Identification of Barriers for Patient Recruitment and Retention in Cell and Gene Therapy Clinical Trials Survey [DRAFT RESULTS SUMMARY]

CIRM is establishing a Patient Support Program (PSP) with financial and logistical assistance to patients being evaluated or enrolled in CIRM-funded clinical trials. The aim of the PSP is to improve access, identification, enrollment, and retention of patients with an emphasis on underserved populations.

To inform PSP development, CIRM is seeking to understand specific barriers to recruitment and retention encountered in cell and gene therapy clinical trials. To inform our understanding, we conducted a survey of medical centers applying to the CIRM Alpha Clinics Network Expansion Award.

Organization responding: N = 7

1. In your experience, rate the barriers below in terms of their impact on patient **RECRUITMENT** to clinical trials. Please use a 1-4 scale where 1 = "Not at all important," 2 = "Slightly Important," 3 = "Important," and 4 = "Very Important."

Responses Where N = 7	Average
1. Travel & Lodging Patient / Care Giver(s)	3.4
2. Lost Wages / Time Away from Work (patient or family members)[1]	3.3
3. Medical co-pays	2.4
4. Childcare	2.1

Individual Responses N = 1 Unless Otherwise Indicated	Average
Concerns about research in general, particularly among some communities	3 (N=2)
Time commitments for busy people	3
Identification of potential participants	2
The possibility of being randomized to PLACEBO arm	1-2
A major barrier to recruitment is insurance authorization, particularly for patients covered by private insurance or who are referred from other states. Medicare and other payor rules differ regionally, while coverage analyses for gene therapy studies my also vary between regions and institutions. Therefore, insurance denials or delays may hinder patient enrollment as cell and gene therapy investigational procedures can be costly at this early stage in the field.	NR
Transportation and lodging in California can be prohibitively expensive, especially for families with children who need accommodations for patient, cell donor, and one or more caregivers.	NR

[1] Note, lost wages and work time ranked “very important” for parents where a child is being treated in the clinical trial.

Distance from sites; lodging and transportation accommodations that meet ADA requirements	NR
Lodging for AYA population is particularly challenging if they are over 18 and can't stay in housing designated for pediatric populations but are treated at pediatric hospital so unable to access adult hospital programs. Families have a difficult time covering the costs of housing during the 7–21-day periods in which they must remain local and outpatient.	NR

2. In your experience, rate the barriers below in terms of their impact on patient **RETENTION** (outside of treatment toxicities or disease progression) to clinical trials. Please use a 1-4 scale where 1 = "Not at all important," 2 = "Slightly Important," 3 = "Important," and 4 = "Very Important."

Responses Where N = 7	**Average**
1. Travel & Lodging Patient / Care Giver(s)	3.7
2. Lost Wages / Time Away from Work (patient or family members)	3.4
3. Medical co-pays	2.3
4. Childcare	2.3

Individual Responses N = 1 Unless Otherwise Indicated	**Average**
Not feeling deriving benefit especially if long distance travel involved	1-2
time commitments	2
Loss of Interest in study	2
Discomfort with study procedures	2
Mobility especially in economically challenged communities	3
During pandemic conditions, families have been reluctant to travel with patients' post-treatment during immune reconstitution and beyond. Therefore, some follow-up visits must accommodate remotely at home institutions and protocols must plan for that with home health visit options, flexible visit dates or other allowances.	4
Scheduling conflicts; ongoing patient education and communication about trial; language barriers for non-native English speakers; insufficient reimbursements or slow turn-around for reimbursements; lodging and transportation accommodations that meet ADA requirements	NR
Families may be able to participate in trials where the coverage analysis is favorable but may not be able to afford long (up to 100 days) post-treatment stays near the treatment center that are often required for early phase cell and gene therapies.	NR

3. What is the typical range of expense/reimbursement for:

   i. Additional medical costs (co-pays) reimbursed

   ii. Lost wages or time away from work

   iii. Childcare

   iv. Transportation or lodging for patients/caregivers

   v. Other costs

Individual Responses N = 1 Unless Otherwise Indicated	
Co-pays should not be reimbursed as this is a potential violation of the Medicare Secondary Payor Rule.	NR
Patients may be reimbursed for time spent from $0 up to $8000 and their caregivers from $0 up to $3000.	NR
Childcare is included in stipends above if applicable	NR
Patients and caregivers may be reimbursed for travel, food and lodging for $0 up to $45,000 for the duration of study participation from screening to end of study (~24-36 months).	NR
Typically, only reimbursements for travel and accommodations are provided. For combination trials that involve standard of care drugs, it is helpful when sponsor provides the drug supply for the SOC drug free of charge to participants.	NR
There is no reimbursement for copays, lost wages from work or childcare.	NR
Reimbursement for ground transportation is dictated by federal/state caps.	NR
For combination trials that involve standard of care drugs, it is helpful when sponsor provides the drug supply for the SOC drug free of charge to participants.	NR
Food allowance is an 'Other' category also usually determined by max daily rates set by university policy.	NR

4. What 3rd party vendors help to facilitate accounting for these types of expenses and reimbursements to patients/caregivers during the clinical trial?

   a. If expenses are submitted to and paid by a 3rd party vendor, how are these transactions processed? (e.g.: Debit card, expense report with receipts…etc.)

