapy should be used to treat rare, hereditary and orphan diseases. 75% of the consultants also mention oncology as their ideal indication for Gene Therapy.

As per Physician 2,"Gene therapy is in experimental stage in India."

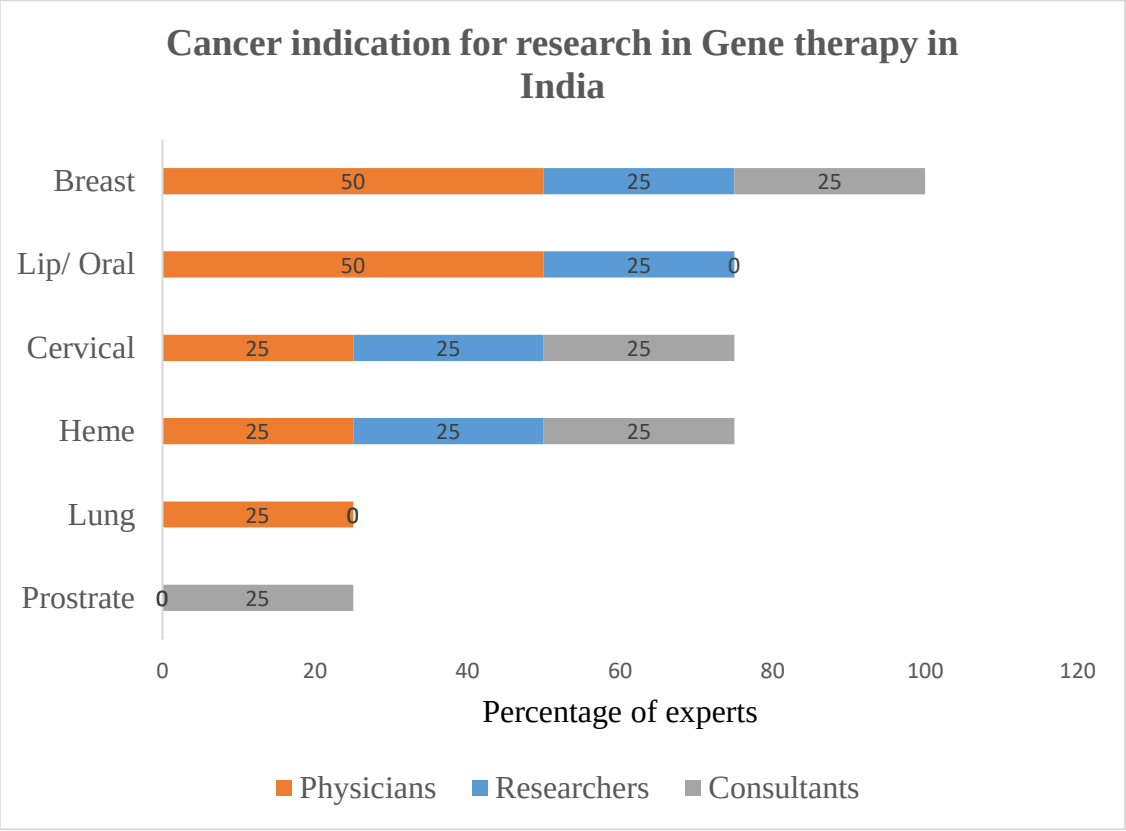
Hence it is only right to work with those indications for which gene therapy has already been tried and tested outside India. This type of therapy should be used for those diseases that are caused by defects or mutations in the genes.

They can either be monogenic that is involving or controlled by a single gene or multigenic which are likely associated with the effects of multiple genes in combination with lifestyle and environmental factors. Monogenic diseases like rare and orphan diseases are comparatively easier to treat with a very defined cause, for example Gaucher's disease. On the other hand, multigenic diseases such as cancer, already have gene therapies being manufactured for their treatment.

To be more specific, one of our experts, Physician 4, comments, "Pediatric oncology should be targeted, as they can be prevented and also the pediatric population is more sensitive and have a higher chance of trade off."

Other indications include diseases with high unmet needs, hereditary diseases, chronic indications that are most prevalent, such as Psoriasis, GI disorders, Ulcerative colitis, Crohn's disease and diseases that do not have a treatment, such as Parkinson's disease with just symptomatic treatments available.

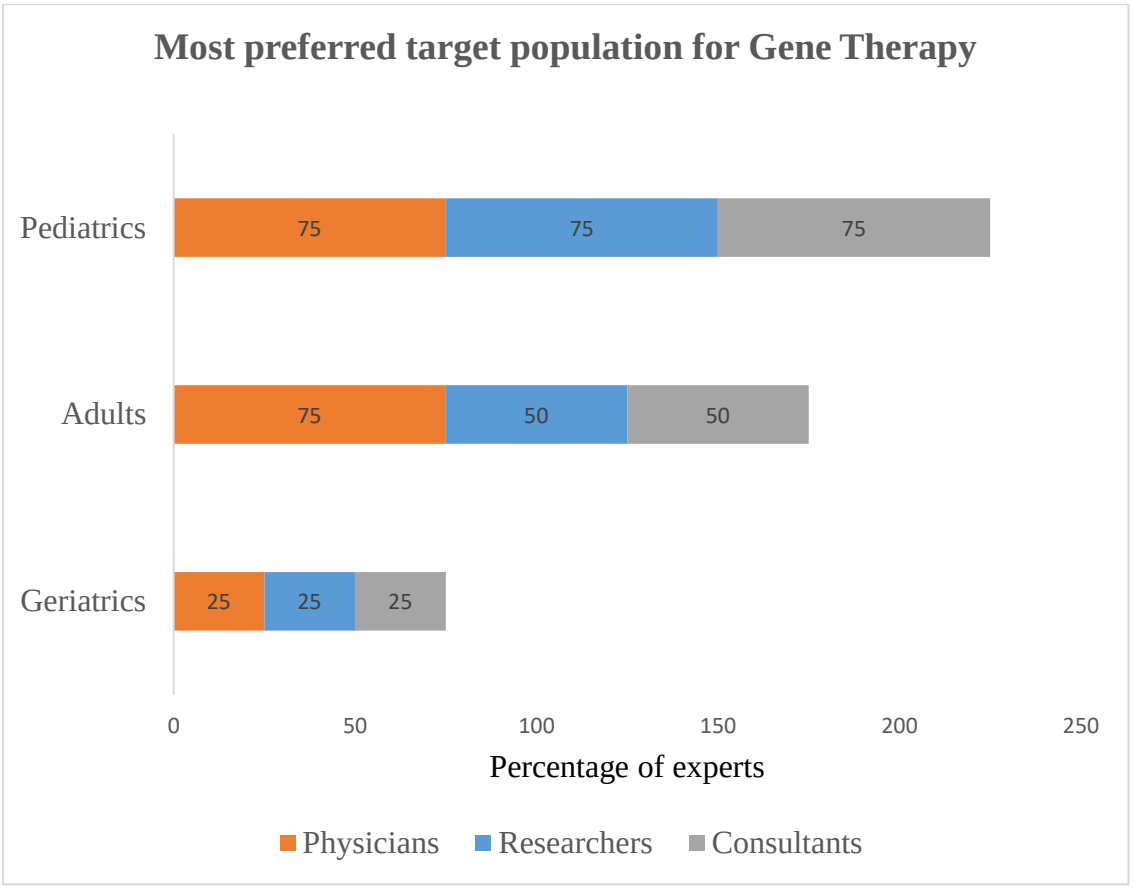
Question: Which cancer indication should be taken up for research in India, to bring a gene therapy product?



Graph 4:Cancer indication for Gene Therapy

50% of the physicians and 25% of researchers and consultants suggest Breast and Lip/Oral cancer should be taken up for research in gene therapy in India.

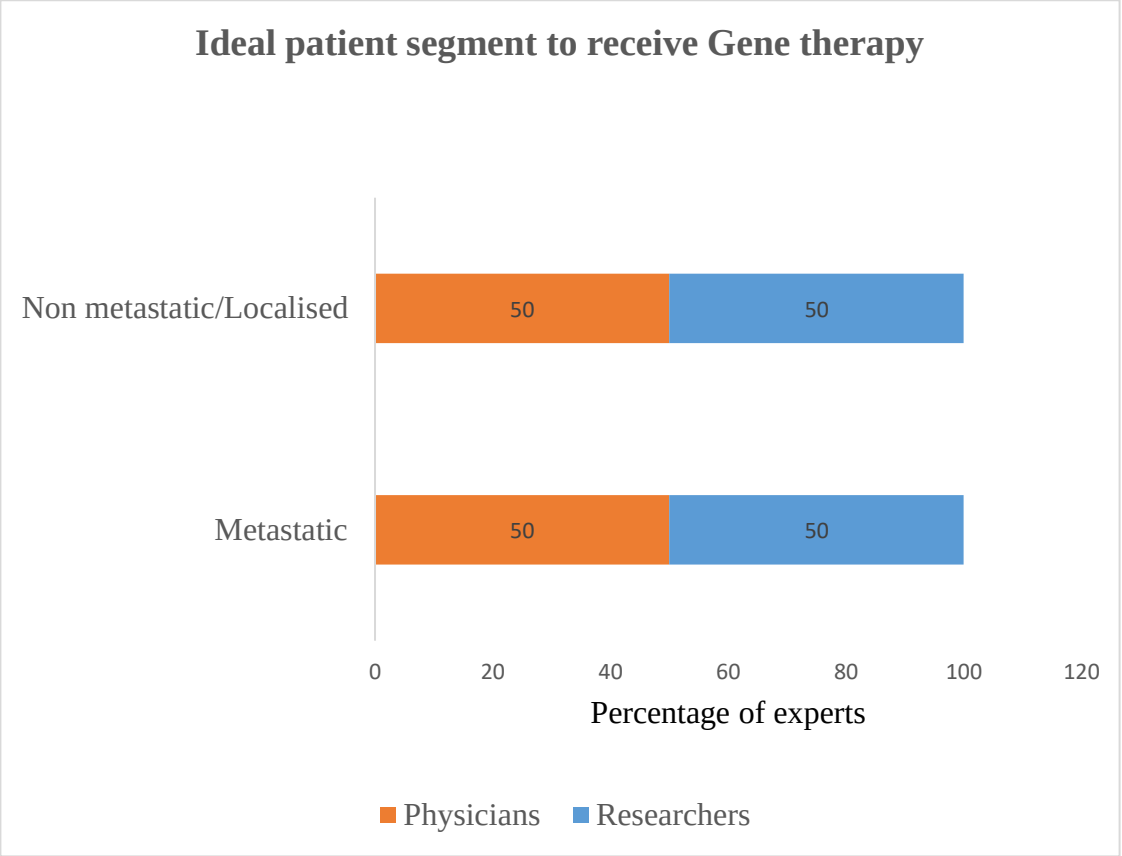
Question: On a scale of 1 - 5, please rate the following as the most preferred target population for gene therapy?



Graph 5: Target population for Gene Therapy

Consultants, Researchers, Physicians rate the pediatric population highest in terms of most preferred target population for Gene Therapy followed by adults and geriatrics.

