The National Expert Group for tixagevimab/cilgavimab (Evusheld) pre-exposure prophylaxis of COVID-19

19 May 2022 14:00-15:30

Via Teams

NOTES OF MEETING

Attendees

Professor Anthony Kessel (Chair) (AK)	Clinical Director, National Clinical Policy, NHS England and NHS Improvement
[redacted]	[redacted] Liverpool School of Tropical Medicine
[redacted]	[redacted], UK Health Security Agency (UKHSA)
[redacted]	[redacted], UKHSA
[redacted]	[redacted] University of Liverpool
[redacted]	[redacted], Alder Hey Children's Hospital
[redacted]	[redacted], Royal Free Hospital
[redacted]	[redacted]
[redacted]	[redacted] The Newcastle Upon Tyne Hospitals NHS Foundation Trust
[redacted]	[redacted] Chelsea and Westminster Hospital
[redacted]	[redacted] Llywodraeth Cymru/ Welsh Government
[redacted]	[redacted] University of Glasgow
[redacted]	[redacted], NICE
[redacted]	[redacted], UKHSA
[redacted]	Department of Health, Northern Ireland
[redacted]	[redacted], Welsh Government
[redacted]	[redacted], The Scottish Government
[redacted]	[redacted] Llywodraeth Cymru/Welsh Government
[redacted]	[redacted]

[redacted]	Department of Health and Social Care Observer
[redacted]	Department of Health and Social Care Observer
[redacted]	[redacted] Specialised Commissioning, NHS England and NHS Improvement
[redacted]	[redacted] NHS England and NHS Improvement
[redacted]	[redacted] Specialised Commissioning, NHS England and NHS Improvement
[redacted]	[redacted] [redacted] Specialised Commissioning, NHS England and NHS Improvement
[redacted]	[redacted], Specialised Commissioning, NHS England and NHS Improvement

Item	Description	Actions

1	**Welcome, apologies and introduction**
	• The chair welcomed the attendees and noted apologies.
	• The chair ensured attendees from all four UK nations were present.
	• The chair provided a brief overview of the RAPID-C19 process for COVID-19 therapies and the role of national expert groups in the development of COVID-19 UK Clinical Commissioning Policies.
	• The chair discussed the background and purpose of the reconvening of the expert group meeting.
	• The chair reminded the attendees of the distinction between formal members of the expert working group and observers and instructed observers to refrain from participating.
	• In advance of this meeting, circulated documents included:
	  ○ an agenda
	  ○ relevant papers containing new data including from UKHSA/Porton Down
	• Attendees agreed not to circulate documents as they are official sensitive.
	
	Apologies received from [redacted], [redacted] [redacted], [redacted] [redacted] [redacted].	

2	**Declarations of interest and review of TOR** The following interests were declared: • [redacted] • [redacted] • [redacted] • [redacted]	

	• The chair explained [redacted] could not attend this meeting due to a new conflict of interest that had arisen; [redacted] lab in Oxford has entered into a financial agreement with AstraZeneca.	
3	[redacted] presented a summary of recent evidence and outlined his position on progression to routine deployment of tixagevimab/cilgavimab as PrEP against COVID-19. Discussion generated the following key points: • There is reasonable clinical data that tixagevimab/cilgavimab is effective as PrEP against pre-Omicron variants. • Only pre-clinical data and antiviral models are available for BA.x variants. • There are concerns regarding reduction in efficacy in the neutralising activity of tixagevimab/cilgavimab. • There are concerns that high-risk groups may modify their behaviour to less risk-avoidant after taking a prophylactic agent – with particular implications if such an agent is of limited effectiveness. • There is insufficient evidence of clinical effectiveness against Omicron variants to justify widespread deployment in the present UK context. •	
4	[redacted] and [redacted] (UKHSA) presented evidence from Virus Neutralization Assays (VNA). Their findings were discussed: • The differential in neutralization concentrations in the studies performed on tixagevimab/cilgavimab against the BA.x variants is small compared to neutralisation concentrations reported for the other variants tested. This suggests that tixagevimab/cilgavimab may have equivalent clinical effect against the panel of variants tested, including BA.x strains. • There is insufficient information (e.g limited samples) from current UKHSA testing to draw definitive conclusions for a clinical policy.	
5	[redacted] presented an updated pharmacokinetic overview of tixagevimab/cilgavimab in the context of in-vitro neutralising activity against BA.x variants, including consideration of all new PK/PD data since the previous meeting: • The expert group was reminded that tixagevimab/cilgavimab antibodies have additional modifications to obviate the effector functions. Therefore, direct neutralisation is the only mechanism of action. • In-vitro data has demonstrated significantly compromised activity for tixagevimab/cilgavimab against the BA.2 subvariant of Omicron. • There are major uncertainties related to the required tissue concentration to achieve neutralisation of SARS-CoV-2, especially in the lungs. There is a need for clinical data to define serum targets for efficacy. • Both antibodies in tixagevimab/cilgavimab were substantially compromised with respect to BA.1 Omicron to an extent that there could be no reasonable expectation of parity with pre-omicron variants. For cilgavimab the neutralisation activity against BA.2 Omicron was restored such that it maintains neutralisation activity comparable to that against the pre-Omicron variants for which it was clinically studied. However, for tixagevimab neutralisation of BA.2 Omicron remains compromised. Therefore, the combination effectively acts as prophylaxis monotherapy against COVID-19.	
9	**Conclusions:** There was an extensive discussion following the presentations which concluded that in the absence of good clinical effectiveness data, the in-vitro data are insufficient to determine a deployment decision. There is, at	

	present, significant scientific uncertainty and clinical equipoise around the efficacy of tixagevimab/cilgavimab as PrEP against COVID-19, especially in the current pandemic context in the UK. The chair asked members of the group (but not observers) to vote on whether a UK-wide clinical commissioning policy should be implemented for PrEP against COVID-19. 1) There was unanimous agreement from the national expert group that tixagevimab/cilgavimab should not currently progress to deployment as PrEP against COVID-19. 2) The necessity of generating clinical data was reiterated. There is the need for more research around the clinical effectiveness of tixagevimab/cilgavimab in the current UK population and present pandemic context. This could be in the form of a pragmatic clinical trial, which would likely be observational using a high-risk patient population. Within such a trial there is an imperative to examine PD/PK data in a sub-group of high-risk patients, so as to helpfully inform clinical pharmacological knowledge.	
	Next steps and close • Minutes will be developed and circulated for comment. • A report and recommendation will be prepared for the CMO.	

Action	**Actionee**
Develop minutes from this meeting	[redacted]
CMO briefing	[redacted]