I BEST OF THE WEEK (7 feb – 13 feb 2022)

Articolo	Abstract	Contenuto e Commento
McCallum M et al. Science Structural basis of SARS-CoV-2 Omicron immune evasion and receptor engagement. https://www.science.org/doi/epdf/10.1126/science.abn8652	Abstract The SARS-CoV-2 Omicron variant of concern evades antibody-mediated immunity that comes from vaccination or infection with earlier variants due to accumulation of numerous spike mutations. To understand the Omicron antigenic shift, we determined cryo-electron microscopy and X-ray crystal structures of the spike protein and the receptor-binding domain bound to the broadly neutralizing sarbecovirus monoclonal antibody (mAb) S309 (the parent mAb of sotrovimab) and to the human ACE2 receptor. We provide a blueprint for understanding the marked reduction of binding of other therapeutic mAbs that leads to dampened neutralizing activity. Remodeling of interactions between the Omicron receptor-binding domain and human ACE2 likely explains the enhanced affinity for the host receptor relative to the ancestral virus.	Questo studio si focalizza sulla variante Omicron, determinandone la struttura cristallina della proteina spike e del "receptor-binding domain" che si lega all'anticorpo monoclonale S309 (simile al sotrovimab) che neutralizza i sarbecovirus e al recettore ACE2 umano. Tale lavoro fornisce le basi molecolari per comprendere più adeguatamente il motivo per cui la variante Omicron sia in grado di evadere estensivamente la risposta immunitaria. Permette inoltre di comprendere l'importanza di disegnare e modellare terapie e vaccini contro quegli epitopi del virus che tendono maggiormente a conservarsi: sarebbe di fondamentale importanza sviluppare delle strategie che possano non solo risolvere l'attuale pandemia, ma anche prepararci nei confronti di future pandemie da sarbecovirus.

Corrao G. et al. The Lancet Persistence of protection against SARS-CoV-2 clinical outcomes up to 9 months since vaccine completion: a retrospective observational analysis in Lombardy, Italy https://doi.org/10.1016/S1473-3099(21)00813-6	Background: Scarce information is available on the duration of the protective effect of COVID-19 vaccination against the risk of SARS-CoV-2 infection and its severe clinical consequences. We investigated the effect of time since vaccine completion on the SARS-CoV-2 infection and its severe forms. Methods: In this retrospective observational analysis using the vaccination campaign integrated platform of the Italian region of Lombardy, 5 351 085 individuals aged 12 years or older who received complete vaccination from Jan 17 to July 31, 2021, were followed up from 14 days after vaccine completion until Oct 20, 2021. Changes over time in outcome rates (ie, SARS-CoV-2 infection and severe illness among vaccinated individuals) were analysed with age-period-cohort models. Trends in vaccine effectiveness (ie, outcomes comparison in vaccinated and unvaccinated individuals) were also measured. Findings: Overall, 14 140 infections and 2450 severe illnesses were documented, corresponding to incidence rates of 6·7 (95% CI 6·6–6·8) and 1·2 (1·1–1·2) cases per 10 000 person-months, respectively. From the first to the ninth month since vaccine completion, rates increased from 4·6 to 10·2 infections, and from 1·0 to 1·7 severe illnesses every 10 000 person-months. These figures correspond to relative reduction of vaccine effectiveness of 54·9% (95% CI 48·3–60·6) for infection and of 40·0% (16·2–57·0) for severe illness. The increasing infection rate was greater for	COMMENTO: Studio osservazionel retrospettivo, finalizzato a valutare la persistenza della protezione nei confronti degli otucomes clinici (infezione e malattia severa) del Sars-Cov2, a nove mesi dal completamento del ciclo vaccinale. In questo studio, 5.351.085 individui sono stati seguiti a 14 giorni dal completamento del ciclo vaccinale tra il gennaio ed il giugno 2021 e poi fino all' ottobre dello stesso anno. In tale lasso di tempo sono stati valutati i cambiamenti nel tempo degli outcomes considerati, come l'infezione e la gravità della stessa nella popolazione vaccinata ed il trend dell'efficacia dei vaccini. In totale sono state osservate 14.140 infezioni e 2450 malattie severe (1.2 casi/10000 persone). Dal primo mese di follow-up fino al mese di ottobre si è osservato un aumento di questo tasso fino al 6.7/10000. Le infezioni più severe sono state riscontrate nella popolazione over60, senza una particolare variazione nella popolazione ricevente un vaccino a mRNA o con vettore virale. Ovviamente tale dato è direttamente proporzionale alla riduzione dell'efficacia della protezione vaccinale nel tempo, ponendo l'attenzione sull'importanza della necessità di una dose booster, con tempistiche non eccessivamente prolungate.

	individuals aged 60 years or older who received adenovirus-vectored vaccines (from 4·0 to 23·5 cases every 10 000 person-months). The increasing severe illness rates were similar for individuals receiving mRNA-based vaccines (from 1·1 to 1·5 every 10 000 person-months) and adenovirus-vectored vaccines (from 0·5 to 0·9 every 10 000 person-months). Interpretation: Although the risk of infection after vaccination, and even more of severe illness, remains low, the gradual increase in clinical outcomes related to SARS-CoV-2 infection suggests that the booster campaign should be accelerated and that social and individual protection measures against COVID-19 spread should not be abandoned	
Garcia-Flores V et al Nature Communications Maternal-fetal immune responses in pregnant women infected with SARS-CoV-2.	Pregnant women are a high-risk population for severe/critical COVID-19 and mortality. However, the maternal-fetal immune responses initiated by SARS-CoV-2 infection, and whether this virus is detectable in the placenta, are still under investigation. Herein, we report that SARS-CoV-2 infection during pregnancy primarily induced specific maternal inflammatory responses in the circulation and at the maternal-fetal interface, the latter being governed by T cells and macrophages. SARS-CoV-2 infection during pregnancy was also associated with a cytokine response in the fetal circulation (i.e. umbilical cord blood) without compromising the cellular immune repertoire. Moreover, SARS-CoV-2 infection neither altered fetal cellular	Studio osservazionale su 15 donne in gravidanza con infezione da SARS-CoV-2, nelle quali si osserva come il virus induca una risposta immunitaria prevalentemente cellulo-mediata nella madre, in assenza di elevati titoli anticorpali nel sangue cordonale. Il virus non è stato rinvenuto in nessun caso nella placenta, confermando il dato che l'infezione transplacentare non sia una evenienza significativa.

https://www.nature.com/articles/s41467-021-27745-z.pdf	immune responses in the placenta nor induced elevated cord blood levels of IgM. Importantly, SARS-CoV-2 was not detected in the placental tissues, nor was the sterility of the placenta compromised by maternal viral infection. This study provides insight into the maternal-fetal immune responses triggered by SARS-CoV-2 and further emphasizes the rarity of placental infection.	