Poster #132608

Opportunities and challenges in linkage of early access databases with the French National claims database: a RWE effectiveness study of AZD7442 for Pre-Exposure prophylaxis against COVID-19 in Immunocompromised patients

Liem Binh Luong Nguyen[1], Anne-sophie Jannot[2], Charles Burdet[3], Laureen Majed[4], Caroline Fabry-Vendrand[4], Théo Cerceau[5], Stephane Bouée[5], Sabada Dube[6], Sylvia Taylor[6], Gabriel Thabut[4], Cécile Artaud[4]

[1]CIC Cochin Pasteur, Assistance Publique Hôpitaux de Paris, Paris, France ; [2]BNDMR, Paris, France ; [3]Institut National de la Santé et de la Recherche Médicale, Infection Antimicrobials Modelling Evolution, Unité Mixte de Recherche, France ; [4]AstraZeneca, Courbevoie, France ; [5]CEMKA, Bourg la Reine, France ; [6]AstraZeneca, Cambridge, UK

Scan here or follow link for e-poster*

www.congresseposter.com

Why did we perform this research?

- AZD7442 was granted early access authorisation for COVID-19 pre-exposure prophylaxis[1]. However, there is no data describing the utilisation of AZD7442 in real-world settings
- Although AZD7442 was proven to be efficacious in the PROVENT trial[2] for the prevention of SARS-CoV-2 infection and hospitalisation/death, real-world setting effectiveness in the French approved patient populations is still unknown. This study aims to fill that gap.
- The PROVENT trial was conducted:
  - In unvaccinated populations
  - During the Alpha variant predominance period while the early access programme included the Omicron variant

Summary

Background

- In 2021, the French Health Authority (FAH) published new guidelines for Early Access Programs (EAPs) for unauthorised pharmaceutical drugs[1].
- These guidelines include obligations for collection of data on product:
  - effectiveness, safety, drug utilisation and patient characteristics.
- Guidelines provide regulatory framework to link EAP databases with the French national claims database (SNDS, for 'Système National des données de santé').
  - SNDS covers 99% of the French population.
- The guidelines provide opportunities for innovative descriptive and effectiveness.

Methods

- Observational, retrospective, matched-control cohort study
- Data sources: SNDS (outcomes and control individuals) and EAP (AZD7442 users) databases
- A propensity score matching based on: calendar time, and confounding clinical characteristics.
  - Individuals exposed to EVUSHELD will be matched to unexposed individual(s) in fixed 1:1
- Comorbidities for which AZD7442 was prescribed

Outcomes: SARS-CoV-2 infections, COVID-19 hospitalisations, and deaths

Results

- 27,782 patients were enrolled in the EAP - administration forms were completed for 13,287 (47.8%).
- AZD7442 prescribers were onco-hematologists (24.2%), nephrologists (19.9%), internal medicine specialists (15.6%), and rheumatologists (6.5%).
- 96.7% of AZD7442 had received at least three COVID-19 vaccine doses.
- Common comorbidities were cancer (34.9%), chronic kidney disease (23.7%), hypertension (23.2%), cardiovascular disease (19.4% >2 CV factors), and diabetes (9.2%).

Conclusions

- The new FHA guidelines for EAP provide opportunities to reuse and enrich EAP data, linked to the SNDS for essential RWE studies for new innovative drugs.
- This study, from AstraZeneca's largest EAP (28,000 patients) will provide valuable insights for future recommendations on COVID-19 prophylaxis in immunocompromised patients

Next Steps: A matched control cohort will be extracted from SNDS to assess effectiveness of AZD7442 for the prevention of COVID-19

Key takeaway

The 2021 EAP reform in France allows linkage between early access database and the SNDS.

The reuse and enrichment of the EAP database linked to SNDS will provide valuable insights for future recommendations on COVID-19 prophylaxis in immunocompromised patients

***E-poster**

Context

Reform of derogatory access to drugs in France[3]

What is the derogatory access

- In France, for 20 years, a patient in a therapeutic impasse may benefit from a drug not authorized for a specific indication
- Several criteria must be met for treatment eligibility to EAP:
  1. Treatment can not be delayed
  2. Efficacy & safety of drug strongly presumed
  3. Serious, rare or disabling disease
  4. Lack of appropriate treatment

Why a reform ?

- To simplify procedures
- To speed up the access to treatment
- To deepen scientific knowledge by strengthening the collection of clinical data and by involving patients.

Early access is an opportunity to collect observational/real-life data in France to document its use and effectiveness to feed into future stages of evaluation by the HTA

Limited data elements are collected in the EAP to reduce burden on clinicians and pharmacists

Other available data: The National claims database SNDS for 'Système National des données de santé' is one of the largest claim database in the world, covering 99% of the French population

An early access authorization of AZD7442 (TIXAGÉVIMAB / CILGAVIMAB) was granted for pre-exposure prophylaxis of COVID-19

AZD7442 Indication

- **Having a deficiency of immunity related to a pathology or treatments and weakly or non-responders after a complete vaccination schedule in accordance with the recommendations in force**
  OR
- **Not eligible for vaccination and at high risk of severe COVID-19**

