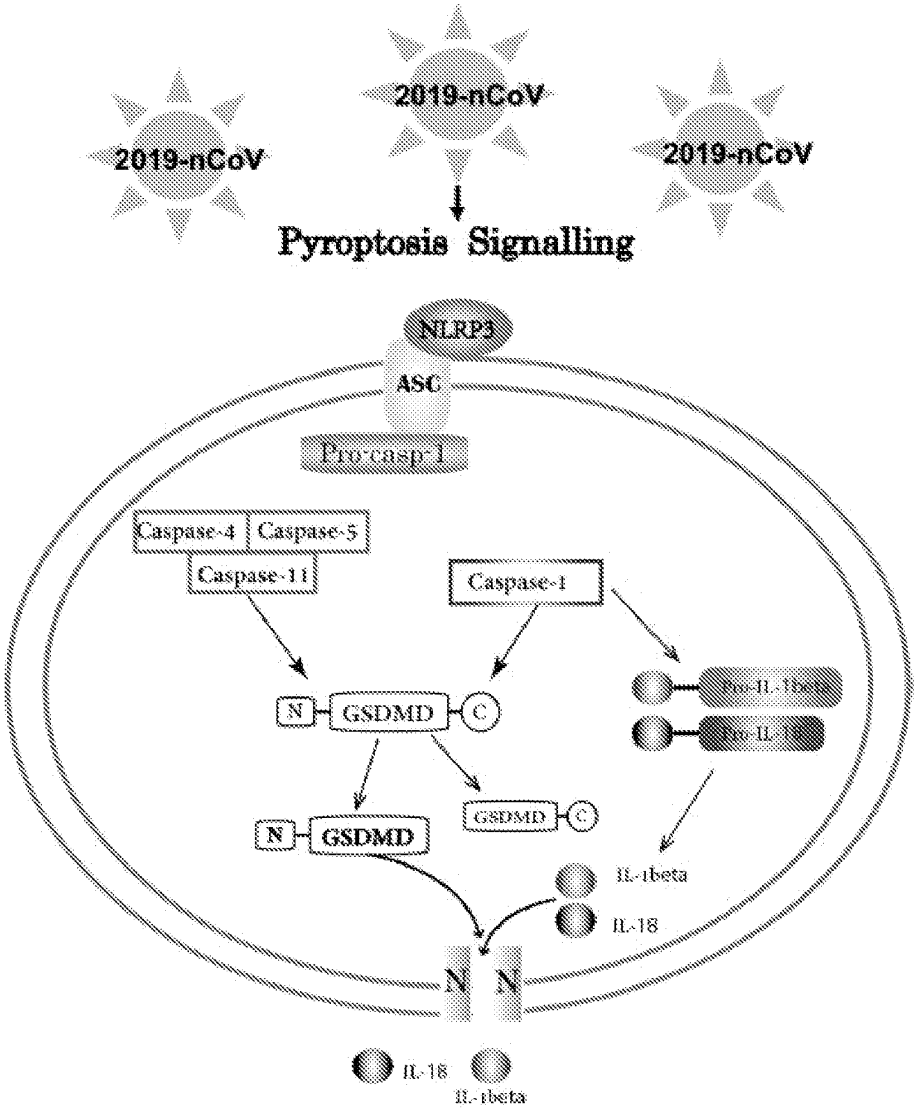
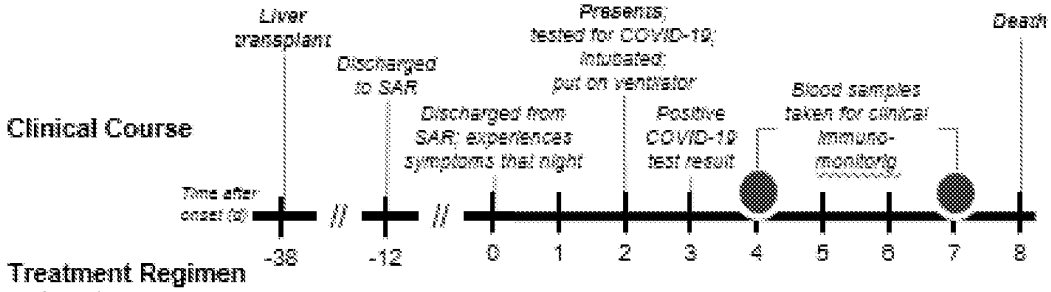