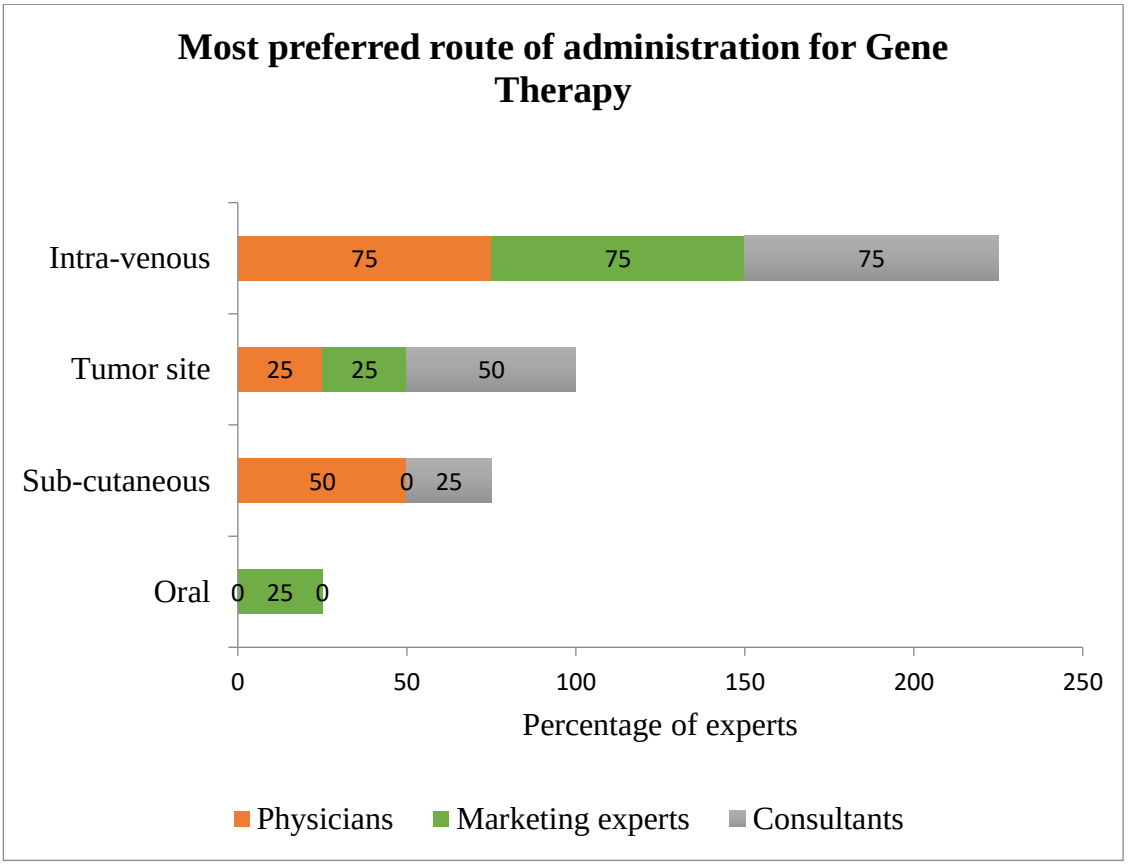
Question: Based on your experience, which among the following patient segments looks to be best suited for receiving gene therapy?



Graph 6: Patient segment for Gene Therapy

50% of physicians and researchers believe gene therapy should be given to patients where the tumor has metastasized, as there is no other option apart from surgery in such cases. The other 50% believe localized tumors, which have a better chance of being cured, should be targeted.

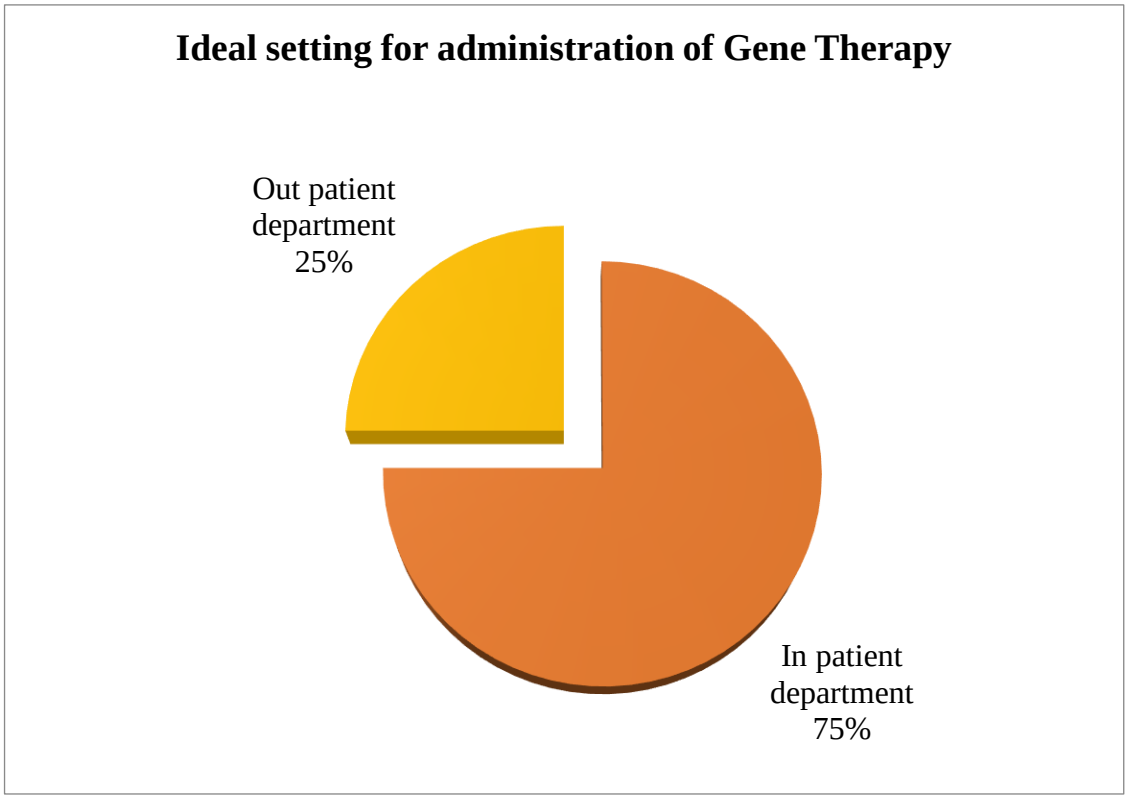
Question: On a scale of 1 - 5, please rate the following as the most preferred route of administration for gene therapy?



Graph 7: Route of administration for Gene Therapy

Physicians, Marketing experts and consultants suggest intra-venous as the most preferred route of administration of Gene therapy. Physicians believe SC would be better than tumor site but the consultants and marketing experts rate tumor site injections higher than SC. Oral route is also an option presented by the marketing experts.

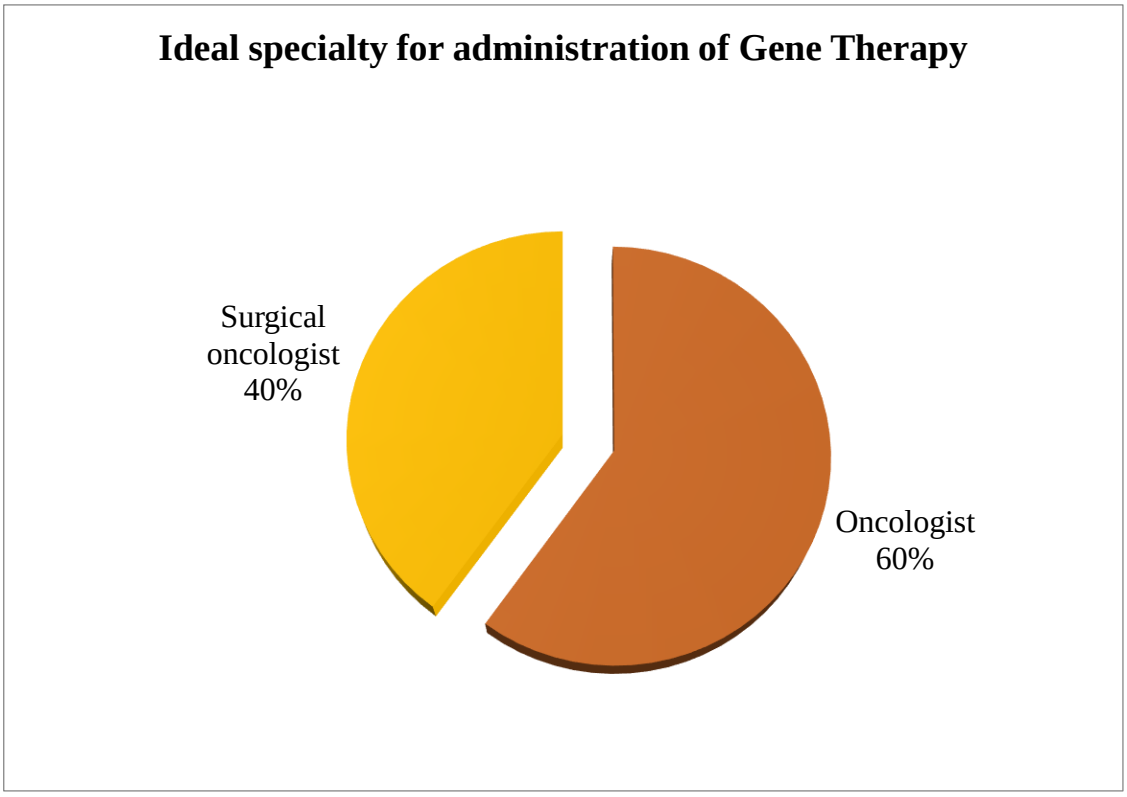
Question: Which setting will be more appropriate to administer gene therapy product?



Graph 8: Ideal setting for administration of Gene Therapy

75% of the physicians believe Gene Therapy should be administered in the-In patient department.

Question: Which specialty will be most suitable to administer this therapy?

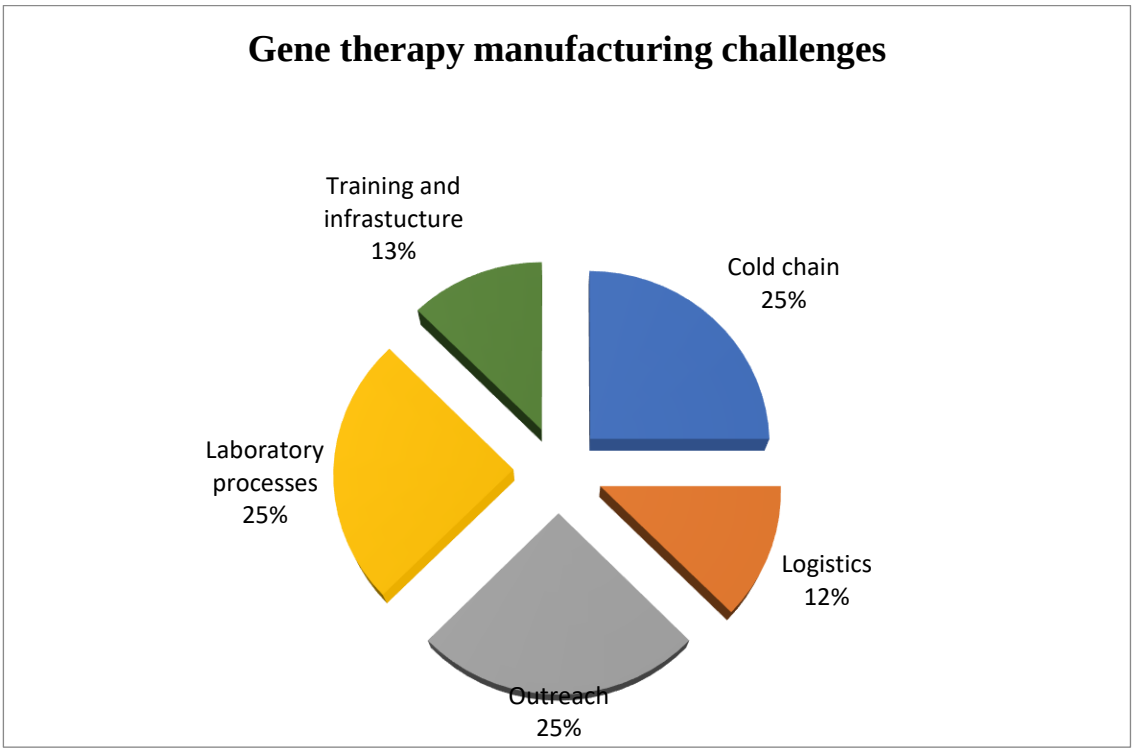


Graph 9: Ideal specialty for administration of Gene Therapy

60% of the physicians believe that oncologists and and 40% believe, surgical oncologists are the ideal specialties for administering Gene Therapy.

