Abstract number: **11125**

Category: Track B: Clinical science, testing (RT-PCR and serologic) and diagnoses, natural history, clinical care, ARDS care, therapeutics

Sofosbuvir and daclatasvir as a potential candidate for moderate or severe COVID-19 treatment, results from a randomised controlled trial

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Background: Sofosbuvir (SOF) and daclatasvir (DCV) show predicted activity against COVID-19 from in silico studies, while DCV has high predicted lung penetration. SOF shows in vitro anti-viral activity against several different viral infections (e.g. Zika, Yellow Fever, Dengue, Chikungunya). This trial evaluated the efficacy of SOF/DCV 400/60mg once daily versus standard care for patients with moderate or severe COVID-19 infection.

Methods: This open-label, multicenter, randomised trial included adults admitted to four Iranian University hospitals. Patients were randomised to standard care (hydroxychloroquine ± lopinavir/ritonavir) either with or without SOF/DCV. The primary efficacy endpoint was clinical recovery within 14 days of starting treatment. Outcomes were analysed by modified intention to treat population, excluding patients who failed major inclusion/exclusion criteria. This study is registered with the Iranian Clinical Trials Registry, IRCT202001238046294N2.

Results: From March-April 2020 four patients failing major inclusion/exclusion criteria were excluded. 66 patients were recruited; 33 to SOF/DCV group and 33 to control. Baseline characteristics were similar across treatment groups. After 14 days of randomised treatment, 29 patients (88%) in the SOF/DCV group achieved clinical recovery versus 22 patients (67%) in the control group (p=0.076). Duration of hospital stay was shorter in the SOF/DCV group versus control (6 [IQR 4-8] vs 8 [IQR 5-13], p=0.029). Using cumulative incidence analysis with competing-risks, median time to hospital discharge was shorter in the SOF/DCV group (6 vs 11 days; Gray's p=0.041). Three patients died in the SOF/DCV group and five in the control group. No serious adverse events were reported.

	SOF/DCV (n=33)	Control (n=33)	p-value
Age, median (IQR)	58 (38-65)	62 (49-72)	0.211
Male, n(%)	20 (61%)	14 (42%)	0.218
Diabetes, n(%)	17 (52%)	11 (33%)	0.213
LPV/r, n(%)	11 (33%)	21 (64%)	0.026
Clinical recovery ≤14 days, n(%)	29 (88%)	22 (67%)	0.076
Duration of hospitalisation (days), median (IQR)	6 (4-8)	8 (5-13)	0.029
Died, n(%)	3 (9%)	5 (15%)	0.708
Time to hospital discharge (days), median (IQR)	6 (4-10)	11 (6-17)	0.041

Conclusions: SOF/DCV with standard care was superior to standard care alone in increasing 14-day clinical recovery rates and reducing the median duration of hospital stay. Larger confirmatory, well controlled randomised trials are required to support worldwide regulatory approval of SOF/DCV to treat COVID-19 infection.

Abstract number: **11803**

Category: Track B: Clinical science, testing (RT-PCR and serologic) and diagnoses, natural history, clinical care, ARDS care, therapeutics

Baseline characteristics associated with clinical improvement and mortality in hospitalized patients with severe COVID-19 treated with remdesivir

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Background: Remdesivir (RDV), a nucleotide analogue prodrug that inhibits viral RNA polymerases, has demonstrated potent in vitro and in vivo activity against SARS-CoV-2 and favorable clinical efficacy and good tolerability in patients with COVID-19 treated through compassionate use. We conducted a randomized, open-label, phase 3 trial of RDV in patients with severe COVID-19. Here we report baseline characteristics associated with clinical improvement and mortality.

Methods: We enrolled hospitalized patients with confirmed SARS-CoV-2 infection, oxygen saturation of ≤94% on room air, and radiological evidence of pneumonia. Patients were randomized 1:1 to receive either 5 or 10 days of intravenous RDV once daily. Baseline demographic and disease characteristics associated with clinical improvement in oxygen support (≥2-point improvement on a 7-category ordinal scale ranging from discharge to death) and all-cause mortality were evaluated using Cox proportional hazards methods.

Results: Of 397 patients treated with RDV, 168 (42%) were ≥65y, 144 (36%) female, 276 (70%) white, 45 (11%) Asian, and 44 (11%) Black. 122 patients (31%) were on high-grade oxygen support (including invasive mechanical ventilation, non-invasive positive pressure ventilation, or high-flow nasal cannula) at baseline. Through median follow-up of 10d (range 1-33d), 256 patients had ≥2-point improvement and 44 had died. In a multivariable model, lower grade respiratory support (low-flow oxygen or room air), age <65y, Black race, ex-Italy regions, and no concomitant biologic medication use were significantly positively associated with ≥2-point clinical improvement (Table). Similarly, high-grade oxygen support, history of COPD, and age ≥65y were significantly associated with increased risk of all-cause mortality in multivariable analyses.

