Sécurité du Comirnaty chez les femmes enceintes : Plan de Gestion des Risques du fabriquant

- Version 1.0 (décembre 2020), pp.58,70

Table 20. Use in pregnancy and while breast feeding

Evidence source:
The safety profile of the vaccine is not known in pregnant or breastfeeding women due to their exclusion from the pivotal clinical study. There may be pregnant women who choose to be vaccinated despite the lack of safety data. It will be important to follow these women for pregnancy and birth outcomes. The timing of vaccination in a pregnant woman and the subsequent immune response may have varying favourable or unfavourable impacts on the embryo/foetus. The clinical consequences of SARS-CoV-2 infection to the woman and foetus during pregnancy is not yet fully understood and the pregnant woman's baseline health status may affect both the clinical course of her pregnancy and the severity of COVID-19. These factors and the extent to which the pregnant woman may be at risk of exposure to SARS-CoV-2 will influence the benefit risk consider

Population in need
The lack of data wil
of COVID-19 mRN

- **Women who are pregnant or breastfeeding**

  Reason for exclusion: To avoid use in a vulnerable population.

  Is it considered to be included as missing information? Yes.

  Rationale: It is not known if maternal vaccination with COVID-19 mRNA vaccine would have unexpected negative consequences to the embryo or foetus.

Sécurité du Comirnaty chez les femmes enceintes : Plan de Gestion des Risques du fabriquant

- Version 2.3 (septembre 2021), p.69

Table 33. Exposure of Special Populations included or not in Clinical Trial Development Programmes

Type of special population	Exposure
Pregnant women	There is limited experience with use of COVID-19 mRNA vaccine in pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryo/foetal development, parturition or post-natal development. Administration of COVID-19 mRNA vaccine in pregnancy should only be considered when the potential benefits outweigh any potential risks for the mother and foetus.

Sécurité du Comirnaty chez les femmes enceintes : Plan de Gestion des Risques du fabriquant

- Version 5.0 (février 2022), p.105

Missing Information: Use in Pregnancy and while breast feeding

Risk-benefit impact

The safety profile of the vaccine is not fully known in pregnant or breastfeeding women due to their initial exclusion from the pivotal clinical study however, post-marketing experience in pregnant women is available.[94] Additionally one clinical study of the safety and immunogenicity of the COVID-19 vaccine in pregnant women is ongoing (C4591015); 2 non-interventional studies (C4591009 and C4591011) to assess whether sub-cohorts of interest, such as pregnant women, experience increased risk of safety events of interest following receipt of the COVID-19 vaccine are planned and another 2 non-interventional studies, C4591021 and C4591022, are ongoing.

It is important to obtain long term follow-up on women who were pregnant at or around the time of vaccination so that any potential negative consequences to the pregnancy can be assessed and weighed against the effects of maternal COVID-19 on the pregnancy.

Sécurité du Comirnaty chez les femmes enceintes : Plan de Gestion des Risques du fabriquant

- Version 9.0 (novembre 2022 = actuelle), pp.93,112,138
  = éléments non modifiés depuis les premières versions

Women who are pregnant or breastfeeding

Reason for exclusion: To avoid use in a vulnerable population.

Is it cons

Rational

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The MAH agrees that monitoring vaccine safety in pregnant women is critical. Given that a pregnancy registry based on primary data collection is susceptible to non-participation, attrition, small sample size and limited or lack of comparator data, Pfizer, on behalf of the

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It is important to obtain long term follow-up on women who were pregnant at or around the time of vaccination so that any potential negative consequences to the pregnancy can be assessed and weighed against the effects of maternal COVID-19 on the pregnancy.

Non-Interventional Post-Approval Safety Studies in Pregnancy

It is anticipated that initial use in pregnancy will be subject to local health authority recommendations regarding which individuals should be vaccinated and likely very limited intentional vaccination of pregnant women; therefore, initially this information will derive from 5 of the real-world safety studies (C4591009, C4591010, C4591011, C4591021 [former

Sécurité du Comirnaty chez les femmes enceintes : Plan de Gestion des Risques du fabriquant

- Version 2.0 (avril 2021), p.28

- C4591015: *A phase 2/3 study to evaluate the safety, tolerability, and immunogenicity of SARS-CoV-2 RNA vaccine candidate (BNT162b2) against COVID-19 in healthy pregnant women 18 years of age and older.*
  Approximately 4000 pregnant women at 24 to 34 weeks gestation are being randomised in a 1:1 ratio to vaccine or placebo.