2. Manufacturing Gene Therapy product

Question: What will be the manufacturing challenges with respect to Gene Therapy Oncology products?



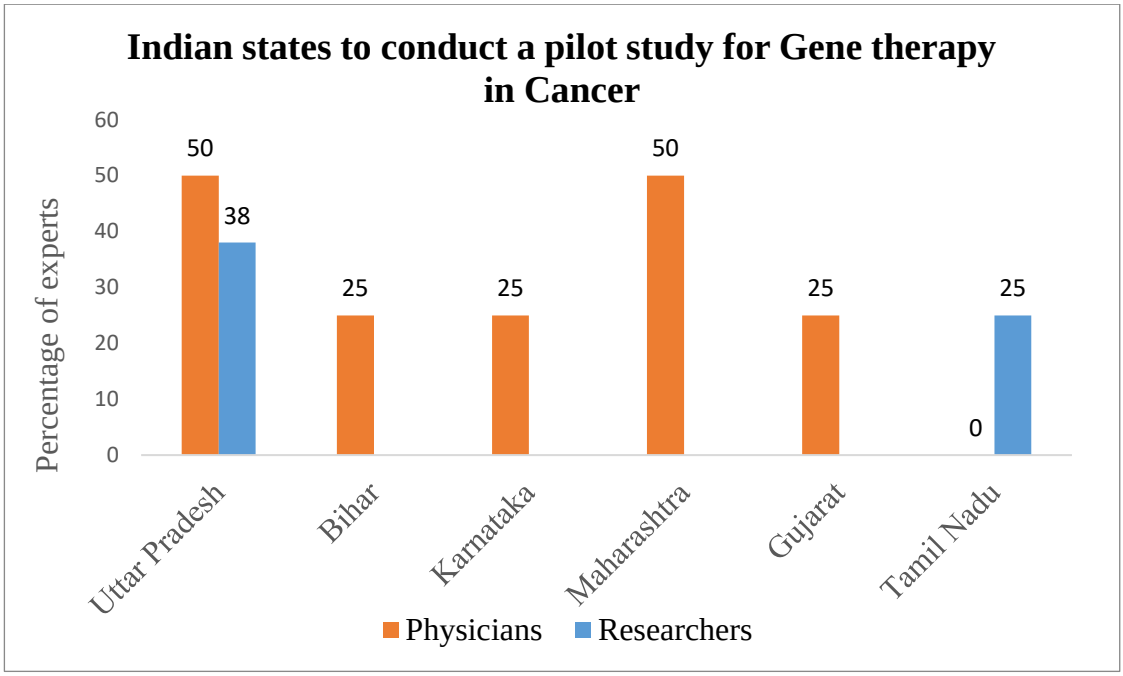
Graph 10: Gene Therapy manufacturing challenges

25% of the researchers believe cold chain, 25% say outreach and another 25% suggest laboratory processes, pose maximum challenge to Gene Therapy manufacturing. Rest of them mentioned logistics and infrastructure as the other challenges.

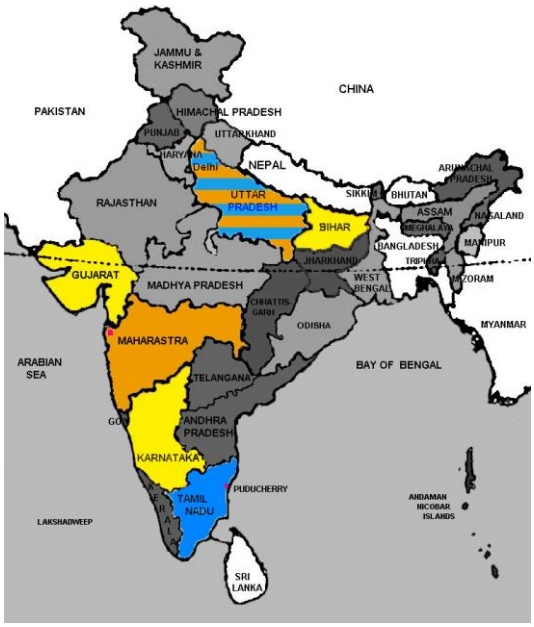
As per the experts, challenges could be seen in mainly two of many laboratory and clinical processes namely, transduction process which includes insertion of genes into the cells and inactive viral vectors in to cells and the delivery process where patients are infused with the therapy.

3. Clinical trials of Gene Therapy products

Question: If you had to recommend India states for conducting a pilot study for gene therapy for cancer, which would they be?



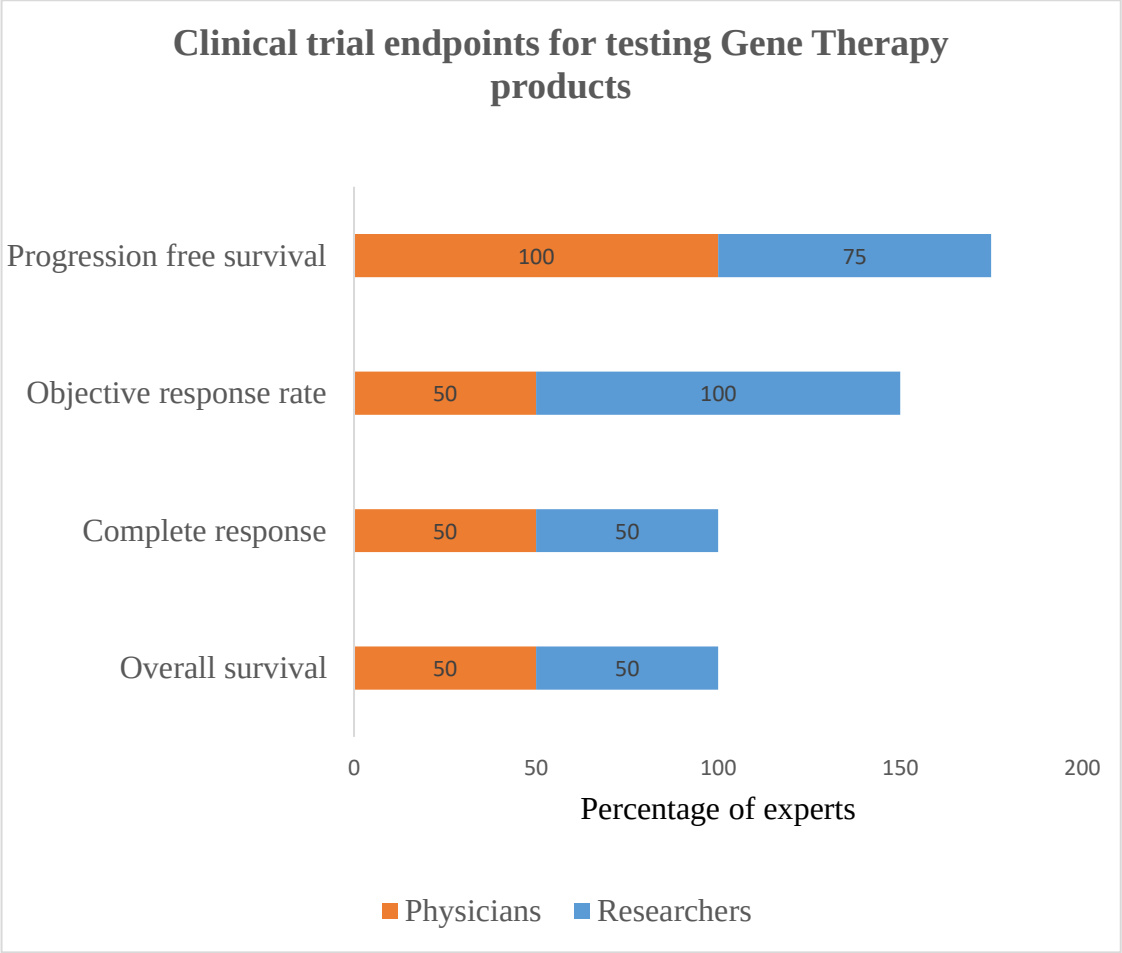
Graph 11: Indian states for conducting clinical trials



50% of physicians think Uttar Pradesh and Maharashtra are the ideal states for conducting a pilot study for gene therapy in India. Researchers suggest Uttar Pradesh and Tamil Nadu as ideal states.

Figure 5:Indian states for clinical trials

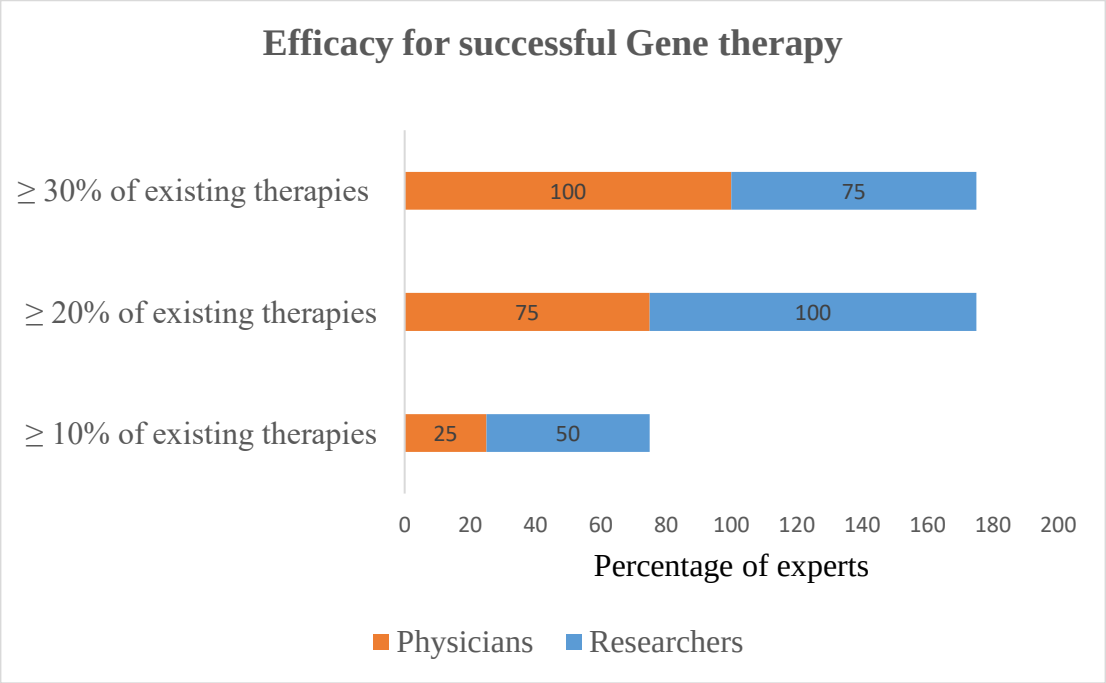
Question: On a scale of 1-5, what should be the clinical trial endpoints for testing gene therapy products?



Graph 12: Clinical trial endpoints for Gene Therapy

Physicians believe ideal clinical trial end point to test gene therapies should be Progression free survival and for Researchers it should be Objective response rate.