Table. Baseline characteristics associated with clinical outcomes in severe COVID-19 patients treated with remdesivir (based on multivariate analyses)

Risk factor: Subgroups	Hazard ratio (95% CI)[a]	p-value
Time to clinical improvement (≥2-point improvement)		
Baseline oxygen support status: Low Flow Oxygen or Room Air vs IMV or HFNC/NIPPV	2.16 (1.50, 3.10)[b]	<0.0001
Age: <65y vs ≥65y	1.93 (1.46, 2.55)[b]	<0.0001
Race: Black vs Asian	3.80 (2.28, 6.35)[b]	<0.0001
Race: White vs Asian	2.45 (1.60, 3.76)[b]	<0.0001
Region: Ex-Italy vs Italy	1.59 (1.07, 2.37)[b]	0.0225
Concomitant biologic medication use[c]: No vs Yes	2. 70 (1.49, 4.88)[b]	0.0010
Time to All-cause Mortality		
Baseline oxygen support status: IMV or HFNC/NIPPV vs Low Flow Oxygen or Room Air	5.47 (2.74, 10.90)[d]	<0.0001
COPD: Yes vs No	3.41 (1.30, 8.94)[d]	0.0125
Age: ≥65y vs <65y	2.30 (1.18, 4.47)[d]	0.0139

CI, confidence interval; COPD, chronic obstructive pulmonary disease; HFNC/NIPPV, high flow nasal cannula oxygen/non-invasive positive pressure ventilation; IMV, invasive mechanical ventilation.

[a] 1.00 (ref)

[b] Cause-specific hazard ratio, its 95% CI, and p-value were based on a competing risk analysis, with death as the competing risk and including RDV treatment arm and all other selected risk factors as covariates

[c] Includes concomitant biologic agents for COVID-19, taken ≥1 days prior to or at any time during RDV

[d] Hazard ratio, its 95% CI, and p-value were based on Cox proportional-hazards models, including RDV treatment arm and all other selected risk factors as covariates

Conclusions: In severe COVID-19 patients who received RDV, baseline oxygen support status, age <65y, Black race, ex-Italy regions, and no concomitant biologic medication were associated with higher rates of clinical improvement. Baseline oxygen support status, medical history of COPD, and age ≥65y were associated with all-cause mortality.

Abstract number: **11384**

Category: Track A: Basic science, pathogenesis, virology, immunology, inflammation

In-utero mother-to-child SARS-CoV-2 transmission - viral detection and fetal immune response

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Background: Pregnancy is known to increase the risk of severe illnesses in response to viral infections. Therefore, the impact of SARS-CoV-2 infection during gestational ages might be detrimental and the potential vertical transmission should be thoroughly studied. Herein, we investigated whether vertical transmission is possible and whether this results in fetal involvement. Additionally, we analyzed the role of the antibody and the inflammatory responses in placenta and plasma from SARS-CoV- 2-positive pregnant women and fetuses.

Methods: 31 SARS-CoV-2 pregnant women were enrolled. Real-time-PCR was performed to detect the virus on maternal and newborns' nasopharyngeal swabs, vaginal swabs, maternal and umbilical cord plasma, placenta and umbilical cord biopsies, amniotic fluids and milk. Maternal and umbilical cord plasma, and milk were tested for specific anti-SARS-CoV-2 antibodies. RNA expression quantification of genes involved in the inflammatory response was performed on four selected placentas. On maternal and umbilical cord plasma of the same subjects, secreted cytokines/chemokines were quantified.