2019-nCoV
2019-nCoV
2019-nCoV
Pyroptosis Signalling
NLRP3
ASC
Pro-casp-1
Caspase-4
Caspase-5
Caspase-11
Caspase-1
N
GSDMD
C
Pro-IL-1beta
Pro-IL-18
N
GSDMD
GSDMD
C
IL-1beta
IL-18
N
N
IL-18
IL-1beta

FIG. 1




**Treatment Regimen**

| | |
|---|---|
| Steroids | ——— |
| Tacrolimus | ——— |
| MMF | ——— |
| Basiliximab | ... .... |
| Azithromycin and Hydroxychloroquine | ——— |

**Absolute Blood Counts** *(K/μL)*

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| WBC [4.0-10.8] | 2.2 | 3.8 | 6.7 | 9.0 | 5.6 | 6.9 | 7.6 | 4.8 | 5.9 | 7.6 |
| Neutrophils [1.7-6.1] | 1.6 | 2.6 | 5.9 | 7.4 | | 6.5 | 7.0 | 4.3 | 5.2 | 6.9 |
| Monocytes [0.1-1.3] | 0.2 | 0.2 | 0.1 | 0.3 | | 0.2 | 0.2 | 0.2 | 0.2 | 0.2 |
| Lymphocytes [0.8-4.9] | 0.2 | 0.3 | 0.3 | 0.2 | | 0.2 | 0.3 | 0.2 | 0.2 | 0.3 |

**Immunomonitoring**

| | | |
|---|---|---|
| CD3 *(/μL)* [518-2607] | 106 | 343 |
| CD20 *(/μL)* [27-443] | 60 | 160 |
| CD16+56+/CD3- *(% of total)* [2.3-24.7] | 14.3 | 11.5 |
| CD3/CD4 *(/μL)* [302-1779] | 56 | 172 |
| CD3/CD8 *(/μL)* [101-951] | 44 | 148 |
| Dendritic Cells *(% of total)* [0.04-0.5] | 0.01 | 0.0 |
| SARS-CoV-2 IgG | Neg | Neg |
| SARS-CoV-2 IgM | Neg | Neg |

**Inflammatory Markers**

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Lactate dehydrogenase *(u/liter)* [84-246] | | 411 | | 373 | | | | |
| CRP *(mg/L)* [0.0-3.0] | | 145 | 158 | 161 | 218 | 227 | 166 | 228 |
| Ferritin *(ng/mL)* [5.0-148.0] | 1,078 | 2,236 | 2,450 | 2,680 | 2,754 | 2,632 | 2,373 | 2,118 |
| D-dimer VTE *(mcg/mL FEU)* [<0.65] | | 11.8 | 5.6 | 4.8 | 5.6 | 5.1 | 7.0 | 16.4 |
| ESR *(mm/hr)* [0-22] | | 75 | 104 | 97 | 128 | 116 | 121 | 123 |