Sécurité du Comirnaty chez les femmes enceintes : Plan de Gestion des Risques du fabriquant

- Version 5.0 (février 2022), p.39

- C4591015[3]: *A phase 2/3 placebo-controlled, randomized, observer-blind study to evaluate the safety, tolerability, and immunogenicity of SARS-CoV-2 RNA vaccine candidate (BNT162b2) against COVID-19 in healthy pregnant women 18 years of age and older.* A total of 348 (209 in phase 2 and 139 in phase 3) pregnant women at 24 to 34 weeks gestation were randomised in a 1:1 ratio to vaccine or placebo.

[3] Enrolment of participants into study C4591015 was stopped on 25 October 2021 due to recruitment challenges as a result of global recommendations for COVID-19 vaccination in pregnant women and the increased availability of COVID-19 vaccines. Participants already enrolled will continue follow up evaluations until study end as planned.

Sécurité du Comirnaty chez les femmes enceintes : Agence Européenne du Médicament (& tutelles françaises)

- Fin décembre 2020

Can pregnant or breast-feeding women be vaccinated with Comirnaty?

Animal studies do not show any harmful effects in pregnancy, however data on the use of Comirnaty during pregnancy are very limited. Although there are no studies on breast-feeding, no risk for breast-feeding is expected.

The decision on whether to use the vaccine in pregnant women should be made in close consultation with a healthcare professional after considering the benefits and risks.

Sécurité du Comirnaty chez les femmes enceintes : Agence Européenne du Médicament (& tutelles françaises)

- Fin novembre 2021

Can pregnant or breast-feeding women be vaccinated with Comirnaty?

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The decision on whether to use the vaccine in pregnant women should be made in close consultation with a healthcare professional after considering the benefits and risks.

Sécurité du Comirnaty chez les femmes enceintes : Agence Européenne du Médicament (& tutelles françaises)

- Début mars 2022

Can pregnant or breast-feeding women be vaccinated with Comirnaty?

Comirnaty can be used during pregnancy. A large amount of data from pregnant women vaccinated with Comirnaty during the second or third trimester of their pregnancy has been analysed and showed no increase in pregnancy complications. Although data in the first trimester of pregnancy are more limited, no increased risk of miscarriage was seen.

Comirnaty can also be used during breast-feeding. Data from women who were breast-feeding after vaccination have not shown a risk of adverse effects in breast-fed babies.

Sécurité du Comirnaty chez les femmes enceintes : Agence Européenne du Médicament (& tutelles françaises)

En France :

- Conseil d'orientation de la stratégie vaccinale (COSV) :
  vaccination de toutes les femmes enceintes
  dès avril 2021

- Haute autorité de santé (HAS) :
  obligation vaccinale des soignants y compris les femmes enceintes
  dès juillet 2021

Sécurité du Comirnaty chez les femmes enceintes : Évaluation d'une balance bénéfices-risques à court terme

À court terme :

- Bénéfices = réduction du risque (absolu) d'événement grave maternel ou péri-natal lié au Covid **(a)**
- Risques = induction du risque (absolu) d'événement grave maternel ou péri-natal lié au vaccin **(b)**
- **(a) >> (b)**

Sécurité du Comirnaty chez les femmes enceintes : Évaluation d'une balance bénéfices-risques à court terme

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- **(a) >> (b)**
- **(a)** ~ entre 0,01 % et 0,001 % (Écosse)

Sécurité du Comirnaty chez les femmes enceintes : Évaluation d'une balance bénéfices-risques à court terme

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- **(a) >> (b)**
- **(a)** ~ entre 0,01 % et 0,001 % (Écosse)
- Pour avoir 95 % de chances de détecter 1 occurrence d'un événement d'une fréquence de 0,01 %, il faudrait un essai randomisé de 60 000 sujets