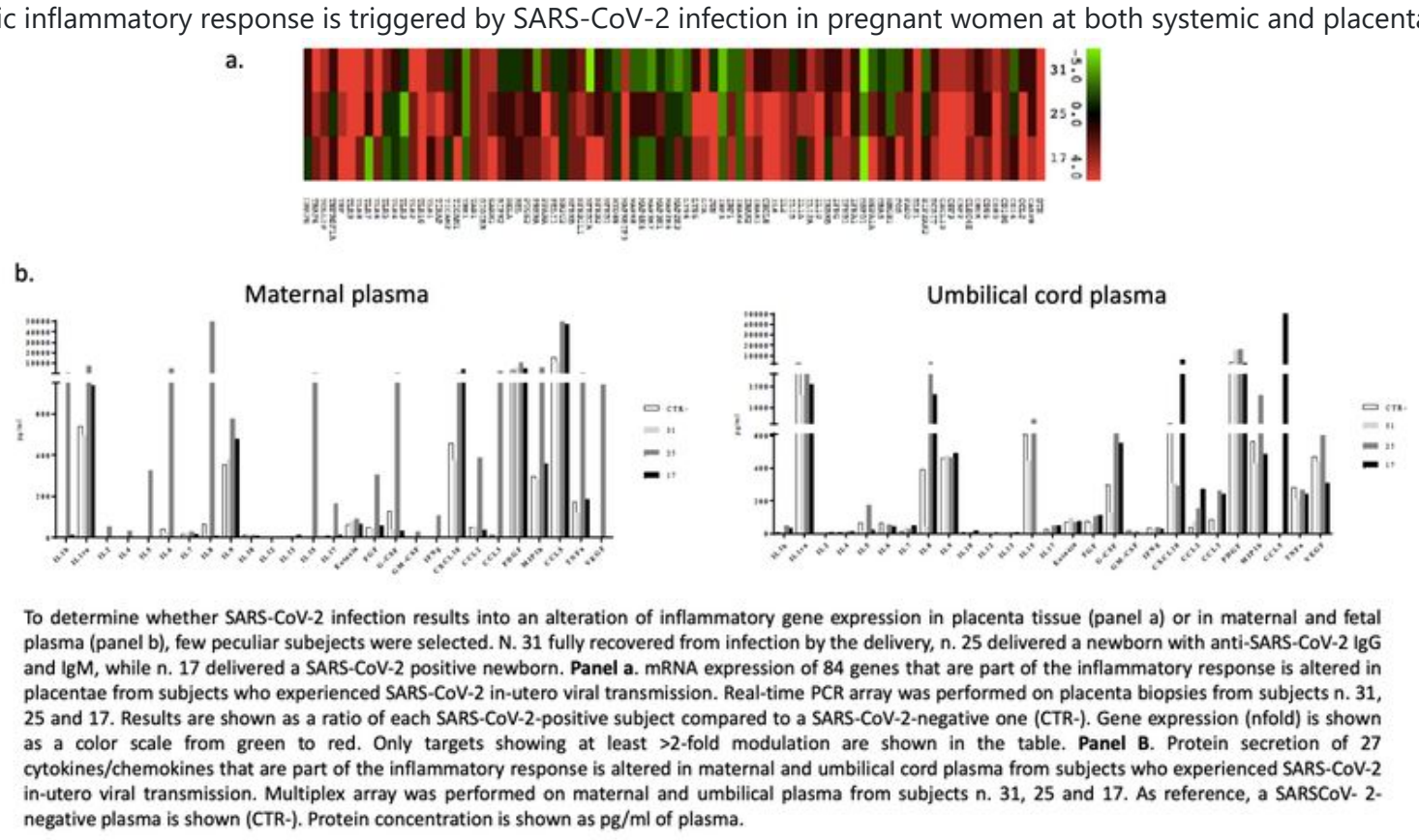
Results: SARS-CoV-2 is found in an at-term placenta and in the umbilical cord blood, in the vagina of a pregnant woman and in milk. Furthermore, we report the presence of specific anti-SARS-CoV-2 IgM and IgG antibodies in the umbilical cord blood of pregnant women, as well as in milk specimens.

Synoptic table of maternal and fetal SARS-CoV-2 virus and anti-SARS-CoV-2 antibody detection correlated to clinical data.