*Red shading denotes that value is outside reference range*

FIG. 2A

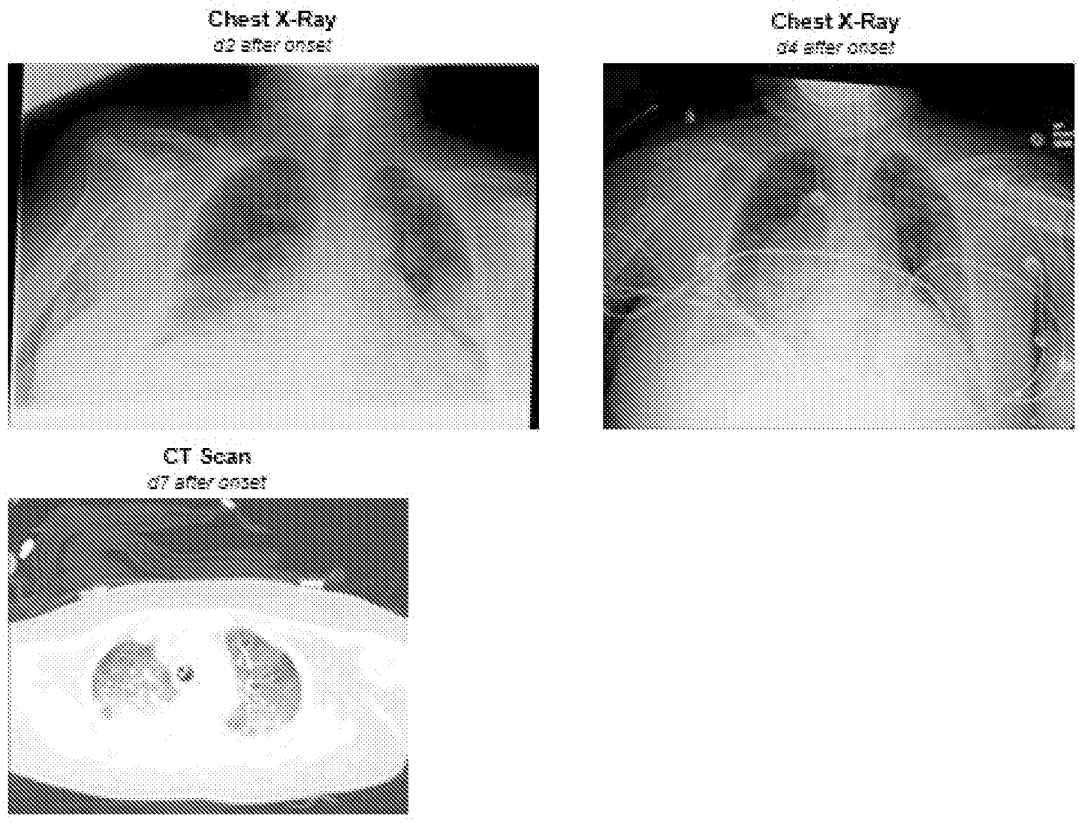
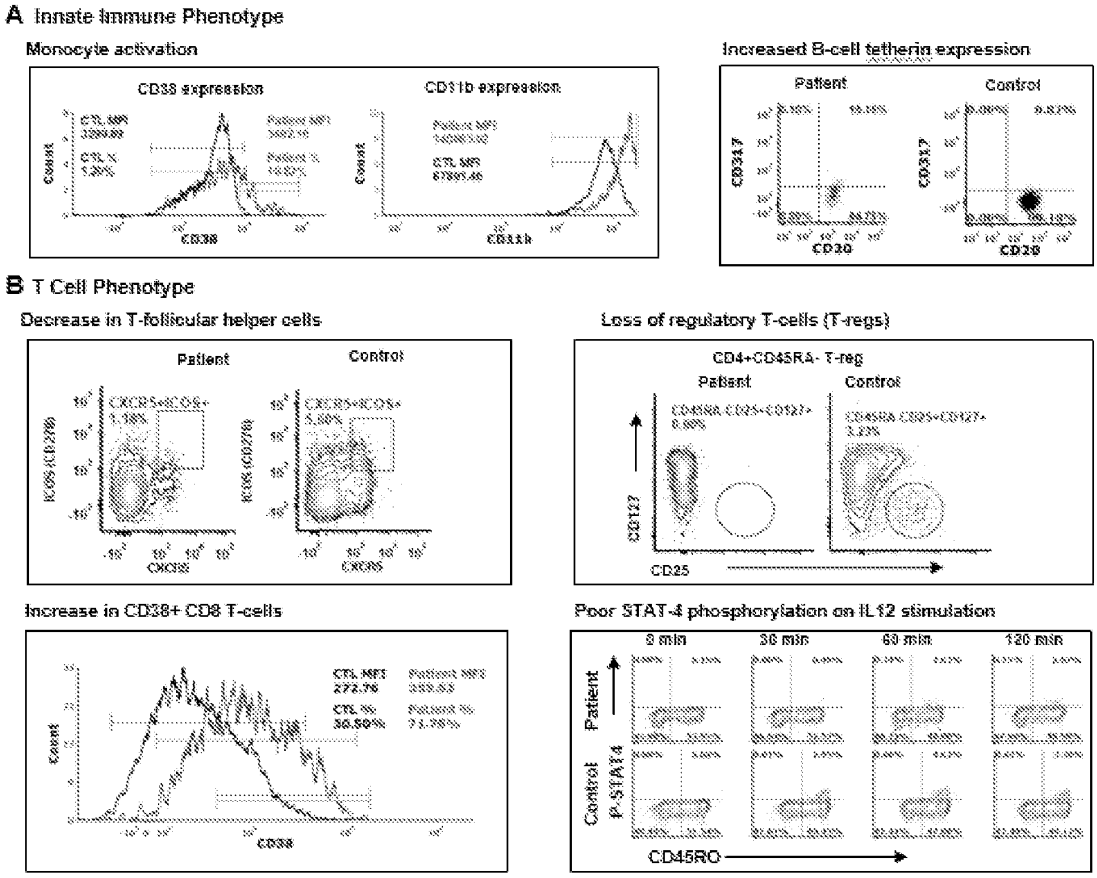
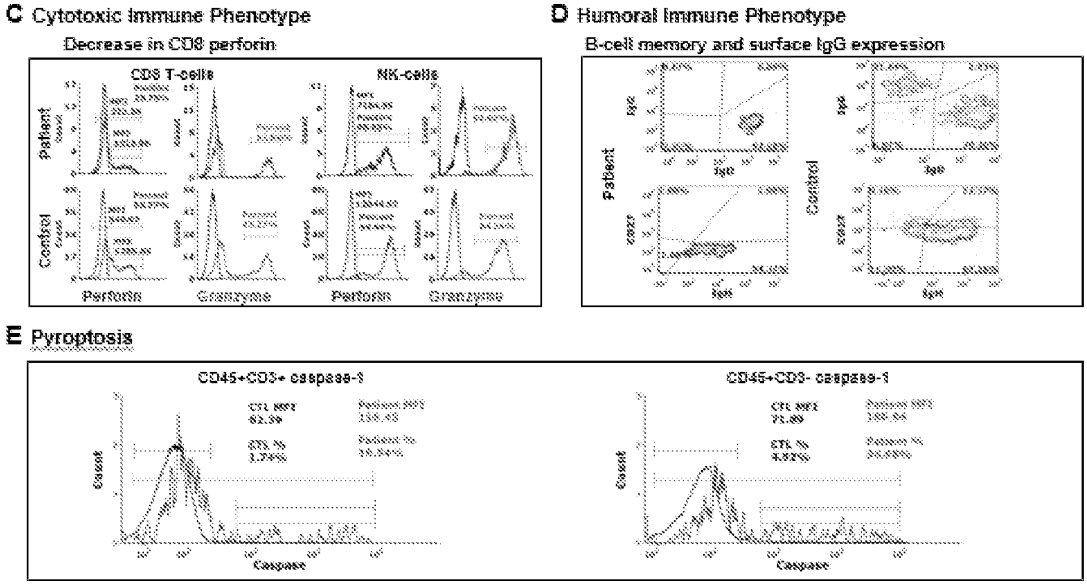

