Physicians' Perspective of the New PLLR: Survey Results

JENNIFER A. NAMAZY, MD

DIVISION OF ALLERGY AND IMMUNOLOGY

SCRIPPS CLINIC

SAN DIEGO, CALIFORNIA

Conflicts

Advisory Board - Genentech

New PLLR

Provide prescriber with relevant information for decision-making when treating pregnant or lactating women

More complete statement of known risks based on available data

Animal data put in context of human exposure

Human data added when available

Statement when no data are available

Questions

Were physicians aware of the change to the PLLR?

How comfortable were physicians with the new PLLR format?

Were clinicians reverting to previous pregnancy letter category system?

Were clinicians finding the necessary information meaningful for critical decision making?

Collaboration with the AAAAI

American Academy of Allergy Asthma and Immunology

Professional organization with over 7,000 members in the United States, Canada and 72 other countries.

This membership includes Allergist / Immunologists, other medical specialists, allied health and related healthcare professionals—all with a special interest in the research and treatment of allergic and immunologic diseases.

Pilot Survey

January – February 2018

Demographics

Awareness

Understanding

Value

Results: Demographics

1500 members received an email invitation to participate in the electronic survey

126 practicing allergists responded

60% in single and multispecialty groups

65% were male

Median age: 56 years old

Results: Awareness

By asking the following questions we were able to assess whether the new PPLR was being used and how often:

- Are you aware that the pregnancy letter categories (A, B, C, D and X) on prescription medication labeling are being replaced with narrative summaries of the risks of using a medication during pregnancy?
- 56% of (126) responders were **not** aware of the new PLLR changes
- How often do you use the medication labeling to obtain prescribing and safety information for your pregnant patients?
- 86% use the medication labelling to obtain prescribing and safety information
- On average, how many pregnant women do you prescribe medications to per month?
- Responders prescribed medications to an average of 2 pregnant women per month

8.1 Pregnancy

Pregnancy Exposure Registry

There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to DRUGABC during pregnancy. Healthcare providers can enroll patients or encourage patients to enroll themselves by calling 1-877-311-8972 or visiting www.mothertobaby.org/asthma.

Risk Summary

The data on pregnancy exposure from the clinical trials are insufficient to inform on drug -associated risk. Monoclonal antibodies, such as drugabc, are transported across the placenta in a linear fashion as pregnancy progresses; therefore, potential effects on a fetus are likely to be greater during the second and third trimester of pregnancy. In a prenatal and postnatal development study conducted in cynomolgus monkeys, there was no evidence of fetal harm with IV administration of drugabc throughout pregnancy at doses that produced exposures up to approximately 30 times the exposure at the maximum recommended human dose (MRHD) of 100 mg SC *[see Data]*.

In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

Clinical Considerations

Disease -Associated Maternal and/or Embryofetal Risk

In women with poorly or moderately controlled asthma, evidence demonstrates that there is an increased risk of preeclampsia in the mother and prematurity, low birth weight, and small for gestational age in the neonate. The level of asthma control should be closely monitored in pregnant women and treatment adjusted as necessary to maintain optimal control.

Data

Animal Data

In a prenatal and postnatal development study, pregnant cynomolgus monkeys received drugabc from gestation days 20 to 140 at doses that produced exposures up to approximately 30 times that achieved with the MRHD (on an AUC basis with maternal IV doses up to 100 mg/kg once every 4 weeks). Drugabc did not elicit adverse effects on fetal or neonatal growth (including immune function) up to 9 months after birth. Examinations for internal or skeletal malformations were not performed. Drugabc crossed the placenta in cynomolgus monkeys. Concentrations of drugabc were approximately 2.4 times higher in infants than in mothers up to day 178 postpartum. Levels of drugabc in milk were less than or equal to 0.5% of maternal serum concentration.

In a fertility, early embryonic, and embryofetal development study, pregnant CD-1 mice received an analogous antibody, which inhibits the activity of murine IL-5, at an IV dose of 50 mg/kg once per week throughout gestation. The analogous antibody was not teratogenic in mice. Embryofetal development of IL-5–deficient mice has been reported to be generally unaffected relative to wild-type mice.

