Message

From: Rob.Orford@gov.wales [Rob.Orford@gov.wales]
Sent: 26/02/2020 15:29:17
To: NR gov.wales]
CC: Chrishan.Kamalan@gov.wales; Andrew Jones (Public Health Wales) [andrew.jones10@wales.nhs.uk]; Gill Richardson (Public Health Wales - No. 2 Capital Quarter) [gill.richardson2@wales.nhs.uk]
Subject: FW: Clinical trials of Remdesivir for treatment of COVID 19

Thanks NR that would be good thank you.

Including colleagues from PHW in copy

From: NR (HSS - DHP - R&D) NR @gov.wales>
Sent: 26 February 2020 15:04
To: Orford, Rob (HSS - Primary Care & Health Science) <Rob.Orford@gov.wales>; Walshe, Kieran (HSS - DHP - R&D) <Kieran.Walshe@gov.wales>
Cc: Atherton, Frank (HSS - Chief Medical Officer) <Frank.Atherton@gov.wales>
Subject: Re: Clinical trials of Remdesivir for treatment of COVID 19

Hi
We've already made arrangements to fast track approvals(ethics etc) for these studies alongside uk counterparts.

I'm not aware of any trials coming soon but will get in touch with nhs England today to find out more ?

Will keep you posted.

NR

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From: Orford, Rob (HSS - Primary Care & Health Science) <Rob.Orford@gov.wales>
Sent: Wednesday, February 26, 2020 2:17 pm
To: Walshe, Kieran (HSS - DHP - R&D)
Cc: NR HSS - DHP - R&D); Atherton, Frank (HSS - Chief Medical Officer)
Subject: FW: Clinical trials of Remdesivir for treatment of COVID 19

Hi Kieran
Are you linked in to any of the NHS England discussions about COVID-19 research trials?
Best wishes
Rob

From: Goulding, David (HSS - DHP Public Health) <David.Goulding@gov.wales>
Sent: 26 February 2020 14:09
To: Orford, Rob (HSS - Primary Care & Health Science) <Rob.Orford@gov.wales>; Gill Richardson (Public Health Wales - No. 2 Capital Quarter) <Gill.Richardson2@wales.nhs.uk>; Kamalan, Chrishan (HSS - DHP Public Health) <Chrishan.Kamalan@gov.wales>; NR (HSS - DHP Public Health) NR @gov.wales>; Lyons, Marion (DHSS - DHP - Public Health) <Marion.Lyons@gov.wales>; NR HSS - DHP Public Health) <NR @gov.wales>; Payne, Heather (HSS-DPH-Population Healthcare) <Heather.Payne@gov.wales>; Atherton,

Frank (HSS - Chief Medical Officer) <Frank.Atherton@gov.wales>
Subject: Re: Clinical trials of Remdesivir for treatment of COVID 19

I doubt we are involved accept maybe via SPI that Marion joined for us. The other way is the CMOs meetings that may receive updates? Copied Frank in

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From: Orford, Rob (HSS - Primary Care & Health Science) <Rob.Orford@gov.wales>
Sent: Wednesday, February 26, 2020 1:38:14 PM
To: Gill Richardson (Public Health Wales - No. 2 Capital Quarter) <Gill.Richardson2@wales.nhs.uk>; Kamalan, Chrishan (HSS - DHP Public Health) <Chrishan.Kamalan@gov.wales>; NR (HSS - DHP Public Health) <NR@gov.wales>; Lyons, Marion (DHSS - DHP - Public Health) <Marion.Lyons@gov.wales>; NR (HSS - DHP Public Health) NR@gov.wales>; Goulding, David (HSS - DHP Public Health) <David.Goulding@gov.wales>; Payne, Heather (HSS-DPH-Population Healthcare) <Heather.Payne@gov.wales>
Subject: RE: Clinical trials of Remdesivir for treatment of COVID 19

Thanks Gill, I am aware that NHS England are purposefully pursuing research trials for COVID interventions – are we linked into the work at a national level? Also will +ve patients in Wales receive Remdesivir?