Chest X-Ray
d2 after onset
Chest X-Ray
d4 after onset
CT Scan
d7 after onset

FIG. 2B


A Innate Immune Phenotype
Monocyte activation
CD38 expression
CD11b expression
Count
CD38
CD11b
Increased B-cell tetherin expression
Patient
Control
CD317
CD20
B T Cell Phenotype
Decrease in T-follicular helper cells
Patient
Control
CXCR5+ICOS+
ICOS (CD278)
CXCR5
Loss of regulatory T-cells (T-regs)
CD4+CD45RA- T-reg
Patient
Control
CD127
CD25
Increase in CD38+ CD8 T-cells
Count
CD38
Poor STAT-4 phosphorylation on IL12 stimulation
0 min
30 min
60 min
120 min
Patient
Control
p-STAT4
CD45RO

FIGS. 3A-3B


C Cytotoxic Immune Phenotype
Decrease in CD8 perforin
CD8 T-cells
NK-cells
Patient
Control
Perforin
Granzyme
Perforin
Granzyme
D Humoral Immune Phenotype
B-cell memory and surface IgG expression
Patient
Control
IgG
IgD
E Pyroptosis
CD45+CD3+ caspase-1
CD45+CD3- caspase-1
Count
Caspase

FIGS. 3C-3E

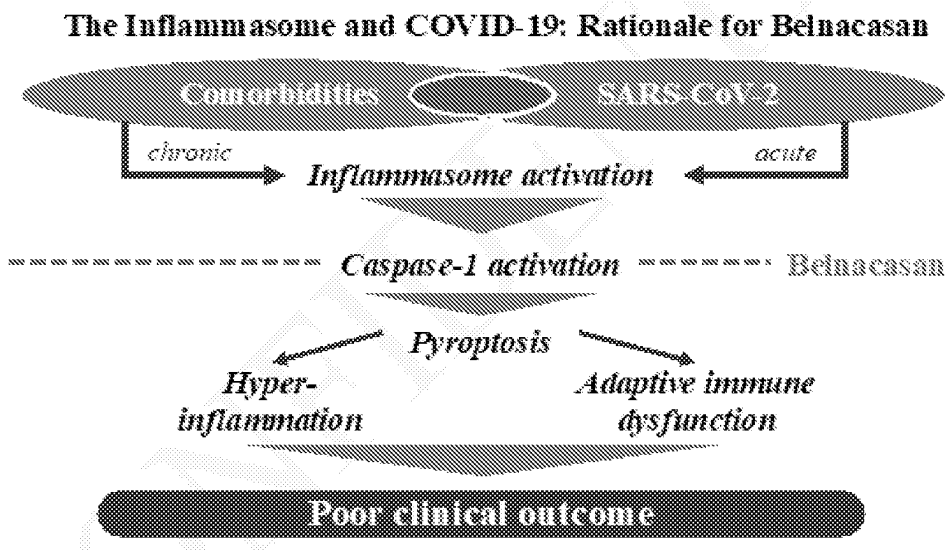

The Inflammasome and COVID-19: Rationale for Belnacasan
Comorbidities
SARS-CoV-2
chronic
acute
Inflammasome activation
Caspase-1 activation
Belnacasan
Pyroptosis
Hyper-inflammation
Adaptive immune dysfunction
Poor clinical outcome