Vaccination des convalescents du Covid

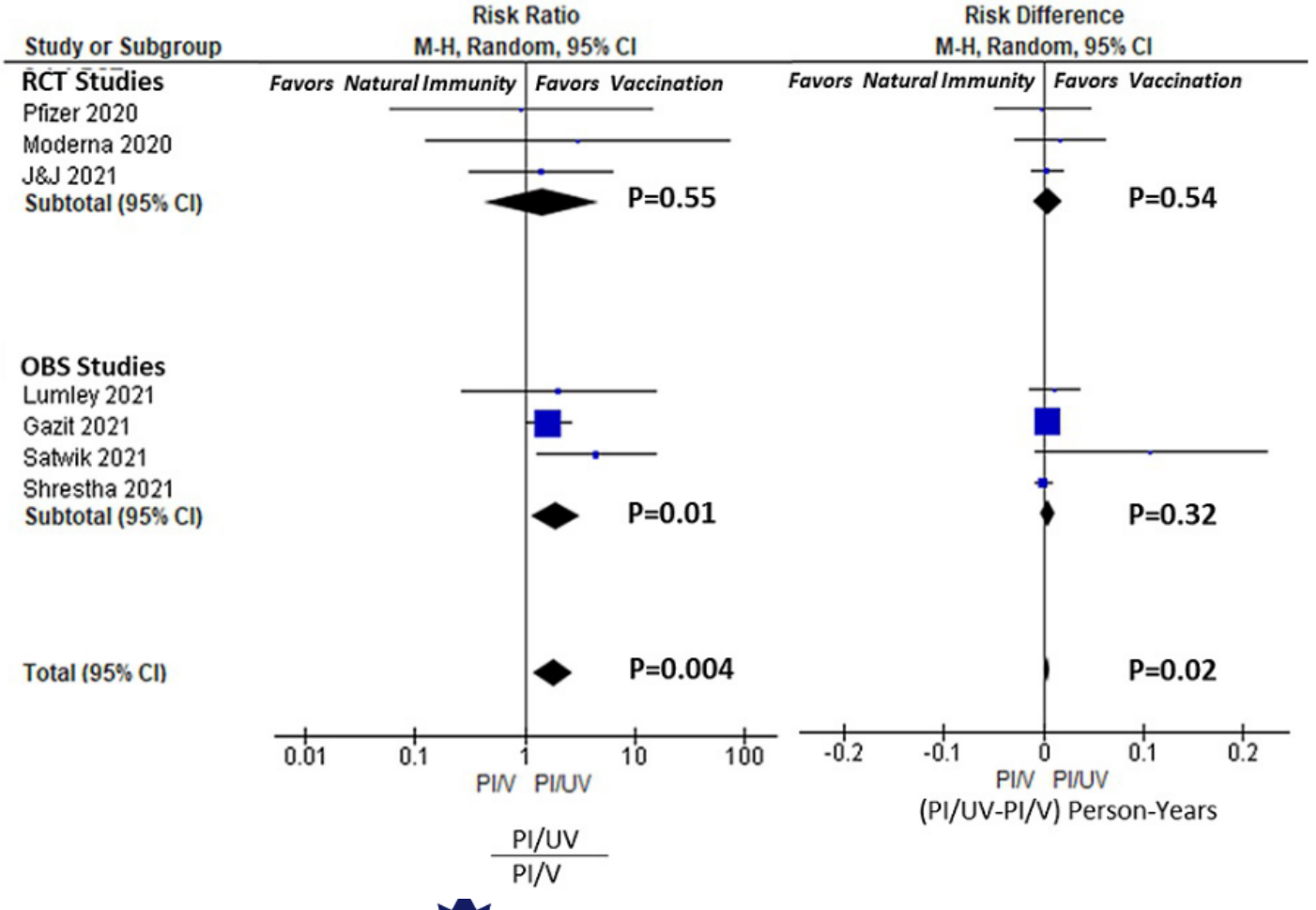
- Stein *et al*. 2023 (*Lancet*), conclusion

Our findings show that immunity from COVID-19 infection confers substantial protection against infection from pre-omicron variants. By comparison, protection against re-infection from the omicron BA.1 variant was substantially reduced and wanes rapidly over time. Protection against severe disease, although based on scarce data, was maintained at a relatively high level up to 1 year after the initial infection for all variants. Our analysis suggests that the level of protection from past infection by variant and over time is at least equivalent if not greater than that provided by two-dose mRNA vaccines.

