Patient-Reported Reasons for not Enrolling in a COVID-19 Therapeutics Trial: Findings from a Multi-Center Investigation

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BACKGROUND

Early in the pandemic, there were **NO EVIDENCE-BASED TREATMENTS** for SARS-CoV-2 and there was an **URGENT NEED TO IDENTIFY EFFECTIVE THERAPEUTICS**.

PUBLIC PARTICIPATION IN MEDICAL RESEARCH IS LOW, 10-20% in U.S. and a common reason why clinical trials are stopped.

Reasons for low enrollment are multifactorial:

- Limited perceived benefit
- Fear of adverse effects
- Physician influence
- Distrust

OBJECTIVES

Report qualitative patient-reported reasons for declining to enroll in a Sarilumab COVID-19 Therapeutics trial.

Identify common themes behind patient decision making.

Determine impact of availability of different treatments on enrollment rates.

METHODOLOGY

Observational study conducted in parallel to an open-label, pragmatic, RCT across 5 VA from April 10, 2020 to February 3, 2021.

Patients SARS-CoV-2 (PCR or Ag +) within 4 weeks of hospitalization for moderate to severe COVID-19.

Informed consent was most often performed virtually via VA-approved video-based platform and expected to take 20 minutes.

Patients not interested in enrolling were asked open-ended question about their reason(s). If unable to provide a reason, several categories were offered.

Enrollment rates by time period were analyzed.

PERIOD 1 (< 6/25/2020): BEFORE EVIDENCE-BASED TREATMENTS WERE AVAILABLE

PERIOD 2 (6/25/2020-8/26/2020): AFTER DEXAMETHASONE AND BEFORE TOCILIZUMAB WAS RECOMMENDED AGAINST

PERIOD 3 (8/27/2020-3/5/2021): UNTIL END OF STUDY PERIOD

Enrollment rates assessed using simple descriptive statistics and qualitative responses were analyzed using direct content analysis.

RESULTS

N=417 SARS-CoV-2 + PATIENTS WERE SCREENED

162 met eligibility criteria

- 102 (62.9%) declined participation
- 53 (32.7%) consented to enroll
- 7 unable to consent; excluded

Table 1: Patient reported reasons for non-enrollment

THEMES	EXAMPLES/PATIENT STATEMENTS
Perceived limited benefit/Distrust 	*Patient factors* - Didn't want to be a guinea pig **(n=1)** - Internet research and thinks it's just another thing we are trying that doesn't work based on what he read **(n=1)** - Patient does not believe in COVID and that it causes pneumonia and does not think it was cause for admission **(n=1)** - Don't want to risk getting worse **(n=1)** - Doesn't like needles **(n=1)** *External factors* - Risk of getting more medication **(n=2)** - Risks of study drug **(n=13)** - It is experimental and don't know if it works **(n=9)** -Been in too many research trials **(n=1)**
Competing priorities /External influences and stressors 	*Patient factors* - Worried about wife, who was admitted to hospital with COVID **(n=1)** - Brother died of COVID 2 weeks prior and too overwhelmed to participate **(n=1)** - A lot going on and very stressed and doesn't want another variable to that stress **(n=3)** - Already enrolled in two other trials **(n=1)**
Clinician/Relative recommendation 	*External factors* - Patient/MD satisfied with current treatment plan **(n=27)** - ID physician recommended not to participate **(n=1)** - Family member against patient's participation **(n=6)** - Doctor told him that he was doing better and he did not need to participate **(n=1)** - Daughter felt trial would be too much **(n=1)**
Comorbidities/ Concern about impact of study drug by treating physicians/ MD satisfied with current treatment plan 	*Patient factors* - Schizophrenia with history of psychiatric decompensations **(n=2)** - Recent aspiration pneumonia **(n=1)** - History of coccidioidomycosis **(n=1)** - History of psychosis **(n=3)** - Concern about kidney issues **(n=1)** - Advanced age **(n=2)** - Admitted for stroke **(n=1)** *External factors* - Per infectious diseases, patient has sepsis/open wound **(n=1)** - On medications for previous kidney transplant, physician determined not a good idea **(n=1)**

RESULTS

Impact on enrollment rates by treatment availability and study period

Period 1 (<dexamethasone) enrollment rate = 10/11 (91%)

Period 2 and 3 (after IL-6 receptor inhibition was recommended against) enrollment rate = 43/144 (30%), p-value <0.0001)

Table 2: Comparison of patients who opted to enroll versus declined to enroll

VARIABLE	SCREENED (N=417)	ELIGIBLE (N=155)	ENROLLED (%) (N=53)	DECLINED TO ENROLL (%) (N=102)	P-VALUE*
SITE					0.220
Site 1	11	10	4 (40%)	6 (60%)	
Site 2	13	8	8 (100%)	0	
Site 3	235	75	26 (35%)	49 (65%)	
Site 4	114	42	14 (33%)	28 (67%)	
SITE 5	44	20	1 (5%)	19 (95%)	
STUDY PERIOD					<0.0001
Period 1 Before Dexamethasone <6/25/2020		11	**10 (91%)**	1 (9%)	
Period 2 & 3 After IL-6 receptor inhibition recommended against 6/25/2020-3/5/2021		144	**43 (30%)**	101 (70%)	

CONCLUSIONS

INCREASING ENROLLMENT INTO COVID-19 THERAPEUTIC TRIALS IS HIGH PRIORITY.

Understanding the reason and attitudes behind declining to enroll may help investigators address them and increase enrollment and retention rates in the future.

SCAN ME

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