Timeline

Date granted (HAS/ANSM*)	December 9th, 2021
Start date of early access	December 15th, 2021
End of data collection	November 30th , 2022
SNDS data availability	Expected in 2024

**HAS: French HTA*
ANSM: French National Agency for Medicines and Health

Study population

- A matched control cohort will be extracted from SNDS.
  - A propensity score matched cohorts based on calendar time, immune category, and confounding clinical characteristics and comorbidities for which AZD7442 was prescribed

Objectives and Methods of the RWE Effectiveness study

Objectives

To demonstrate AZD7442 clinical value through confirmation of effectiveness and safety in real world setting in all targeted population, and in sub-groups of interests

- To assess AZD7442 effectiveness on COVID-19 hospitalizations up to 6 months following its initial administration
- To compare all-cause mortality up to 6 months following the initial dose of AZD7442, among subjects who did and did not receive AZD7442

To assess AZD7442 economic value and impact on COVID-19-related Health Care Resource Utilization (HCRU)

Figure 1: Overview of databases

Methods

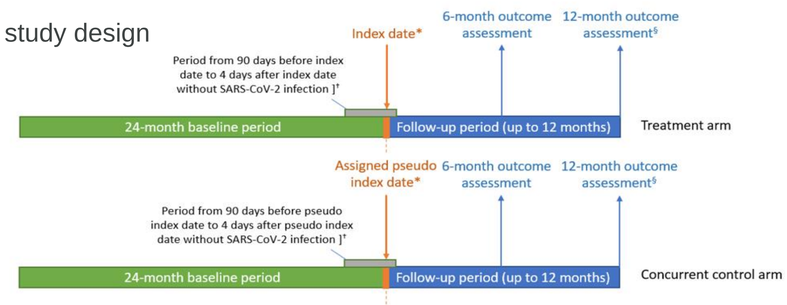
Two databases will be linked:

- The EAP database which includes the identification of patients who were treated with AZD7442 and the description of patients;
- The SNDS claims database which will be used to identify outcomes of interest (e.g., overall deaths and hospitalizations due to COVID-19 infection)

Propensity score is used to match patients and controls with a ratio 1:1

Cox proportional hazards regression models to estimate unadjusted and adjusted hazard ratios

Figure 2: Overview of study design



Preliminary results: description of patient charateristics

Requests for treatment

27,782 patients

Number of patient with confirmed exposure*

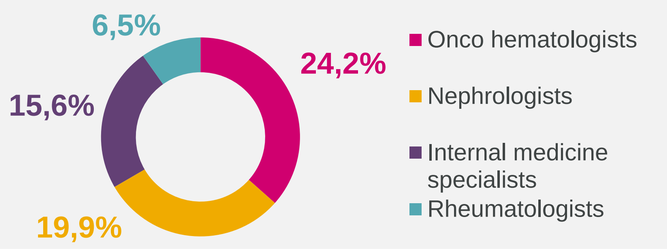
13,287 (47.8%) patients had confirmation of AZD7442 administration

*treatment administration form completed

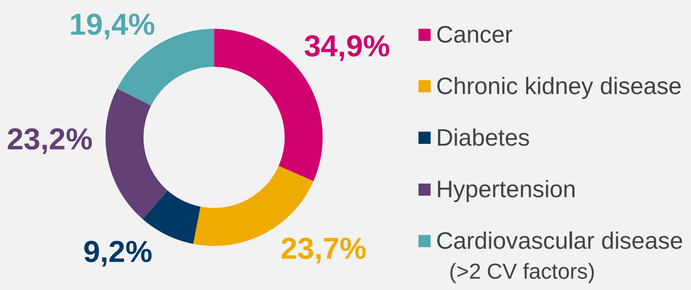
Most patients (96.7%) had received at least 3 vaccine doses at inclusion

Median (min-max) age 64 (13-100) years

Prescription of AZD7442 according to medical specialty



Most common comorbidities in the study population



CONCLUSION

| An innovative project

This study presents a comparative RWE effectiveness study combining multiple sources of data through a new technological AGORIA Santé

| Unique challenges

Single administration prophylactic treatments are challenging to assess with the constraints of an EAP without additional data

| Opportunities

The reuse and enrichment of data collected during EAP and linked to the SNDS will lead to promising RWE studies for new innovative drugs

The largest AstraZeneca's EAP worldwide with 28,000 patients included

This study will provide valuable insights for future recommendations on COVID-19 prophylaxis in immunocompromised patients

Disclosures

- The study was sponsored by AstraZeneca France.
- Cerceau T and Bouee S are employees at CEMKA, a French consulting firms in the field of evaluation of products, programs and organizations in Health.
- Nguyen L, Jannot AS, Burdet C received honoraria from AZ. Majed L, Fabry-Vendrand C, Taylor S Artaud C Thabut S are employees at AZ.

References

1. https://www.has-sante.fr/jcms/p_3304034/fr/evusheld-tixagevimab/cilgavimab-covid-19-adultes
2. https://www.nejm.org/doi/full/10.1056/NEJMoa2116620
3. https://www.has-sante.fr/upload/docs/application/pdf/2021-06/acces_precoces_-_doctrine.pdf

Presented at ISPOR | November 12–15, 2023 | Copenhagen, Denmark