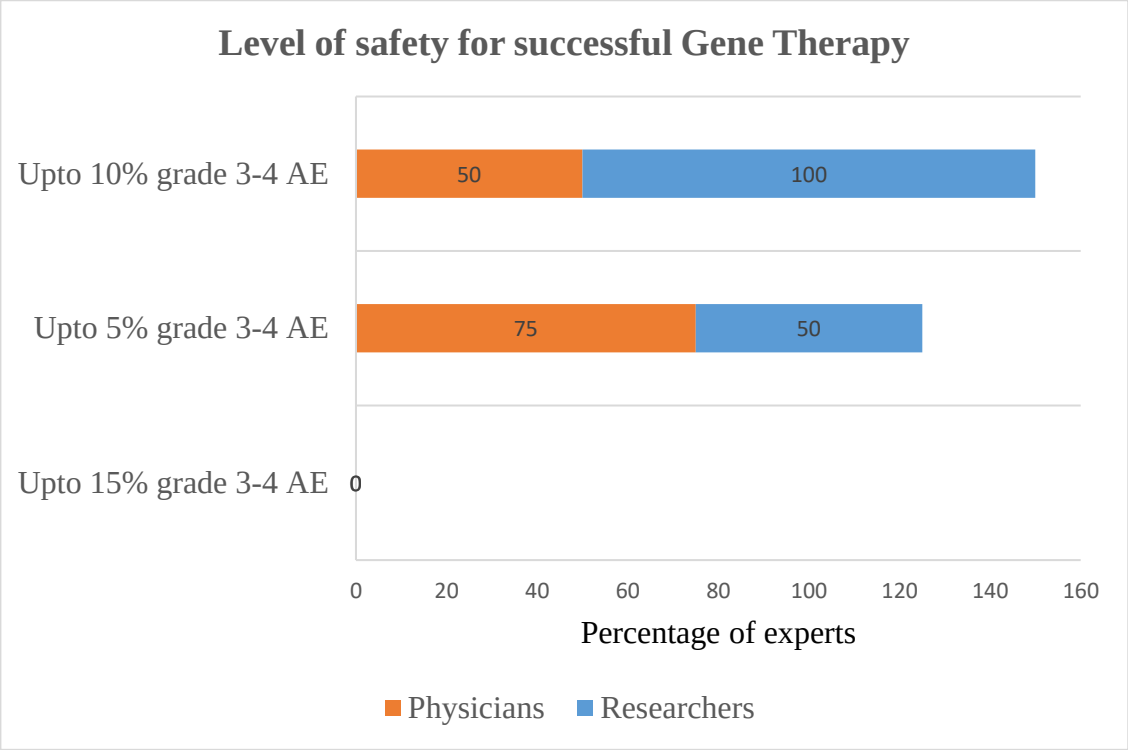
Question: On a scale of 1-5, what should be the efficacy of gene therapy for it to be successful in India?



Graph 13: Efficacy for successful Gene Therapy

Researchers believe efficacy of gene therapy has to ≥ 20% of existing therapies and Physicians believe gene therapy has to be ≥ 30% of existing therapies, for it to be successful in India.

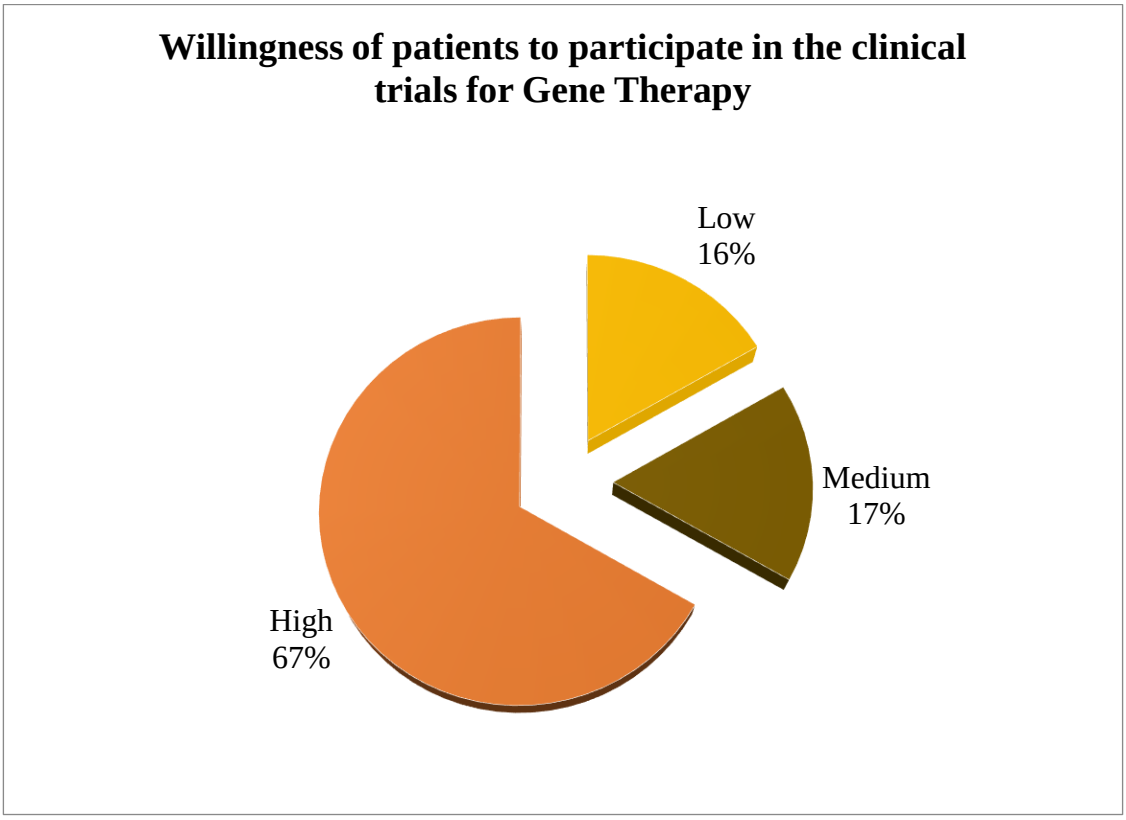
Question: On a scale of 1-5, what should be the level of safety of gene therapy for it to be successful in India?



Graph 14: Safety for successful Gene Therapy

According to the physicians adverse events upto 5% grade 3-4 is acceptable. According to the researchers, up to 10% grade 3-4 AE is acceptable.

Question: On a scale of 1-5, if a clinical trial is held for gene therapy cancer product in India, what will be the level of willingness of patients to participate in the trial?

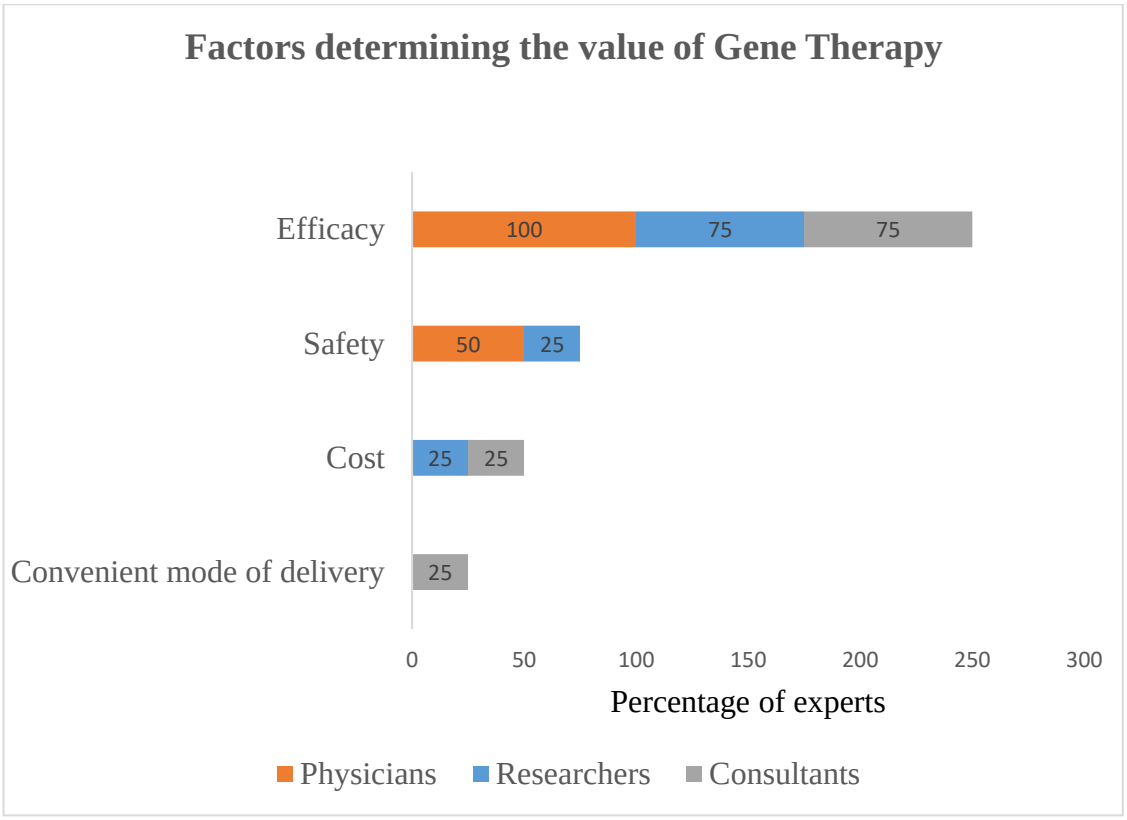


Graph 14: Willingness of patients to participate on Gene Therapy clinical trials

67% of the physicians believe that the level of willingness of the patients to participate in clinical trials for Gene Therapy will be high.

According to Physician 3, "If trial population is given free treatment then 100% of population will be willing (this includes people of all strata, caste and creed)."

Question: Which among the following, is the most important factor to determine the value of a gene therapy oncology product?



Graph 15: Factors determining value of Gene Therapy

100% of the physicians and 75% of consultants and researchers believe efficacy is the most important factor followed by safety. Cost also has a role to play as affordability is turning out to be an important factor in gene therapy.

Consultant 4 adds, "Convenient mode of delivery that is, it should be less painful and definitely duration of treatment, the shorter the better."