COVID-19 Forecasting Team
Caroline Stein, Hasan Nassereldine, Reed J D Sorensen, Joanne O Amlag, Catherine Bisignano, Sam Byrne, Emma Castro, Kaleb Coberly

Vaccination des convalescents du Covid

- Shenai *et al*. 2021 (*Cureus*), fig.3



Vaccination des convalescents du Covid

- Shenai *et al*. 2021 (*Cureus*), conclusion

This disparity in NNT highlights the muted absolute benefit of vaccination to COVID-recovered individuals, compared to that enjoyed by COVID-naïve individuals. While our systematic review did not specifically cover the risk of vaccination, recent studies have shown that vaccinations have a small but excess risk of adverse events appears in the range of 2-80 events per 100,000 [31]. There are also some reports, though no consensus, that previously infected individuals may have an increased risk of local and systemic adverse effects [32]. Therefore, while vaccination is overwhelmingly safe for the general population, and even for most COVID-recovered individuals, higher-risk subgroups are subject to a distinctly different risk/benefit calculus and narrower therapeutic window, suggesting that individual factors with clinical equipoise should be utilized. Further evaluation of adverse events specifically within COVID-recovered individuals is warranted, as is a formal evaluation of the risk/benefit calculus. Civil policies, including vaccine mandates, should strongly consider automatic exemption from vaccination based on a history of prior infection or serological evidence of immunity until the risk/benefit is better delineated.

Vaccination des convalescents du Covid

- Sainton 2021 (note à la HAS), conclusion

La raison éthique et médicale voudrait que l'on s'abstienne de vacciner de façon systématique les convalescents.

La raison scientifique voudrait aussi que l'on s'abstienne de vacciner la population entière avec une technique expérimentale, ne serait-ce que pour rester en capacité de mesurer les effets de cette technique à moyen et à long terme (par comparaison avec les autres types de population : naïve non vaccinée, convalescente non vaccinée).

La raison scientifique rejoint la raison éthique et médicale : ne pas supprimer les témoins.

Surestimation de l'efficacité vaccinale : biais extra- et intra-méthodologiques

1) Efficacité relative *versus* efficacité absolue

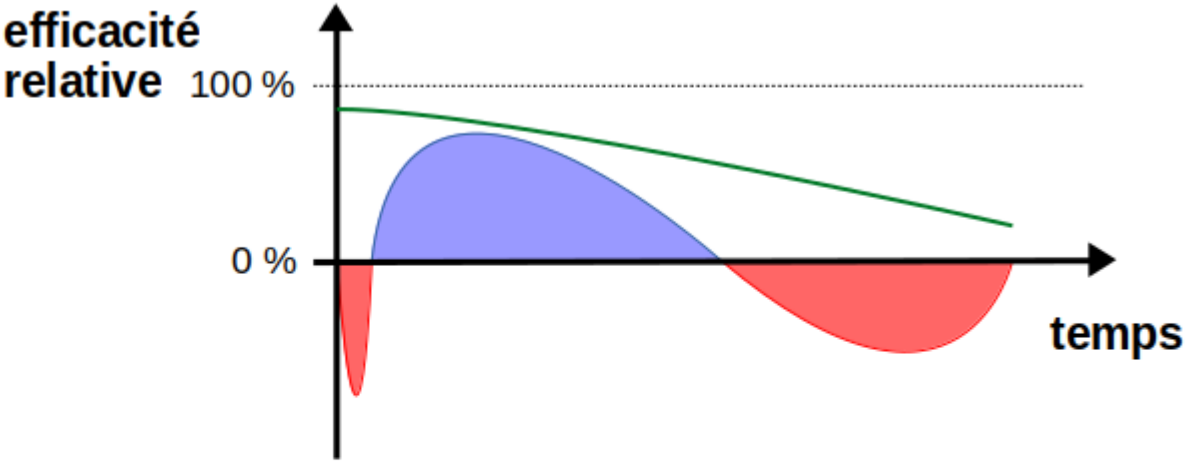
> **2. Provide absolute risks, not just relative risks.** Patients are unduly influenced when risk information is presented using a relative risk approach; this can result in suboptimal decisions. Thus, an absolute risk format should be used.