Best wishes
Rob

From: Gill Richardson (Public Health Wales - No. 2 Capital Quarter) <Gill.Richardson2@wales.nhs.uk>
Sent: 26 February 2020 12:46
To: Kamalan, Chrishan (HSS - DHP Public Health) <Chrishan.Kamalan@gov.wales>; NR (HSS - DHP Public Health) NR@gov.wales>; Lyons, Marion (DHSS - DHP - Public Health) <Marion.Lyons@gov.wales>; NR NR (HSS - DHP Public Health) NR@gov.wales>; Goulding, David (HSS - DHP Public Health) <David.Goulding@gov.wales>; Orford, Rob (HSS - Primary Care & Health Science) <Rob.Orford@gov.wales>
Subject: FW: Clinical trials of Remdesivir for treatment of COVID 19

For info

PD
Dr Gillian Richardson, MBChB, MRCGP, MPH, FFPH, MRCPHMI, MInstLM

Dr Gill Richardson
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Dr Gill Richardson
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Rydym yn croesawu gohebiaeth yn Gymraeg. Byddwn yn ymateb yn Gymraeg heb oedi.
We welcome correspondence in Welsh. We will respond in Welsh without delay.

Arhoswch! Meddyliwch am yr amgylchedd - oes angen argraffu'r ebost yma?
Please consider the environment - do you really need to print this email?

From: John Watkins (Public Health Wales) <John.Watkins@wales.nhs.uk>
Sent: 26 February 2020 12:03
To: Quentin Sandifer (Public Health Wales - No. 2 Capital Quarter) <Quentin.Sandifer@wales.nhs.uk>; Tracey Cooper (Public Health Wales - No. 2 Capital Quarter) <Tracey.Cooper3@wales.nhs.uk>; NR (Public Health Wales - No. 2 Capital Quarter) NR @wales.nhs.uk>; NR (Public Health Wales - Matrix House) NR @wales.nhs.uk>; NR (Public Health Wales - No. 2 Capital Quarter) NR @wales.nhs.uk>; NR (Public Health Wales - No. 2 Capital Quarter) NR @wales.nhs.uk>; NR (Public Health Wales - No. 2 Capital Quarter) NR @wales.nhs.uk>; NR (Public Health Wales - Matrix House) NR @wales.nhs.uk>; NR Public Health Wales - No. 2 Capital Quarter) < NR @wales.nhs.uk>; NR (Public Health Wales) NR @wales.nhs.uk>; NR (Public Health Wales - No. 2 Capital Quarter)

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Cc: NR (Public Health Wales - No. 2 Capital Quarter) NR @wales.nhs.uk>
Subject: Clinical trials of Remdesivir for treatment of COVID 19

Hi

Just thought I would give you an update on a fast moving story. Remdesivir is an antiviral drug produced by Gilead Pharmaceuticals, initially for the treatment of Ebola, among other viruses. However, the clinical trials showed that it was ineffective against Ebola but has been subsequently shown to be effective against coronaviruses, notably SARS in animal trials. The company stockpiled Remdesivir in anticipation that it would be effective against Ebola and this stockpile is now available for clinical trials and humanitarian use against COVID 19.

The clinical trials for Ebola showed the drug is safe and last month it was used on a patient in the US who had developed respiratory symptoms on return from China and tested positive for COVID 19. It is reported he made a dramatic improvement within 24 hours. On the basis of this two clinical trials have been started in China, one in patients with severe symptoms and the other in those with milder disease. These trials started a couple of weeks ago and results are expected in early April. The third trial, which is being led by NHH in the USA and based out of Nebraska, see link https://www.nih.gov/news-events/news-releases/nih-clinical-trial-remdesivir-treat-covid-19-begins, will recruit patients globally.