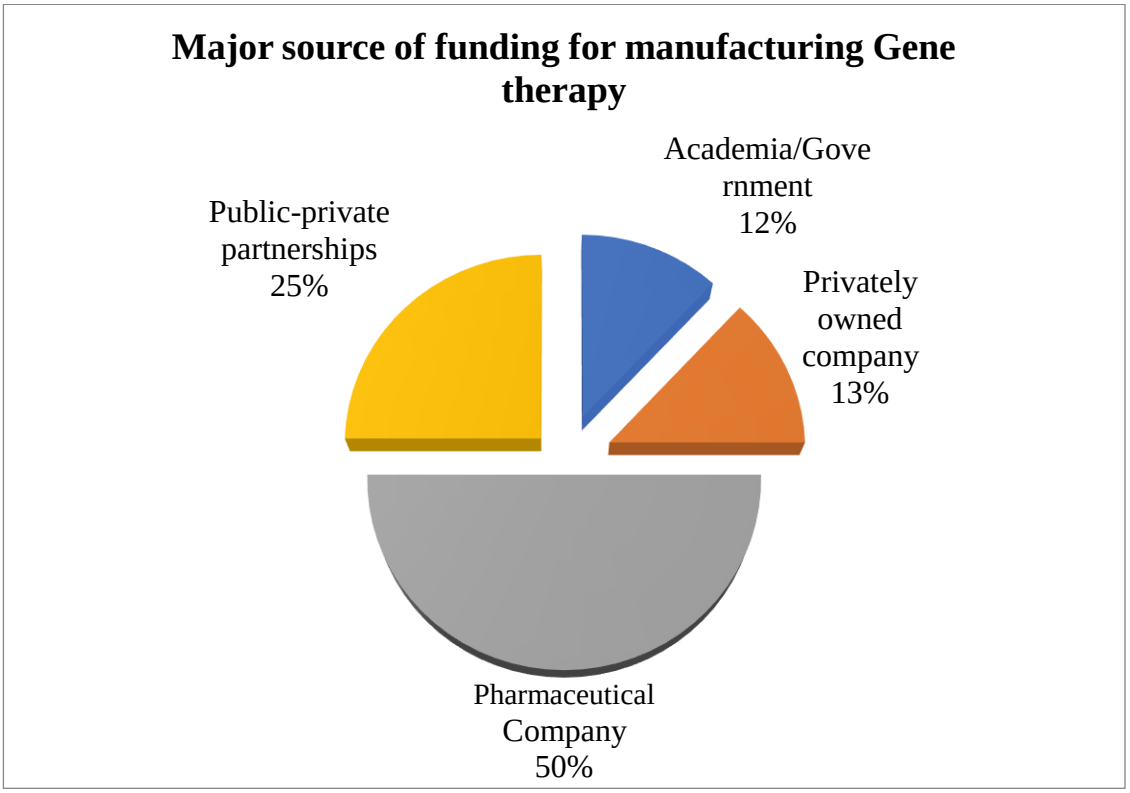
Question: Will industries be willing to conduct clinical trials for gene therapy in India? Any specific company in mind? 

100% of the researchers believe that industries will be willing to conduct clinical trials for Gene Therapy in India.

The various industries could be willing to conduct clinical trials include, Novartis, Xydus, Cadila and Biocon BMS.

As per Researcher 3, "Xydus, Cadila- already in India for malaria. Public, private vaccine companies", positively confirmed one of the experts. Another was of the view that Industries will most definitely be willing to conduct clinical trials such as, "Biocon collab BMS centre- Bangalore."

Question: Which can be a major source of funding for gene therapy oncology product?

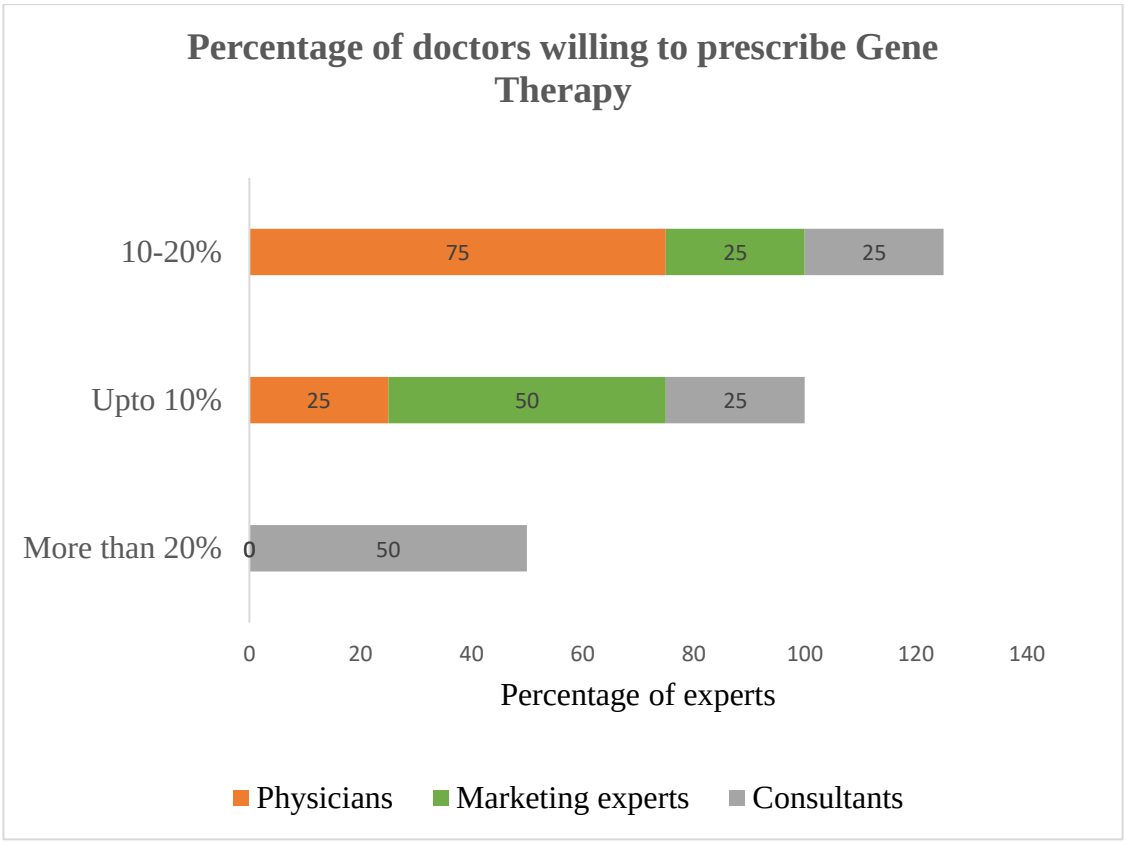


Graph 16: Funding sources for Gene Therapy manufacturing

50% of the researchers believe that pharmaceutical companies will be the major source of funding for manufacturing Gene Therapy. 25% believe public-private partnerships can help whereas rest thinks privately owned companies and Academia/Government collaborations can act as funding sources.

4. Commercialization of Gene Therapy for Oncology in India

Question: If gene therapy is launched in India, what percentage of doctors do you think will prescribe it?

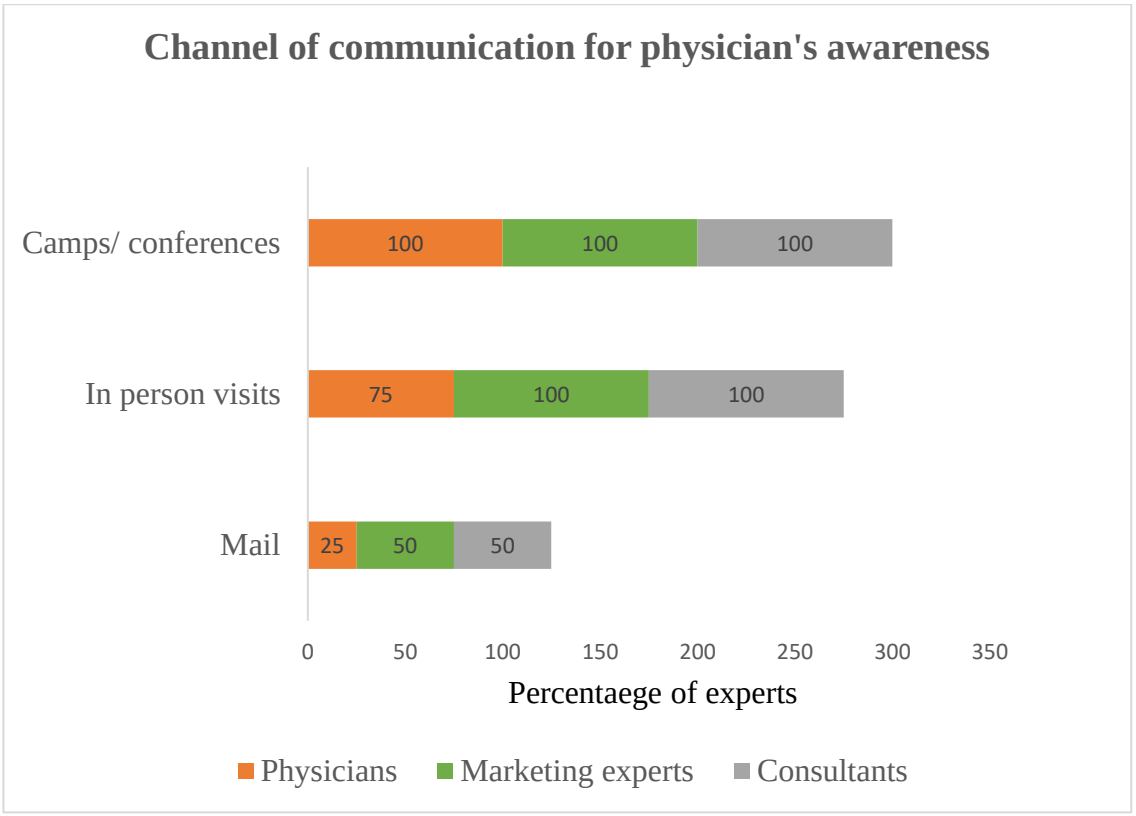


Graph 17: Percentage of doctors willing to prescribe Gene Therapy

75% of the physicians and 25% of consultants and marketing experts are of the view that only 10-20% of doctors will be willing to prescribe Gene Therapies to their patients.

Reason for such low percentage could be that, this therapy is a first of its kind in the Indian market with very high cost and equally low awareness.

Question: On a scale of 1 - 5, which channel of communication would be most suitable for physician's awareness about gene therapy product?

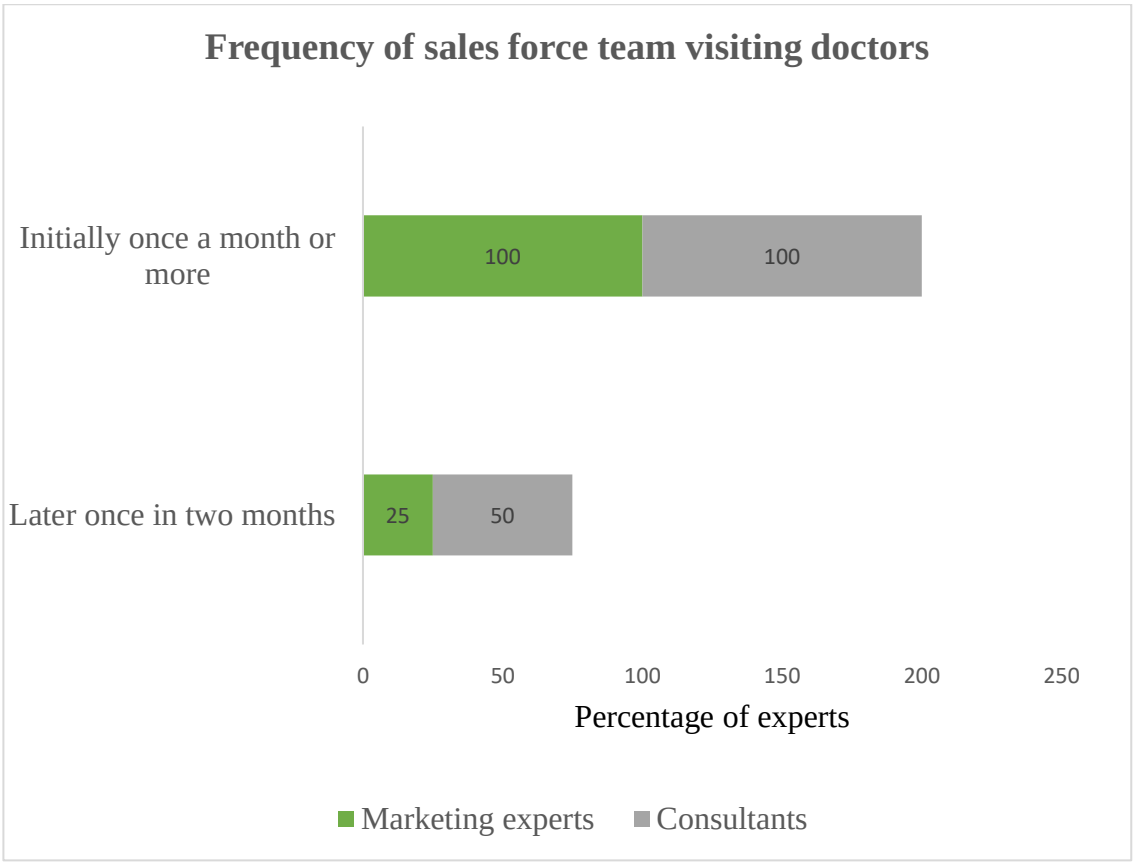


Graph 18: Channel of communication for physicians awareness of Gene Therapy

Physicians, Consultants and Marketing experts have given highest importance to camps and conferences followed by In-person visits and mails for raising awareness among physicians about gene therapies by the sales and marketing team of pharmaceutical companies.

