STUDY OF COMPLIANCE WITH THE ISOTRETINOIN PREGNANCY PREVENTION PROGRAMME REGARDING PREGNANCY TESTING IN FRANCE USING THE EGB DATABASE

Marie-Laure Veyries, Marion Bertrand, Sara Miranda, Patrick Maison, Mahmoud Zureik
The French National Agency for Medicines and Health Products Safety (ANSM), 143-147 boulevard Anatole France, 93285 Saint Denis Cedex, France

INTRODUCTION

Isotretinoin, an effective treatment in severe acne, is known to be a potent teratogen. The European Pregnancy Prevention Programme (PPP) includes a pregnancy test (PT) before each prescription and a final one 5 weeks after treatment discontinuation, and dispensing no later than 7 days post-prescription.

OBJECTIVES

The main objective was to evaluate compliance with PT recommendations in France from 2007 to 2013 in new female isotretinoin users aged 11-50 years.

METHODS

This is a retrospective cohort study using the EGB database (1/97 Sample of Health Insurance Beneficiaries), which provides sociodemographic characteristics and healthcare consumption data of a permanent representative sample of the population covered by the French national health insurance. It currently includes more than 600 000 beneficiaries[1]. Reimbursed PTs have been investigated in accordance with more or less stringent time intervals regarding prescription and dispensing. The link between the rate of PTs, patient characteristics and those of the course of treatment was estimated using logistic regression models.

RESULTS

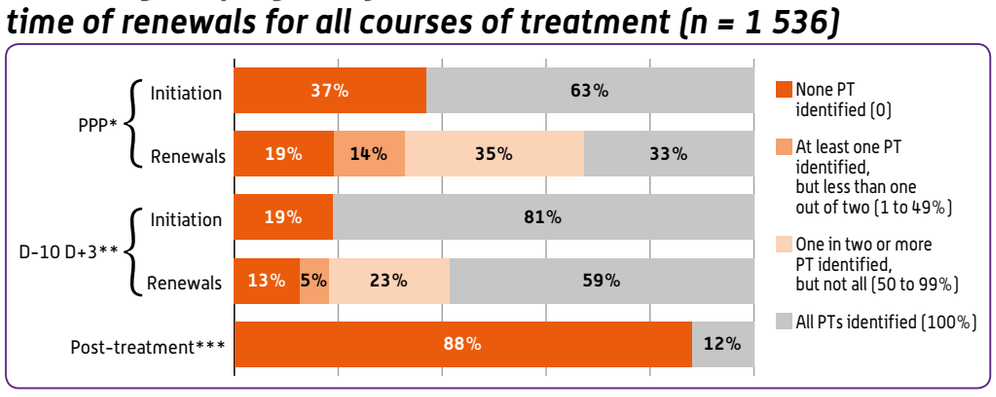
Characteristics of new isotretinoin users and patterns of use (n = 1 367 females aged 11-50 years)

Age at inclusion date* (years) (mean age ± sd)	25.4 ± 9.0
Age category	
11-14	5.3%
15-18	25.0%
19-25	25.4%
26-35	28.2%
36-50	16.1%
Deprivation index at inclusion date** (mean ± sd)	2.7 ± 1.4
Course of treatment (n)	**1 536**
Duration, mean ± sd (months)	6.2 ± 2.9
Total dose, mean ± sd (g)	5.4 ± 2.8
Initial dosage, mean ± sd (mg/d)	27.0 ± 9.3
Prescriber (n [% with knowledge of prescriber's specialty])	**8 179 [94.3%]**
Dermatologist	89.2%
General Practitioner	10.3%

* Inclusion date = Date on which isotretinoin was first dispensed during the study period
** The deprivation index is a 1 to 5 scale, 1 is for the most affluent population and 5 for the poorer population

The cohort included 1 367 female patients who completed 1 536 courses of treatment. Almost 90% received only one course of treatment, and 9% received 2. Dermatologists issued 89% of prescriptions.

Percentage of pregnancy tests identified at initiation and at the time of renewals for all courses of treatment (n = 1 536)



Non-compliance with PT recommendations is rather low at the time of treatment initiation (37% according to PPP* - 19% according to less stringent criteria** had no PT identified). It is much higher for renewals (67%* - 41%** subjects did not have all PTs) and very high after treatment discontinuation (88% had no PT identified).

* PT investigated according to PPP criteria: within 3 days before prescription, dispensing no later than 7 days post-prescription
** PT investigated according to less stringent criteria: from 10 days before dispensing to 3 days after dispensing
*** Post-treatment: PT between 4 to 6 weeks after treatment discontinuation in subjects with at least one 10-week follow-up period after the last dispensing (4-week treatment + 6-week follow-up)

Risk factors for low compliance with PPP recommendations during the first course of isotretinoin treatment

	O.R. [95% CI]	
	No PT before initiation	**Less than 1 out of 2 PTs among renewals (0-49%)**
Age, year	1.03 [0.97-1.10]§	1.02 [0.96-1.08]§
Deprivation index	1.01 [0.93-1.10]	1.10 [1.0-1.20]
Inclusion year		
2007	1.0	1.0
2008	0.75 [0.45-1.26]*	0.85 [0.56-1.67]*
2009	0.52 [0.31-0.87]*	0.88 [0.51-1.50]*
2010	0.34 [0.22-0.63]*	0.43 [0.24-0.77]*
2011	0.55 [0.32-0.94]*	0.93 [0.53-1.62]*
2012	0.59 [0.35-1.00]*	0.75 [0.43-1.31]*
2013	0.54 [0.32-0.92]*	0.64 [0.36-1.12]*
No. of courses: Several / One	1.28 [0.90-1.82]	1.26 [0.88-1.82]
Duration	0.96 [0.92-1.00]†	0.94 [0.89-0.99]*†
Total dose	0.93 [0.88-0.98]*	0.87 [0.82-0.92]*
Initial dosage,	1.21 [1.03-1.42]*§§	1.16 [1.0-1.37]*§§
Period of isotretinoin initiation:		
March – Aug / Sept – Feb	1.04 [0.81-1.32]	1.29 [1.01-1.66]
Prescriber: GP / Dermatologist	2.83 [1.83-4.37]*	2.64 [1.70-4.08]*

* Odds ratio and 95% confidence intervals using logistic regression models, backward stepwise method for covariate selection. Covariates included in the model: age category, deprivation index, inclusion year, number of courses of treatment (1 or > 1), total dose, initial dosage, season, prescriber, patented pharmaceutical product
† Same model as (*) with duration of course of treatment instead of total dose
§ Risk a 5-year increase
§§ Risk a 10 mg increase

Predictors of non-compliance with pregnancy tests:
Prescriptions issued by general practitioners compared to dermatologists were associated with lower PT compliance, regardless of the treatment stage, i.e. initiation, renewal or post-treatment. The other studied factors did not appear to affect PT compliance, even if an improvement was observed in recent years compared to 2007.

CONCLUSION

These results warrant a thorough evaluation of the PPP and the reasons behind poor compliance.

- Knowledge of how the isotretinoin PPP is implemented in daily practice and an assessment of its efficacy are essential in order to benefit fully from this approach.
- This is the first French database study focusing on PT compliance in relation to the isotretinoin PPP.

Conflict of interest statement

None of the authors has conflict of interest to disclose.

1. ITMO Santé publique. EGB- SNIIR-AM - Échantillon Généraliste de Bénéficiaires - SNIIR-AM. Available at: https://epidemiologie-france.aviesan.fr/catalog/sheet/detail.jsp?id=2456&langSheet=fr&vid=1&readOnlyForcedContrib