subject n.	clinical outcome	Δ T1-T0 (days)	maternal plasma			vaginal swab	Placenta	Umbilical cord plasma			umbilical cord	milk		
			virus	IgM	IgG	virus	virus	virus	IgM	IgG	virus	virus	IgM	IgG
1	SEVERE	2	-	-	-	-	-	-	-	-	-	+	+	-
2	MILD	1	-	-	-	-	-	N/A	N/A	N/A	-	-	-	-
3	MILD	1	-	-	-	-	-	-	-	-	-	-	-	N/A
4	SEVERE	2	+	-	+	-	-	-	-	-	-	-	-	-
5	MILD	7	-	-	-	-	-	-	-	-	-	N/A	N/A	N/A
6	MILD	1	-	+	+	-	-	-	-	-	-	-	N/A	-
7	MILD	12	-	+	+	-	-	-	-	-	-	-	-	-
8	SEVERE	6	-	+	+	-	-	-	-	-	-	N/A	N/A	N/A
9	MILD	1	N/A	N/A	N/A	-	-	-	-	-	-	-	-	-
10	MILD	1	-	-	-	-	-	-	-	-	-	-	-	-
11	MILD	5	-	-	-	-	-	-	-	-	-	-	-	-
12	MILD	4	-	-	+	-	-	-	-	-	N/A	N/A	N/A	N/A
13	MILD	3	-	-	+	-	-	-	-	+	-	-	-	-
14	MILD	3	-	-	+	-	-	-	-	+	N/A	N/A	N/A	N/A
15	MILD	4	-	-	-	-	-	-	-	-	N/A	N/A	N/A	N/A
16	MILD	2	-	-	-	-	-	-	-	-	N/A	N/A	N/A	N/A
17	SEVERE	6	+	+	+	+	+	+	-	+	N/A	N/A	N/A	N/A
18	MILD	2	-	-	+	-	-	-	-	+	N/A	N/A	N/A	N/A
19	MILD	9	-	+	+	-	-	-	-	+	N/A	N/A	N/A	N/A
20	MILD	3	-	+	+	-	-	-	-	+	N/A	N/A	N/A	N/A
21	MILD	13	-	-	+	-	-	-	-	-	N/A	N/A	N/A	N/A
22	MILD	10	-	-	-	-	-	-	-	-	N/A	N/A	N/A	N/A
23	MILD	9	-	-	-	-	-	-	-	-	N/A	N/A	N/A	N/A
24	MILD	12	-	-	-	-	-	-	-	-	N/A	N/A	N/A	N/A
25	MILD	17	-	+	+	-	-	-	+	+	N/A	N/A	N/A	N/A
26	MILD	13	-	+	+	-	-	-	-	+	N/A	N/A	N/A	N/A
27	MILD	1	-	-	+	-	-	-	-	+	N/A	N/A	N/A	N/A
28	MILD	3	-	+	+	-	-	-	-	+	N/A	N/A	N/A	N/A
29	MILD	2	-	-	+	-	-	-	-	-	N/A	-	-	-
30	MILD	1	-	-	+	-	-	-	-	+	N/A	N/A	N/A	N/A
31	recovered	N/A	-	-	+	N/A	-	-	-	+	N/A	N/A	N/A	N/A

N/A = not available

Finally, a specific inflammatory response is triggered by SARS-CoV-2 infection in pregnant women at both systemic and placental level, and in umbilical-cord blood plasma.



To determine whether SARS-CoV-2 infection results into an alteration of inflammatory gene expression in placenta tissue (panel a) or in maternal and fetal plasma (panel b), few peculiar subejects were selected. N. 31 fully recovered from infection by the delivery, n. 25 delivered a newborn with anti-SARS-CoV-2 IgG and IgM, while n. 17 delivered a SARS-CoV-2 positive newborn. **Panel a**. mRNA expression of 84 genes that are part of the inflammatory response is altered in placentae from subjects who experienced SARS-CoV-2 in-utero viral transmission. Real-time PCR array was performed on placenta biopsies from subjects n. 31, 25 and 17. Results are shown as a ratio of each SARS-CoV-2-positive subject compared to a SARS-CoV-2-negative one (CTR-). Gene expression (nfold) is shown as a color scale from green to red. Only targets showing at least >2-fold modulation are shown in the table. **Panel B**. Protein secretion of 27 cytokines/chemokines that are part of the inflammatory response is altered in maternal and umbilical cord plasma from subjects who experienced SARS-CoV-2 in-utero viral transmission. Multiplex array was performed on maternal and umbilical plasma from subjects n. 31, 25 and 17. As reference, a SARSCoV- 2-negative plasma is shown (CTR-). Protein concentration is shown as pg/ml of plasma.

Conclusions: Data strongly support that in-utero vertical transmission is possible in SARS-CoV-2 positive women. This is essential for defining proper obstetric management of COVID-19 pregnant women.