This depends on the phase of product launch. Initially the main stakeholders, that is the physicians have to be made aware by conducting camps and conferences which would include the key opinion leaders. Second would be in person visit for discounts etc. directly to the physicians. Third would be mail that is after convincing the KOL and doctors and to keep reminding and updating them with the latest scenario.

Question: How many times should the sales force teams visit doctors for successful commercialization of gene therapy products in India?

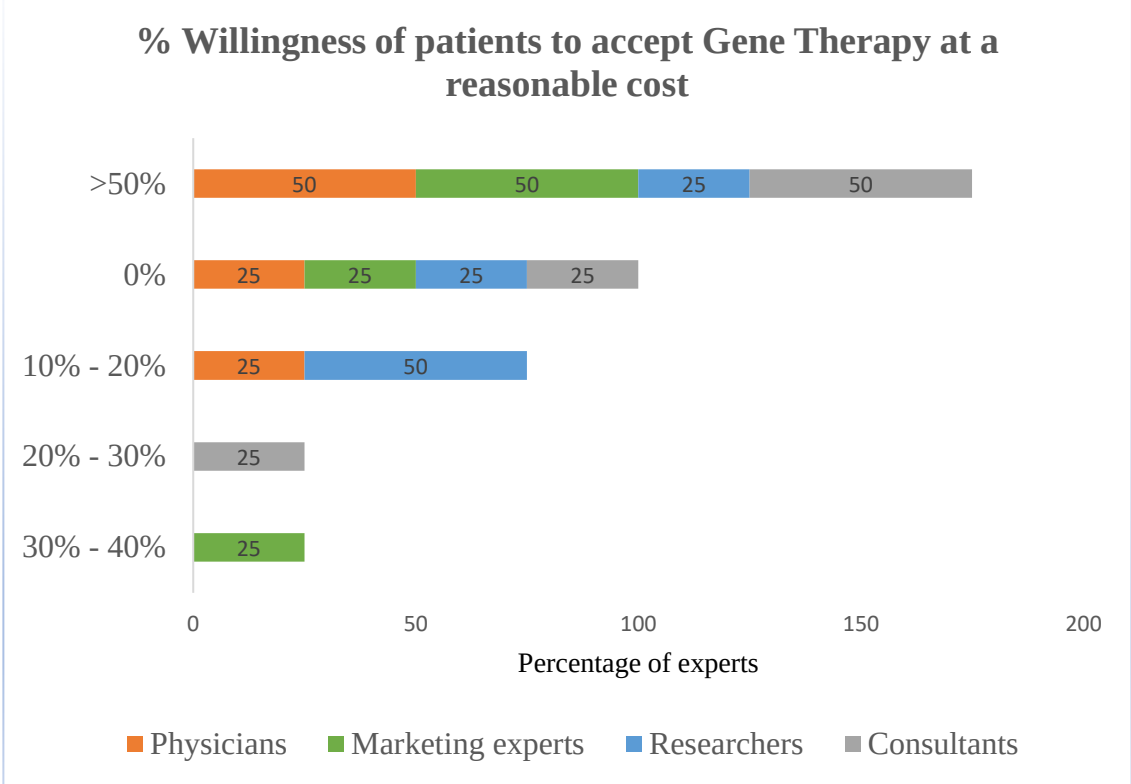


Graph 19: Frequency of sales team visiting doctors

100% of the consultants and marketing experts believe that the sales force team should visit the doctors at least once a month initially when the product is newly launched. Later the frequency can be tapered down to once in two months.

Question: Based on your experience, what percentage of cancer patients will be willing to take gene therapy?

a. If Gene Therapy comes at reasonable/comparable cost to existing therapies

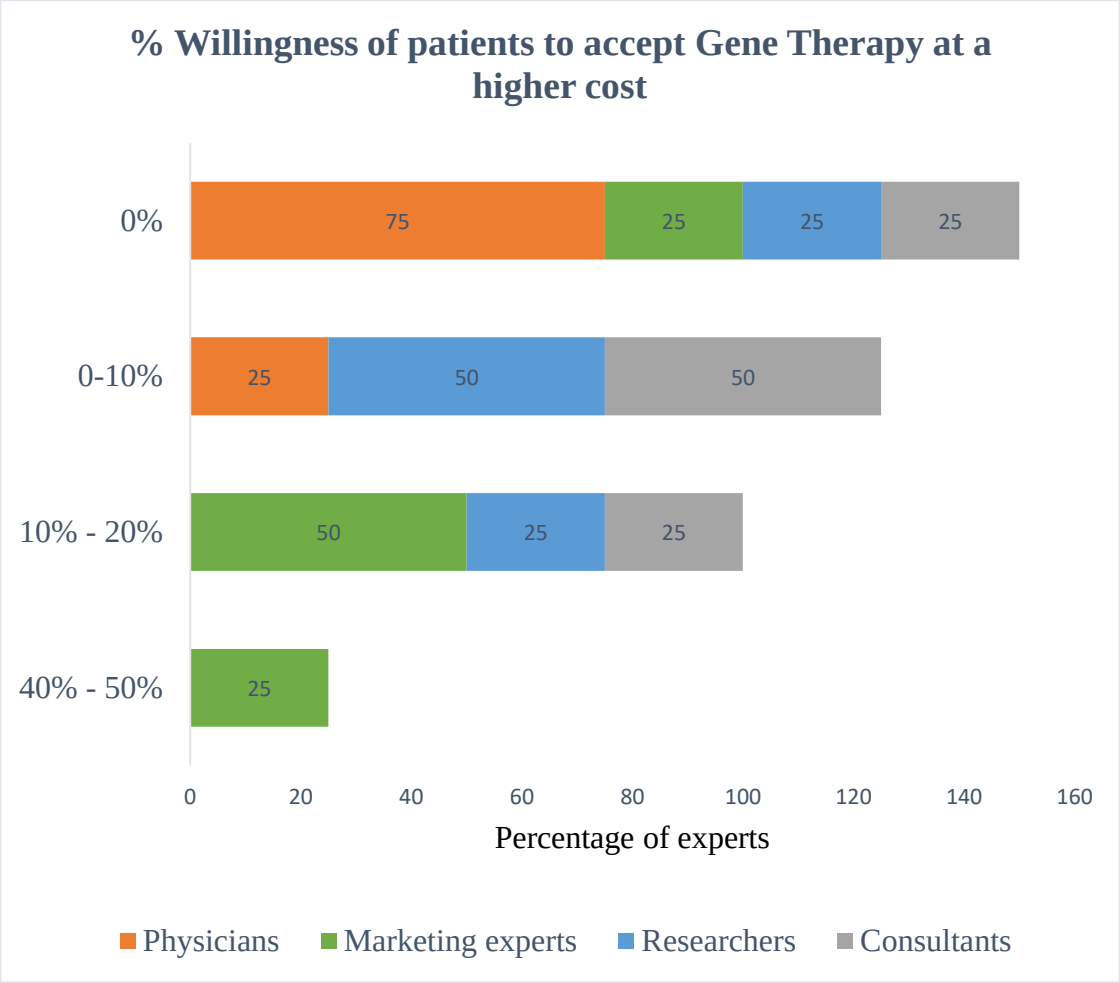


Graph 20: % willingness of patients to accept Gene Therapy at a reasonable cost

Almost 50% of the experts are of the view that if Gene Therapy comes at a reasonable/ comparable cost to existing therapies then more that 50% of the cancer patients will be willing to take up this specific therapy. However one-fourth of the experts also think that it is inaccessible to and unaffordable by most of the Indian population.

Cost of existing gene therapy is $475,000 that is Rs 3,16,44,500 which is far beyond the buying capacity of an average Indian. Although it is a single time treatment and if proven efficacious and suggested by the physicians to their patients, only a handful of people convinced by their treating physicians will be able to afford such a treatment.

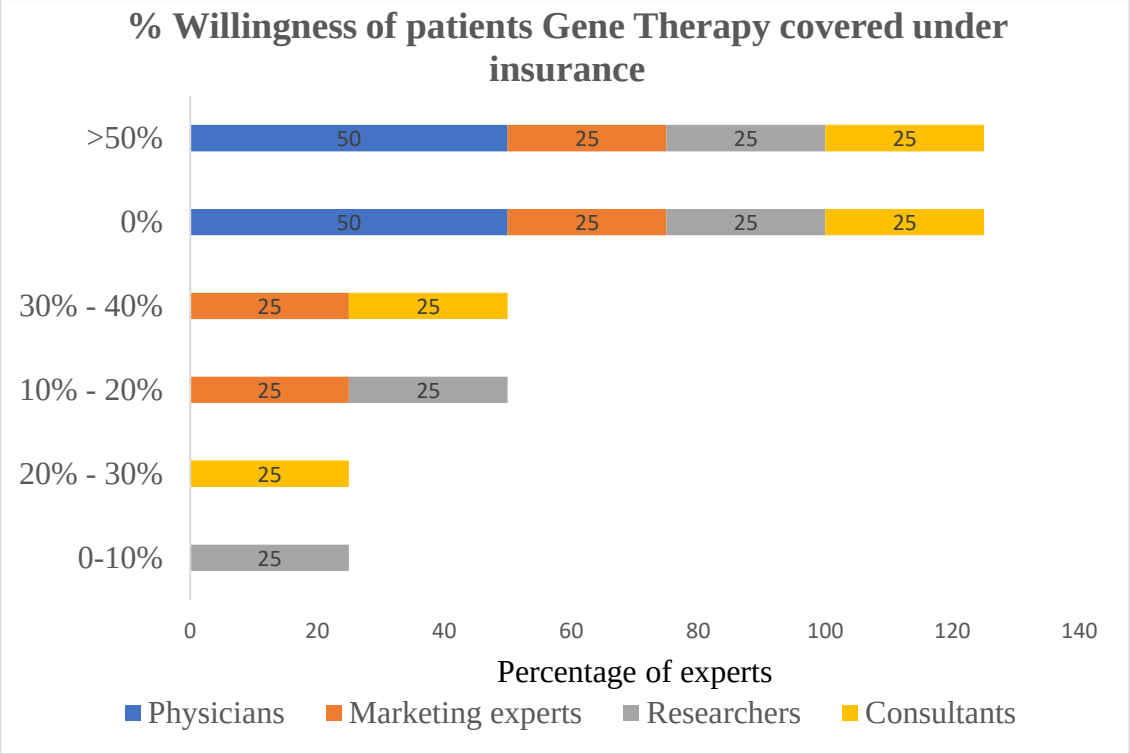
b. If Gene Therapy comes at higher cost?