Results: Understanding

- **How much do you agree or disagree that the narrative summary labeling of DRUGABC is clear and concise:**
- 49% of responders felt the narrative summary was clear
- 29% felt the narrative summary was concise
- Comments included:
- “unclear and impossible to use”
- “ on a busy clinical day this is a lot of reading
- “ hard to interpret this information”

Results: Understanding

- Do you have experience referring pregnant women to a pregnancy exposure registry (an online database that gathers information about how prescription drugs or vaccines affect a pregnant woman and her fetus)?
- Only 25% of responders had experience referring pregnant women to a pregnancy exposure registry
- After reading the information about the pregnancy exposure registry for DRUGABC, would you refer your pregnant patient to the pregnancy exposure registry?
- After reading the provided information 54% of responders were likely to refer their pregnancy patient to the pregnancy registry
- How helpful or unhelpful is the **background risk information** under the **Risk Summary** heading?
- How helpful or unhelpful is the **disease-associated risk information** under the **Clinical Considerations** heading?
- 73% of (120) responders found the background risk and disease-associated risk information to be helpful
- How helpful or unhelpful is the **Animal Data** section?
- 65% of responders found the animal data to be helpful

Results: Value

- Overall, how helpful or unhelpful is the narrative summary labeling for DRUGABC compared to the pregnancy letter category (A,B,C,D and X) that used to appear on drug labels?

62% of responders found the narrative summary compared with previous pregnancy categories to be **unhelpful**

Comments:

- "It will …lead me to prescribe LESS medications to pregnant patients"
- "too complicated"
- How often do you use the pregnancy risk letter categories (A,B,C, D and X)instead of the narrative summary to make prescribing decisions for pregnant women?
- 76% of responders use the pregnancy risk letter categories instead of the narrative summary

Comments:

- "quicker and easier"
- "easier for patients to grasp"
- Overall, do you think the new labeling has brought more meaningful information to you and your patients compared to prior labeling?
- 57% of responders felt that the new labeling **DID NOT** bring more meaningful information to them and their patients.
- After reading the narrative summary labeling for DRUGABC 63% were unsure if they would prescribe the medication

Conclusions

The goal of the new PLLR is to bring a more complete statement of the known risks based on the available data

This survey provides a first look at the impact of the new labelling:

- The majority of responders did not know of the new PLLR changes
- Most responders were reverting back to letter categories when counseling patients
- Most of the responders found the risk information included in labelling to be helpful
- More than half of responders felt that the new labelling did not bring more meaningful information to them or their patients and that compared with past letter categories was unhelpful

Physician Time in Ambulatory Care

57 physicians across specialties– observed for 430 hours

27% of time spent on direct patient care

49.2% of time spent on EHR and desk work

While in a room with patients only 50% was spent direct face to face

The mean time spent with a patient across specialties was 20.8 minutes.

Sinsky C, et al. Allocation of Physician Time in Ambulatory Practice: A Time and Motion Study in 4 Specialties. Ann Int Med. 2016

Physician Undertreatment

Of pregnant asthmatics presenting to the ER with acute asthma only 38% were treated with oral corticosteroids. (50% vs 74%) - McCallister JW, Benninger CG, Frey HA, Phillips GS, Mastronarde JG. Pregnancy related treatment disparities of acute asthma exacerbations in the emergency department. Respir Med. 2011

Over a quarter of family physicians have said they would instruct their pregnant patients to decrease or discontinue asthma medications during pregnancy when asthma was well controlled with current therapy - Lim AS, Stewart K, Abramson MJ, George J. Management of asthma in pregnant women by general practitioners: a cross sectional survey. BMC Fam Pract. 2011

What's next?

Based on this survey, the new labelling is not meeting the perceived needs regarding prescribing during pregnancy of a majority of responding allergy/immunology clinicians

Many clinicians still do not know of the new PLLR labelling changes

Many clinicians lack the time to navigate through information and present it in a clear way to their patients

Continued education of clinicians of the new PLLR changes is essential

Continue to use this survey among clinicians from all specialties as a tool of understanding and value of the new PLLR