For more info on Remdesivir, please see https://en.wikipedia.org/wiki/Remdesivir .

Watch this space.

Best wishes

John

Professor John Watkins
Consultant Epidemiologist

[See recipients listed above]

[See recipients listed above]

All

Further to my previous E mail and Nigel's response below, some further information;

The ability of viruses such as Influenza to infect humans is dependent, in their case, on the presence and distribution of binding sites for the neuraminidase, sialic acid, expressed on the surface of cells.

In the case of human influenza viruses the neuraminidase binds to Sialic Acid receptors Type A, found in the upper respiratory tract, humans have Type B receptors in the lungs. In contrast Birds have Type B receptors at both these sites. This distribution of receptors explains why Avian Influenza does not transmit easily person to person but is lethal if inhaled deep into the lungs where viruses can bind and gain entry into cells.

When we take this knowledge into SARS coronaviruses, it is found that they, in common with many other coronaviruses (and probably this Wuhan strain), bind to Angiotensin Converting Enzyme 2, ACE2, receptors. These ACE2 receptors are

found in the lungs, gut and on arterial and venous cell surfaces, see Hamming, Timmens, et al; https://doi.org/10.1002/path.1570

.....oral and nasal mucosa, nasopharynx, lung, stomach, small intestine, colon, skin, lymph nodes, thymus, bone marrow, spleen, liver, kidney, and brain). The most remarkable finding was the surface expression of ACE2 protein on lung alveolar epithelial cells and enterocytes of the small intestine. Furthermore, ACE2 was present in arterial and venous endothelial cells and arterial smooth muscle cells in all organs studied.

This distribution would explain the widespread pathogenesis of these novel coronaviruses and also why the viral pneumonial lung damage increases as viral load declines. This pathogenesis, probably explained by the age based innate cytokine response that I highlighted in my previous Email.

The presence of ACE2 receptors in the nasal and oropharynx in humans would aid person to person spread but maybe ACE2 binding to coronaviruses are not as strong, or the receptors as plentiful, as Sialic Acid binding sites for the influenza virus, making it less easily spread by this route, with viral capture occurring in the gut and lung. In the case of SARS one of the epidemiological routes of transmission was surface contamination in the corridor of an Hong Kong hotel by an infected doctor who had contracted the disease, became ill in the hotel and vomited.

As an additional bit of info, which may be relevant, or not, coronaviruses also bind to sialic acid binding sites on cell walls.

Best wishes

John

From **NR**

Thanks John.

As it happens I had already seen it when I looked for what we know about this disease.

Also found that this paper exists – have not seen the full paper yet but suggests this could relatively easily mutate into a more infectious form for humans. I would how labile the genome is.
https://www.sciencedaily.com/releases/2020/01/200131114755.htm

If you get any more info I will be interested.

NR

[See recipients listed above]

[See recipients listed above]

[See recipients listed above]

Dear All

Just in case you missed it, please find attached a paper from Lancet looking at the clinical features of coronavirus cases.

In addition, the interesting thing about this particular epidemic, at present, is, in common with SARS and MERS-CoV, the low number of children reported to be infected, with deaths occurring in older adults. Children are classically the 'super spreaders' of these viral diseases and it is likely that the children are being infected but asymptomatic. Teenagers and adults seem to have similar symptoms and those with chronic conditions the worst outcomes. All of this would fit with the age based innate immune system, the young, not new-born, being immuno-tolerant, young adults, post puberty, have a very aggressive response (known as a cytokine storm), while the older age group cannot react to novelty. We see this in influenza pandemics when it is young adults who are worst affected by viral pneumonia, while the elderly develop secondary complications. Chickenpox in young adults is also a case in point. In addition there seems to be some indication that this virus spreads more readily, person to person but with lower morbidity and mortality than the other two recent CoV epidemics. Time will tell.

Best wishes

John

Professor John Watkins
Consultant Epidemiologist
Public Health Wales/Cardiff University