Graph 21: % willingness of patients to accept Gene Therapy at a higher cost

At a higher cost than the existing therapies, 75% of the physicians and quarter of the rest of the experts believe that the patients will not be able to afford this therapy

c. If covered under insurance



Graph 22: % willingness of patients to accept Gene Therapy covered under insurance

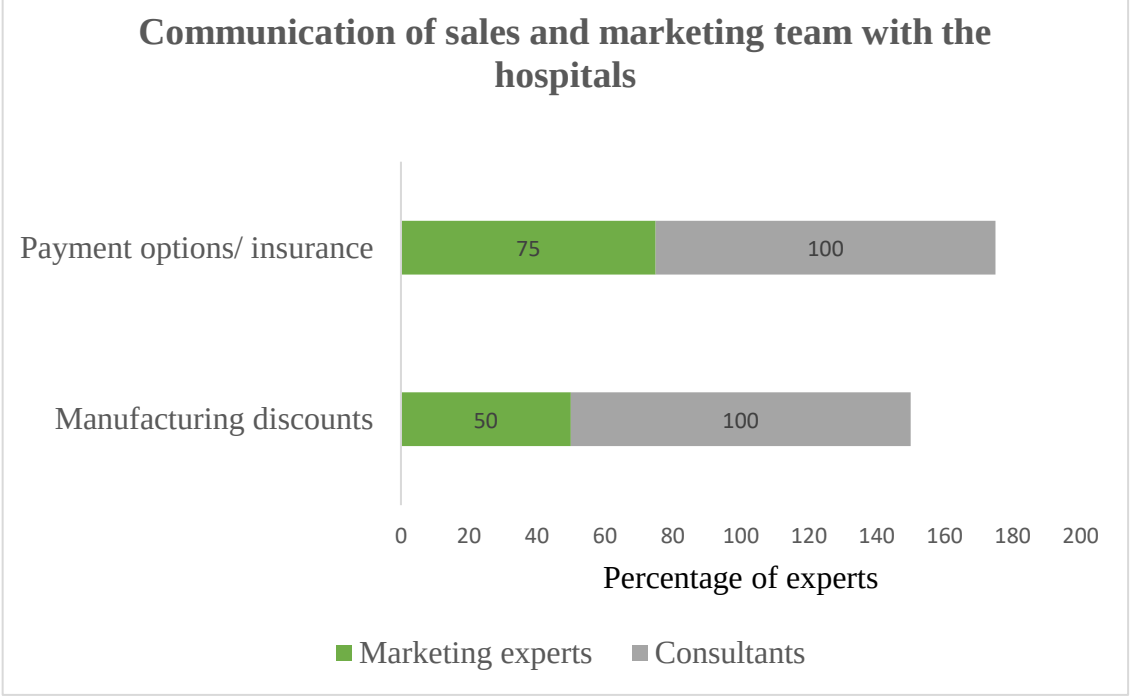
If Gene Therapy is covered under insurance then half the physicians and 25% of other experts believe that patients will be highly willing to take it up.

As the insurance system in India is not that strong, to believe that Gene Therapy will be covered under insurance seems a like a distant reality. However if it does happen, then most patients will be willing to go for Gene Therapy as a treatment option for cancer.

Marketing expert 3 adds, "It will not help as insurance coverage is very less in India."

Insurance in India is mostly private or for Govt employees and hence the chance of having such an option is practically impossible.

Question: On a scale of 1-5, how important is it for the gene therapy marketing and sales team to provide the following, while visiting hospitals for their products?



Graph 23: Communication of sales and marketing team with hospitals

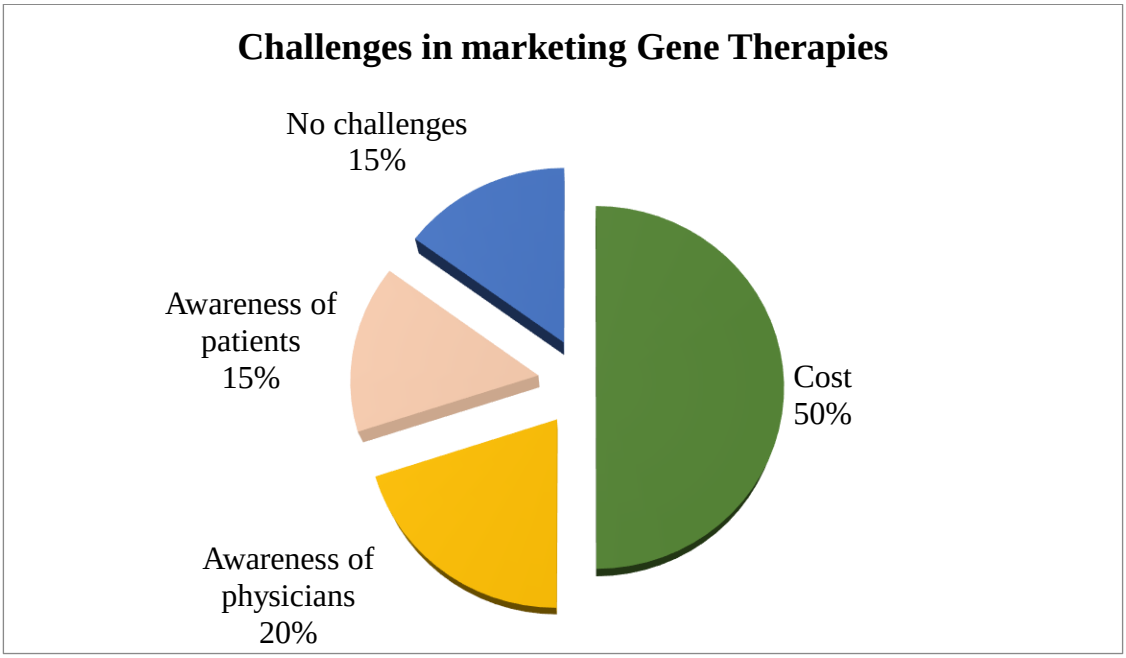
Both consultants and marketing experts believe discussing payment options/ insurance details with the hospitals during visits by the sales and marketing team would help in commercialization of the product.

Question: Do you think marketing for gene therapy products would need a special team with relevant subject matter experience? 

100% of the marketing experts believe that in order to market Gene Therapy Oncology products in India, one needs a special team with relevant subject matter experience.

Marketing for Gene therapy products would definitely benefit from a special team with relevant subject matter experience. This is because gene therapy being such a specialized subject, physicians would rather like to listen to people who can make them understand the mechanism of action clearly with scientific terms. Here comes in the concept of pharmaceutical companies needing doctors and staff with a medical background (Medical Science liaison) who can “sell the concept to the physicians.”

Question: How challenging will it be to market gene therapy oncology product in India?

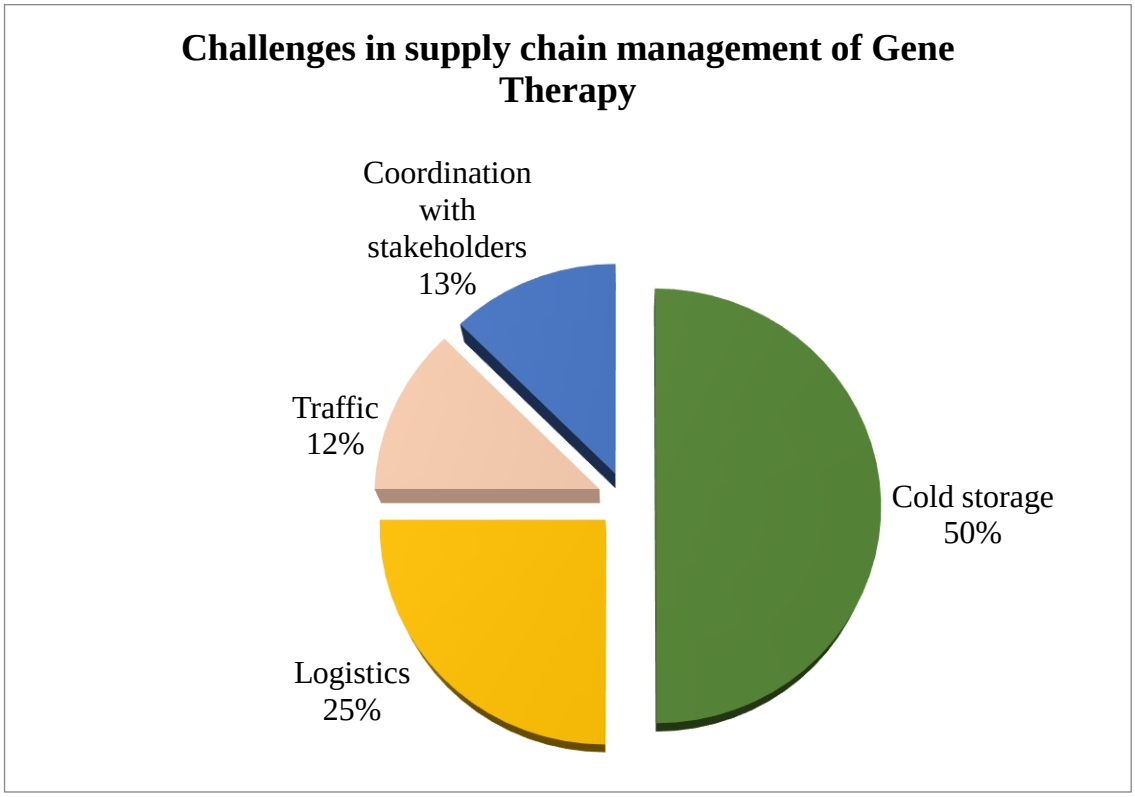


Graph 24: Challenges in marketing Gene Therapies

50% of the Marketing experts believe that the biggest challenge in Gene Therapies is related to the expected high cost of the therapy. 20% believe that awareness of physicians and 15% believe awareness of patients about gene therapies could be potential challenge. 15% also believes that if the therapy has proven its efficacy and the population is aware of it, then marketing such therapies would not have any significant challenges.

According to Marketing expert 2 , "It will be difficult if the price is high, no insurance, no patient awareness, no patient compliance. The solution would be to train physicians and also counsel patients by conducting patient campaigns etc. At first it is essential to create a base by imparting knowledge and education about the subject."

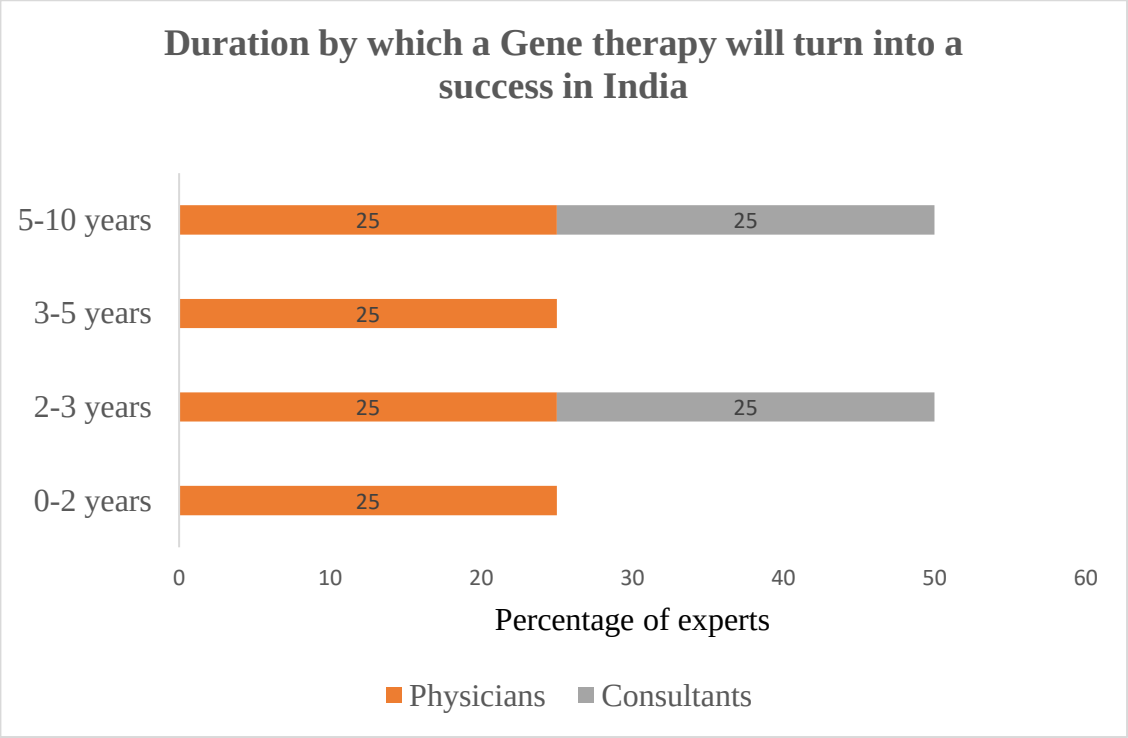
Question: What could be the challenges for supply chain management?



