Pregnancy-Related Adverse Events with Tyrosine Kinase Inhibitor Use: A FAERS Database Analysis (2001–2024)

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Introduction

Tyrosine kinase inhibitors (TKIs) are essential therapies for chronic myeloid leukemia (CML), yet their safety during pregnancy remains poorly characterized. Due to potential placental transfer, TKI exposure may carry varying risks for both maternal and fetal outcomes. Current evidence is limited and association with adverse pregnancy outcomes has not been previously evaluated. We aimed to address this gap, providing pharmacovigilance data using FDA Adverse Event Reporting System (FAERS).

Aims

- The study aims to assess maternal and fetal complications associated with tyrosine kinase inhibitor (TKI) use, including imatinib, nilotinib, dasatinib, ponatinib, and asciminib.
- By analyzing real-world pharmacovigilance data, we sought to identify safety signals and provide evidence to guide management of pregnant patients with chronic myeloid leukemia.
- The findings highlight the need for prospective studies to establish clear safety guidelines for TKI use in pregnancy.

Methods

- We conducted a retrospective analysis of pregnancy-related adverse events reported in the publicly available FAERS from January 2001 through December 2024.
- The database was queried for reports involving TKI exposure during pregnancy. TKIs of interest included imatinib, nilotinib, dasatinib, ponatinib, and asciminib, as well as any reported biosimilar variants.
- Descriptive statistics were used to summarize the frequency and distribution of adverse events associated with each TKI.

Results

- A total of 647 pregnancy-related events associated with TKI exposure were identified. These included 450 exposures to imatinib, 118 to nilotinib, 64 to dasatinib, 13 to ponatinib, and 2 to asciminib.
- Spontaneous abortion was the most frequently reported adverse event with 260 cases (35.4%), primarily associated with imatinib (n= 168; 26.0%), followed by nilotinib (n= 55; 8.5%), dasatinib (n= 24; 3.7%), ponatinib (n= 11; 1.7%), and asciminib (n=2; 0.3%).
- Premature delivery was also a common adverse event (n= 219; 33.8%), with most cases occurring among those receiving imatinib (n= 168; 24.3%), followed by nilotinib (n= 32; 12.8%) and dasatinib (n= 19; 12.9%).
- The most frequent adverse perinatal outcomes included stillbirth (n= 17; 2.6%) and fetal growth restriction (n= 12; 1.7%), with most cases occurring in patients receiving imatinib (n= 36; 5.2%; n= 40; 5.8%, respectively).
- Other notable adverse outcomes among TKIs included polyhydramnios (n= 28; 4.3%) and pre-eclampsia (n= 12; 1.7%).
- Imatinib was the most frequently reported TKI across nearly all adverse outcomes.

Adverse Event	Total	Imatinib	Dasatinib	Nilotinib	Ponatinib	Asciminib
Duration	-	2001-2024	2006-2024	2007-2024	2012-2024	2021-2024
FDA year of approval for CML	-	2001	2006	2007	2012	2021
Maternal complications						
Abortion (spontaneous, induced, selective, or threatened)	260	168	24	55	11	2
Polyhydramnios	28	15	10	3	-	-
Twin pregnancy	12	6	4	2	-	-
Pre-eclampsia	11	7	-	4	-	-
Gestational diabetes	9	8	-	1	-	-
Preterm Premature Rupture of Membranes (PPROM)	16	11	-	5	-	-
Gestational hypertension	6	4	1	1	-	-
Retroplacental hematoma	6	6	-	-	-	-
Ectopic pregnancy	6	5	-	1	-	-
Anembryonic gestation	5	1	-	3	1	-
Postpartum hemorrhage	5	3	-	2	-	-
Fetal/neonatal complications						
Premature delivery/premature baby/premature labor	219	168	19	32	-	-
Low birth weight baby	29	28	-	-	1	-
Stillbirth	17	11	-	6	-	-
Fetal growth restriction	12	8	2	2	-	-
Hydrops fetalis	6	1	4	1	-	-

Conclusion

Pregnancy-related adverse events have been reported across all TKIs, with imatinib accounting for the majority of cases. These findings highlight the need for prospective data to better guide clinical decision-making regarding TKI use during pregnancy.

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