Abstract number: **11343**

Category: Track C: Epidemiology, transmission dynamics, prevention, vaccines

High prevalence of asymptomatic SARS-CoV-2 infection found in a Latinx population in San Francisco in a mass testing campaign

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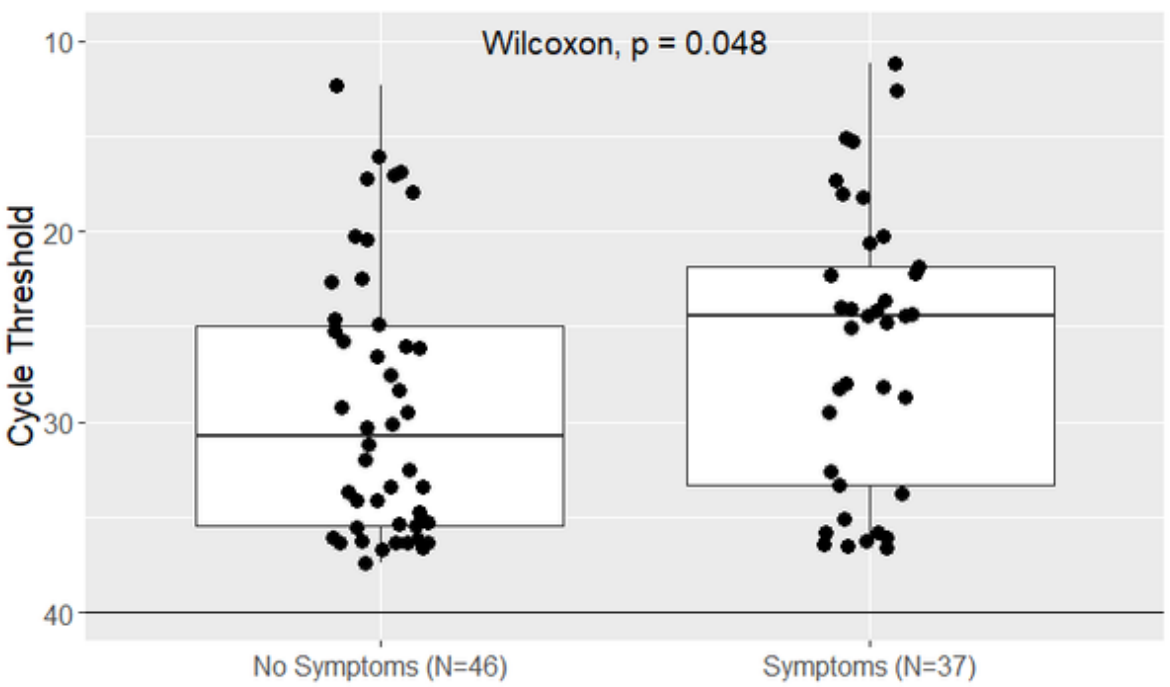
Background: We performed one of the first SARS-CoV-2 mass-testing campaigns in the U.S. in a predominantly Latinx San Francisco community to determine prevalence and characteristics of active infection.

Methods: Six weeks into San Francisco's shelter-in-place, we offered community-based SARS-CoV-2 testing, regardless of symptoms, to our study population of all residents (>4 years) of San Francisco census tract 022901 (5174 residents, 58% Latinx) and individuals working in the tract. The campaign was advertised door-to-door and conducted in partnership with the Latino Task Force-COVID-19. We collected demographic, socioeconomic and clinical information and performed oropharyngeal/mid-turbinate swabs for reverse transcription-PCR for SARS-CoV-2. We determined point prevalence of SARS-CoV-2 infection among residents adjusting for testing participation and test characteristics, determined risk factors for PCR-positivity and compared SARS-CoV-2 levels in PCR+ persons with and without symptoms.

Results: We tested 3,871 people over 4 days (2,598 tract residents; 450 tract workers; 823 neighboring-tract residents), of whom 41% were Latinx, 41% White, 9% Asian/Pacific Islander, 2% Black. Overall, 83/3,871 (2.1%) tested PCR+: 95% (79/83) were Latinx; median age was 38; 76% were male. Estimated point prevalence was 5.8% (95%CI: 2.6-9.1) among Latinx vs. 0.03% (95%CI: 0-0.3%) among non-Latinx tract residents. Comparing PCR-positive vs. negative people: 91% vs. 55% reported inability to shelter-in-place and maintain income; 64% vs. 27% ($p<0.001$) worked frontline-service jobs; 88% vs. 38% ($p<0.001$) had household income <$50,000/year; and 86% vs. 63% ($p=0.002$) had >3 persons/home. Among PCR-positive individuals, 55% were asymptomatic at time of testing. Though median levels of virus were higher among symptomatic persons, a large proportion of asymptomatic persons had high levels of virus (Figure).



Conclusions: Low-income, Latinx people unable to shelter-in-place had a high prevalence of active SARS-CoV-2 infection six-weeks into San Francisco's shelter-in-place. Symptom-based testing would have missed the majority of infections. Low-barrier testing and economic support programs for most-affected communities are needed.