Graph 25: Challenges in supply chain management of Gene Therapies

50% of the marketing experts think cold storage is the biggest challenge in supply chain management of Gene Therapy. These experts also think that the other challenges include transportation problems such as traffic in India, logistics and overall coordination among stakeholders like physicians, insurance companies etc.

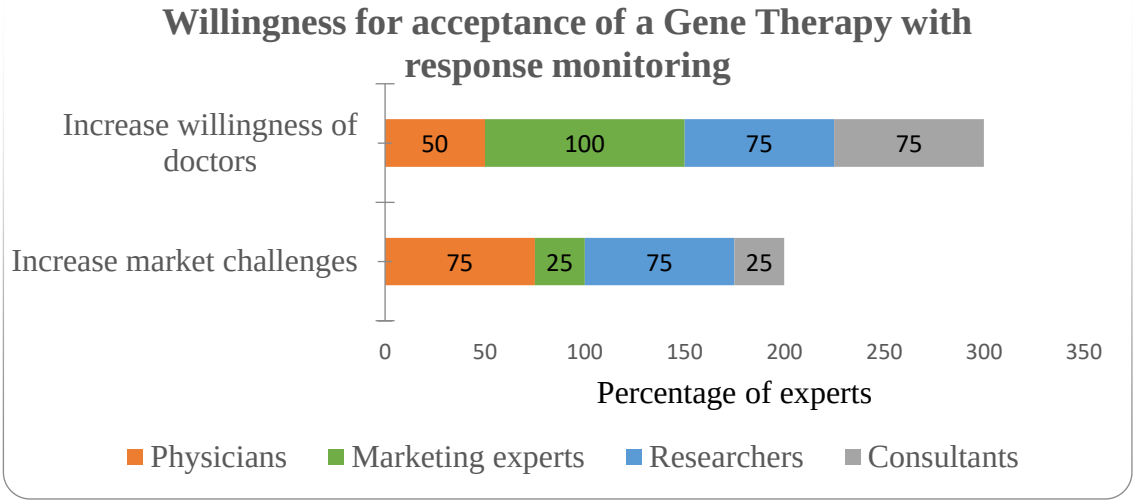
Question: If a gene therapy product with good efficacy is launched in India, how early can it turn into a successful therapy?



Graph 26: Duration by which Gene Therapy will turn into a success in India

Consultants and Physicians believe it would take at least 5-10 years, but if proper reimbursement strategies are made, then in 2-3 years India could see a gene therapy in its market.

Question: If gene therapy comes with a feature of diagnostic test that can be used for response monitoring, will it increase the willingness of the doctors to prescribe it and how challenging will it be to market such a product?



Graph 27: Willingness for acceptance of a Gene Therapy with response monitoring

Only 50% of the physicians believe such a product will increase the willingness of doctors to prescribe such a product and 75% of them believe this will increase the marketing challenges. However according to the marketing experts, 100% of them support the fact that it'll increase the willingness of doctors to prescribe this product and only 25% of them think that it'll increase the market challenges.

75% of the Researchers believe it'll increase both willingness of doctors to prescribe such a product and at the same time increase marketing challenges. Consultants on the other hand believe although it'll increase the willingness of the doctors to prescribe such a product, it will not be so challenging to market such a product.

Discussion

Gene therapy is a procedure that can be used to cure diseases with no current treatment modalities and also extend and enhance life of patients suffering from rare and orphan diseases. According to the American Medical Association there are 4000 diseases related to genetic disorders. Hence the scope of treatment using Gene Therapy is huge. In India, one of the major causes of mortality is cancer. Cancer can also be related to genetic mutations and hence there are already Gene Therapies in pipeline for treatment of cancer. According to the experts, cancer especially breast and oral cancer, should be targeted for treatment using Gene Therapy in India. These cancers account for greater than 50% all deaths due to Cancer in India. Another group of cancers that could be targeted is Pediatric cancer. As there are already Gene Therapies for diseases like Acute Lymphoblastic Leukemia, it could also be an option.

Gene Therapy, being such a specialized subject, requires high level of infrastructure and trained personnel to manufacture it. As the procedure involves genetic engineering, where in viruses and bacteria are used as vectors to transfer the required genes, it is extremely necessary to have high end laboratories and also facilities to fulfill its cold storage needs.

Only of the Gene Therapies in Europe was discontinued as there was only one center, in Italy, that provided the therapy, which could not be transported anywhere else due to its storage issues. Hence people could not afford to first fly to Italy and then pay for the treatment also. Therefore is it required to make accessible to the population.

In order to administer Gene Therapy, the experts suggest intra- venous as the most preferred route and hence to be delivered in the IPD by an oncologist.

For Gene Therapy to be successful, especially for indications like cancer, the efficacy needs to be high, at least greater than 30% of existing therapies and also low levels of adverse events. If incentives are given to the patients and also surety regarding the treatment, patients should be willing to take part in clinical trials for the same. Also in order to conduct clinical trials, one needs funding and sponsors. The Government seems like a positive ray of hope to aid in funding for such trials.

Once the clinical trial is successful, comes the commercialization challenges. Two of the most important challenges are awareness and cost. The way to reach to the patients for Gene Therapy is via doctors. In India it is only the doctors who consult and advise patients regarding treatment modalities. Hence in order to make the doctors aware, and indirectly the patients, it is important to talk about Gene Therapies in conferences involving Key Opinion Leaders. Next, in person visits to various hospitals, discussing about payment options and discounts, and finally mails to keep them updated, is what the experts suggest.

For Gene Therapy sales and marketing, the team involved should be specialized in this field as the subject is quite scientific and requires in depth knowledge. Once there is enough awareness, the willingness of patients and doctors to use Gene Therapy will rise.

The last and most important issue with Gene Therapy is its sky-high price. Strengthening the health insurance system in India could be one of the solutions to this problem. Other options could be offering discounts and loans to the patients. Also, involving patients in clinical trials could benefit the stakeholders, the manufacturers and the payers.

Conclusion

Along with an exciting opportunity, Gene Therapy also poses certain challenges. In India clinical trials in Gene Therapy should be conducted for oncology specifically breast and oral cancer as they have the highest incidence and mortality rates. Ideal efficacy of the therapy should be greater than 30% of existing therapies and adverse events less that 5% grade 3-4 AE. Highly specialized laboratories and trained specialists are required with funding from the Government and public-private partnerships to manufacture Gene Therapy products.

The two biggest challenges for gene therapy are cost and lack of awareness among the population. Doctors need to be convinced first followed by the rest of the stakeholders to choose Gene Therpay as a treatment modality. The health insurance system in India should be strengthened to make the therapy accessible to the population.

It would take at least 5-10 years for Gene Therapy for Cancer to arrive in India that too with proper funding and commercialization strategies.

Recommendations

Gene Therapy is a one-time treatment modality that can be used to treat various diseases, including Cancer.

1. In order to bring Gene Therapy to the Indian market one has to specify the target population. Research should be conducted for diseases that have high prevalence in India and is difficult to treat with already existing modalities. Cancers such as Breast and Oral cancer along with Pediatric cancers like Acute Lymphoblastic Leukemia should be targeted
2. Research efforts of scientists have to be strengthened to manufacture Gene Therapies. One of the ways could be, conducting and attending conferences where in they could interact with Gene Therapy experts already involved in designing successful Gene Therapies. Extended programs like continuing medical education (CME) should be held with such experts
3. Similarly awareness of doctors prescribing the Therapy should be taken care of by involving them in similar conferences because they are the ones who will be actually advising the patients to use the treatment
4. Once there is enough awareness and sufficient infrastructure to manufacture the Gene Therapy, only then can strategies can be made to run clinical trials and market the product

Reference

Cancer Key facts [Internet]: [WHO]; 2018 Feb 01 [Cited 2018 Apr 27]. Available from: http://www.who.int/mediacentre/factsheets/fs297/en/

Call for Action: Expanding cancer care in India: [Place unknown]: Ernst and Young; 2015 July [Cited 2018 Apr 27]. Available from: http://www.ey.com/Publication/vwLUAssets/EY-Call-for-action-expanding-cancer-care-in-india/%24FILE/EY-Call-for-action-expanding-cancer-care-in-india.pdf

Frédéric Biemar and Margaret Foti; Global progress against cancer—challenges and opportunities; Cancer Biol Med. 2013 Dec; Cited 2018 Apr 27]; Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3860343/

Swadesh K. Das, Mitchell E. Menezes, Shilpa Bhatia, Xiang-Yang Wang,Luni Emdad,Devanand Sarkar,and Paul B. Fisher; Gene Therapies for Cancer: Strategies, Challenges and Successes;[Place unknown]; 2016 Feb 1; Cited 2018 Apr 29] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4363073/

Global & US Gene Therapy Market Forecast to 2020; [Internet]; [Global]; 2018 February 14; [Cited 2018 April 29]; Available from: https://www.wiseguyreports.com/reports/2997455-global-us-gene-therapy-market-forecast-to-2020

Cellular & Gene Therapy Products; [Internet]; [Place unknown]; 2018 February 2; [Cited 2018 April 27]; Available from: https://www.fda.gov/BiologicsBloodVaccines/CellularGeneTherapyProducts/default.htm

Guidance for Industry on Submission of Clinical Trial Application for Evaluating Safety and Efficacy; [Internet]; [Place unknown]; [Cited 2018 Apr 27]; Available from: http://www.cdsco.nic.in/writereaddata/CDSCO-GuidanceForIndustry.pdf

Historic Overview of Gene Therapy; [Internet]; [Place unknown]; [Cited 2018 Apr 27]; Available from: http://www.genetherapynet.com/historic-overview-of-gene-therapy.html

FDA approval brings first gene therapy to the United States; [Internet]; [Place unknow]; 2017 August 30]; Available from: https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm574058.htm

Gene therapy in India: A focus;[Internet]; [Place unknown]; [Cited 2018 Apr 24]; Available from: https://www.researchgate.net/publication/261995699_Gene_therapy_in_India_A_focus

Grace Hampson, Adrian Towse, Steven D Pearson, William B Dreitlein & Chris Henshall; Gene therapy: evidence, value and affordability in the US health care system ; [Place unknown]; Journal of comparative effectiveness research Vol. 7, no. 1; [Cited 2018 Apr 29];Available from: https://www.futuremedicine.com/doi/full/10.2217/cer-2017-0068