      - We highly recommend using third-party vendors for travel and reimbursements: (1) They set travel policy and expectations impartially with families;

(2) They protect confidentiality between patients and sponsors;
(3) They can negotiate travel discounts;
(4) They are more efficient at booking and change management than internal study teams;
(5) They remove the heavy administrative burden of arranging travel from the sites.
(6) They usually have a card system to load reimbursements vs. reimbursing by cash or check. Vendors we work with are [multiple contractors identified].

- [Contractor] actually arranged flights, hotel rooms, and transportation between airport/hotel/ clinics. Since the contract with the 3rd party vendor was directly with the sponsor and not with Alpha Clinic, we do not know how transactions were processed.
- Please note these reimbursements and partnerships depend on what clinical trial the patient is on and patient diagnosis: Partnership vary with different sponsors (including commercial) and different patient foundations like [various patient foundation listed by respondent].
- There are institutional funds, sometimes grant/trial funding, and several foundations (e.g. LLS and ACS) offer assistance.
- Generally covered by trial sponsors, may be billed as part of care for cancer trials.
- Sometimes via debit card, stipend card or reimbursed prepayment (N=3)

b. Is the reimbursement paid/allocated retroactively, or in advance of the expense?

- Reimbursements are usually allocated retroactively with proof of visit and receipts. Reimbursements per diem are occasionally provided in advance in cases with long stays.
- [Contractor] handled all arrangements and paid expenses. Since the contract with the 3rd party vendor was directly with the sponsor, we do not know how transactions were processed.
- Retroactively

5. If you could solve the biggest issue impacting clinical trial recruitment and retention, what would it be and how would you solve it?

- We usually have patients very interested to enroll and so no big issues. Would advocate for more education and public awareness

- Combination of informing potential subjects of the importance and safety of trials and making connections with them for recruitment, based on work in largely underserved and economically disadvantaged communities. Solution is to provide information and conduct recruitment with trusted community members such as community health workers.

- Would ask patients, but these issues came up:
    - clinical trials need better integration into clinical ecosystem

  - patients should be better educated about clinical trial options
  - need more funding for out-of-pocket costs, travel, follow-up
  - need a broader range of clinical trials for community patients

- For the pediatric CAR-T trial supported by a CIRM, the biggest challenge is that the patients receive repeat infusions for which they must stay inpatient and outpatient at site for up to two weeks at a time. Patients and their families travel to site every 4-6 weeks, and have extensive out of pocket housing, food, and living expenses that accumulate over time. Additionally, families do not have the same flow of income while their children are receiving treatment, as one caregiver must be with the patient during the duration of their treatment (and therefore is out of work). This disadvantages families without the resources to accommodate for these expenses.

- Below we share the collective thoughts of our team members so that they have a voice and can share their experiences. In summary, economic barriers rank as biggest impediment to clinical trial participation. These barriers need to be taken into consideration during protocol design. Therefore, resources for sponsors need to be developed. Clinical sites need resources (tech and community engagement tools and strategies) for how to reach under-represented communities and training on EDI competency for staff. Depending on the trial, missing work/income for extended periods of time or missing work often due to frequent study visits is most challenging. Our university has options for caregivers for inpatient stays and that is very helpful to offset the cost for long inpatient study visits. Travel reimbursements are a burden for patients from a financial standpoint and a burden on staffing who need to process those reimbursements. Having a 3rd party vendor handle that would be amazing. As it relates to low-income patients, often the lost income, not having reliable ground transportation, or the challenges with public transportation often impact retention. Addressing those financial/transportation barriers should be a priority, followed by cultural sensitivity and diversity training for research staff. The Good Clinical Practices training that most clinical research must have should be supplemented by these other trainings and be requirements of funding agencies. There is a huge body of literature available that addresses the challenges and possible solutions. Finally, many patients would benefit from genomics screening, yet obtaining insurance authorization before-hand is problematic and patients get stuck with bills. We suggest finding resources to cover this cost.

- Cell and gene therapies may be lengthy and disrupt work and childcare which may exclude families who can't take time off. Secondarily, access to novel therapies may be limited to those whose insurance plans will agree to cover them. This may exclude adults in California, those covered by private plans or. out of state or international patient referrals.

- For Recruitment: Advertising and Marketing. We would get more online presence and social media involvement.

- For Retention: Provide travel/lodging for studies that do not include a travel vendor. Or contract directly with a 3rd party vendor that can assist with studies where vendors are not provided by the sponsor.