FIG. 4

# Subject Diary – Overview of Study Events

| | Days | | | | | | |
|---|---|---|---|---|---|---|---|
| **Week 1** | 1 | 2 | 3 | 4 | 5 | 6 | 7 |
| **Week 2** | 8 | 9 | 10 | 11 | 12 | 13 | 14 |
| **Week 3** | 15 | 16 | 17 | 18 | 19 | 20 | 21 |
| **Week 4** | 22 | 23 | 24 | 25 | 26 | 27 | 28 |
| **Week 5** | 29 | 30 | 31 | 32 | 33 | 34 | 35 |
| **Week 6** | 36 | 37 | 38 | 39 | 40 | 41 | 42 |
| **Week 7** | 43 | 44 | 45 | 46 | 47 | 48 | 49 |
| **Week 8** | 50 | 51 | 52 | 53 | 54 | 55 | 56 |
| **Week 9** | 57 | 58 | 59 | 60 | 61 | 62 | 63 |

*Legend*

***Days 1-28**: On every day take study drug three times; take your temperature two times; log your general impressions and symptoms once; and engage with Telemetry Care Team*

***Days 1, 4, 10, 42, 60**: Receive phone calls from Study Team*

***Days 7, 14, 21, 28**: Visit Study Center in person*

***Days 7, 14, 21, 28**: Give Study Team last 7 days of Diary pages*

FIG. 5A

# Subject Diary – Sample Daily Log – Page 1

Date: _____ Subject Number: _____

## Common COVID-19 Symptoms

Time you are filling this out today: _____

What was the SEVERITY of these symptoms at their worst in the last 24 hours? Place an X

| | None | Mild | Moderate | Severe |
|---|---|---|---|---|
| Stuffy or runny nose | | | | |
| Sore throat | | | | |
| Shortness of breath at rest | | | | |
| Shortness of breath with exertion | | | | |
| Cough | | | | |
| Low energy or tiredness | | | | |
| Muscle or body aches | | | | |
| Headache | | | | |
| Chills or shivering | | | | |
| Feeling hot or feverish | | | | |
| Nausea | | | | |

In the last 24 hours, how often did you have these ISSUES? Place an X

| | 0 times | 1-2 times | 3-4 times | 5 or more times |
|---|---|---|---|---|
| Vomit (throw up) | | | | |
| Diarrhea (loose or watery stools) | | | | |

In the last 24 hours, how would you rate your SENSES? Place an X

| | SAME as usual | LESS than usual | I have NO sense |
|---|---|---|---|
| Sense of smell | | | |
| Sense of taste | | | |

Over the last 24 hours, if there were any other symptoms beyond the ones listed above that you experienced, please describe them here:

FIG. 5B

# Subject Diary – Sample Daily Log – Page 2

Date: _____ Subject Number: _____

## Medication

Place an X to note that you have taken 3 tablets of the STUDY DRUG and note the time you took them

| Morning | Mid-Day | Evening |
|---|---|---|
| | | |
| am | _m | pm |

Note any OTHER medications, vitamins, or supplements you took, other than those you told us at enrollment that you take on a regular basis; use the back of this page if you need more space

| Name | Dose | Time |
|---|---|---|
| | | |
| | | |
| | | |
| | | |

## Temperature

Note your temperature from the thermometer and note the time you took the measurement

| Morning | Evening |
|---|---|
| °F | °F |
| am | pm |

## Global Impression

Time you are filling this out today: _____

Place an X

| | None | Mild | Moderate | Severe |
|---|---|---|---|---|
| In the past 24 hours, what was the severity of your OVERALL COVID-19-related symptoms at their worst? | | | | |

Place an X

| | Yes | No |
|---|---|---|
| In the past 24 hours, have you returned to your usual HEALTH (before your COVID-19 illness)? | | |
| In the past 24 hours, have you returned to your usual ACTIVITIES (before your COVID-19 illness)? | | |

FIG. 5C