FDA 2011, p.60
Guide sur la communication en matière de risques et de bénéfices dans le cadre de la médecine fondée sur les preuves

Voir aussi Michel Cucchi 2022

Surestimation de l'efficacité vaccinale : biais extra- et intra-méthodologiques

2) Efficacité vaccinale non prise en compte

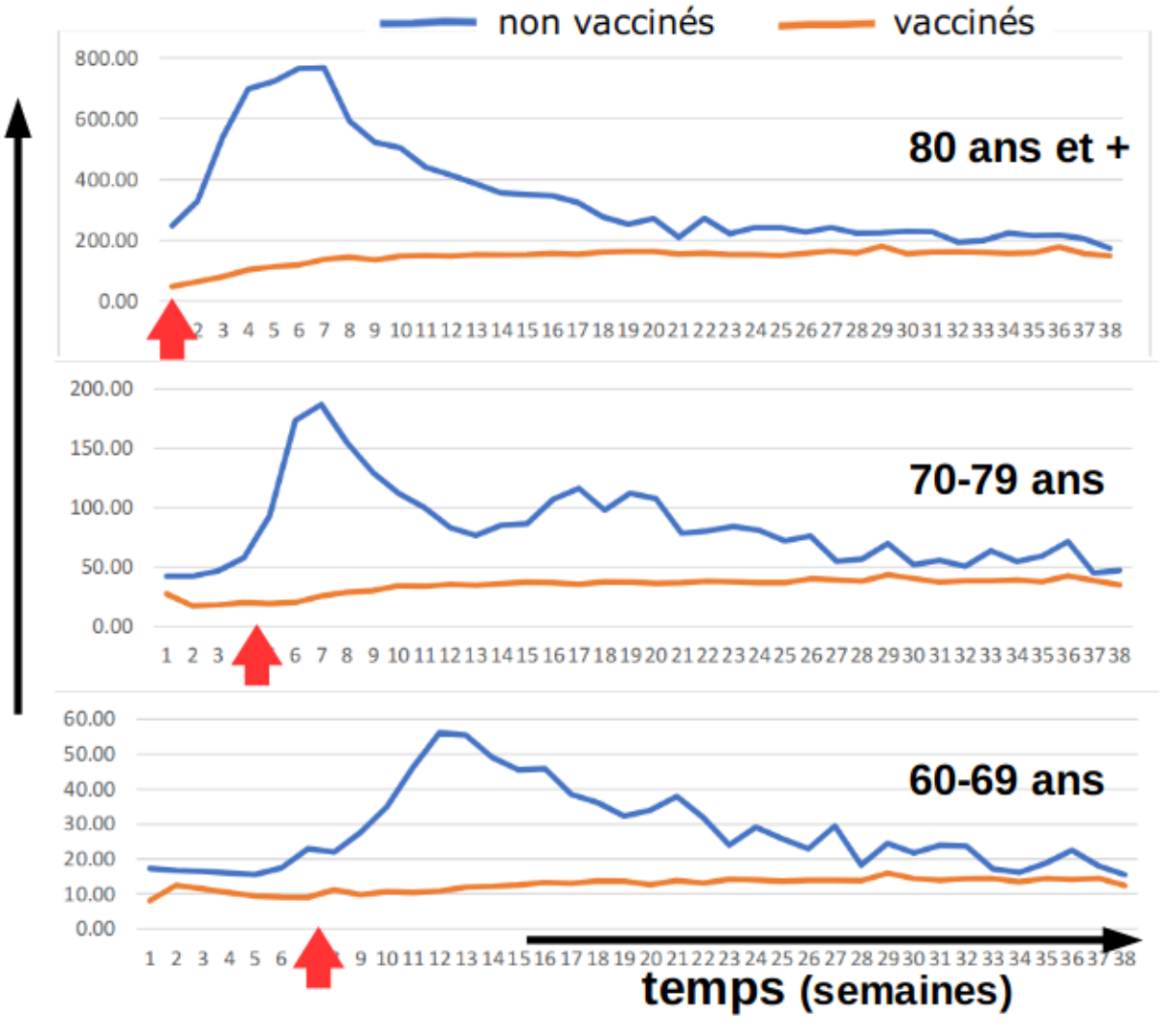


Évolution dans le temps de l'efficacité de l'immunité acquise contre le risque d'infection au Covid :

- efficacité de l'immunité naturelle
- efficacité vaccinale positive
- efficacité vaccinale négative

Surestimation de l'efficacité vaccinale : biais extra- et intra-méthodologiques

3) Statut vaccinal



Neil et al. 2022
(fig. 10,9,8)