Transcript Details
This is a transcript of an educational program. Details about the program and additional media formats for the program are accessible by visiting: https://reachmd.com/programs/medical-industry-feature/ph-cml-and-treatment-adherence-rethinking-nilotinib-formulations-and-fasting-restrictions/33045/

ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

Ph+ CML and Treatment Adherence: Rethinking Nilotinib Formulations and Fasting Restrictions

Announcer:
Welcome to ReachMD. This medical industry feature, titled "Ph+ CML and Adherence: Rethinking Nilotinib Formulations and Fasting Restrictions," is sponsored by Azurity Pharmaceuticals. And now, here's your host, Dr. Jennifer Caudle.

Dr. Caudle:
This is ReachMD, and I'm your host Dr. Jennifer Caudle. And today, we'll be exploring the role of adherence in managing patients with Philadelphia chromosome-positive chronic myeloid leukemia, also known as Philadelphia-positive CML. We'll also discuss Danziten™, nilotinib tablets, a formulation without fasting restrictions.[1]

Joining me today is Dr. Michael Mauro, the Director of the ChronicMyeloid Leukemia Program at Memorial Sloan Kettering Cancer Center as well as a Professor at Weill Cornell Medicine in New York City. Dr. Mauro is a paid consultant of Azurity Pharmaceuticals. Dr. Mauro, welcome to the program.

Dr. Mauro:
Thanks for having me.

Dr. Caudle:
Of course, well let's begin by examining treatment for Philadelphia-positive CML with nilotinib. Now in your experience, what are some of the challenges adult patients might face when taking capsule formulations of nilotinib?

Dr. Mauro:
Well, tyrosine kinase inhibitors, or TKIs, have really transformed the prognosis for patients with CML,[2] and nilotinib is an established therapy option for over 17 years due to its efficacy, safety, and tolerability.[1] Of course, I want to make sure my patients can adhere to their treatment regimen to support long-term outcomes, but that's where I've seen some challenges. And we know that this issue of adherence is widespread.[2-4] One study found that about 44 percent of adult patients across three TKIs demonstrated suboptimal adherence of less than 90 percent.[2]

This is worth noting because in another study examining the TKI imatinib, adherence was directly correlated with clinical outcomes. Adult patients who took imatinib as prescribed 85 percent of the time or less had about a 36 percent chance of losing their complete cytogenetic response. In comparison, for adult patients who remained highly adherent, this risk was around one percent.[3] So adherence isn't just about convenience for our adult patients—it could also impact outcomes.

So let's take a look at nilotinib capsules. Tasigna's bioavailability, or the amount of drug absorbed into the bloodstream, is quite variable depending on food intake. And when Tasigna is taken 30 minutes after a high-fat meal, we've seen that systemic drug concentrations can rise by as much as 82 percent, which could increase cardiotoxicity risk.[5]

That's part of the reason why twice-daily dosing with Tasigna comes with strict fasting restrictions: no food two hours before and one hour after each dose. Practically, this totals about six hours per day, which may significantly impact patients' routines.[5,6] So some patients have difficulty fully adhering to the fasting restrictions or the administrations directions due to their schedules.[6,7]

Dr. Caudle:
Now, let's shift our focus to Danziten, a tablet formulation of nilotinib that was approved by the FDA in November of 2024. But before we do, let's take a moment to hear some Important Safety Information on Danziten.

[Voiceover]

IMPORTANT SAFETY INFORMATION
DANZITEN™ (nilotinib) tablets, for oral use

DANZITEN is a kinase inhibitor indicated for the treatment of:

- Adult patients with newly diagnosed Philadelphia chromosome positive chronic myeloid leukemia (Ph+ CML) in chronic phase.
- Adult patients with chronic phase (CP) and accelerated phase (AP) Ph+ CML resistant to or intolerant to prior therapy that included imatinib.

WARNING: QT PROLONGATION and SUDDEN DEATHS
See Full Prescribing Information for complete Boxed Warning.

- Nilotinib prolongs the QT interval. Prior to DANZITEN administration and periodically, monitor for hypokalemia or hypomagnesemia and correct deficiencies. (5.3) Obtain ECGs to monitor the QTc at baseline, seven days after initiation, and periodically thereafter, and following any dose adjustments. (5.3, 5.4, 5.8, 5.12)
- Sudden deaths have been reported in patients receiving nilotinib. (5.4) Do not administer DANZITEN to patients with hypokalemia, hypomagnesemia, or long QT syndrome. (4, 5.3)
- Avoid use of concomitant drugs known to prolong the QT interval and strong CYP3A4 inhibitors. (7.1, 7.2)

Stay tuned for more Important Safety Information during this program.

Dr. Caudle:
And now that we've heard that Important Safety Information, Dr. Mauro, what sets Danziten, nilotinib tablets, apart from nilotinib capsules?

Dr. Mauro:
Danziten nilotinib tablets received approval through the 505(b)(2) pathway, which allows the FDA to consider existing data from an already approved reference drug—in this case, Tasigna nilotinib capsules.[1]

So Danziten tablets are indicated for adult patients with newly diagnosed chronic phase Philadelphia-positive CML as well as adult patients with chronic phase and accelerated phase Philadelphia-positive CML that's resistant to or intolerant to prior therapy that included imatinib.[1]

The difference is that Danziten is a re-engineered formulation of nilotinib that doesn't require fasting restrictions[1]. It uses a different salt form of nilotinib and an amorphous solid dispersion technology.[1,5] This design increases the bioavailability of nilotinib while also controlling its release, allowing it to be absorbed in the GI tract rather than the stomach and likely minimizing drug-food interactions.[1]

Danziten has also shown consistent pharmacokinetics, regardless of whether patients are fasting or have eaten, or what type of meal they've had.[1,8] Specifically, Danziten tablets maintain more stable drug exposure after both low- and high-fat meals, which is distinctly different from other nilotinib formulations. So as a result, adult patients can achieve consistent drug exposure regardless of meal timing.[8] They'll still need to avoid grapefruit products and CYP3A4 inhibitors at any time during treatment.[1] So this makes Danziten the first and only nilotinib formulation to be approved without mealtime or fasting restrictions. Now, Danziten does carry a Boxed Warning for concentration-dependent QT prolongation.[1]

While nilotinib is associated with concentration-dependent QT prolongation, no new significant QT findings were observed in healthy subjects with single doses of Danziten given with or without food, and no QT prolongation events were noted in any of the 14 PK studies that were associated with Danziten.[1] At the same time, it's important to recognize that the risk of QT prolongation—and broader concerns about cardiotoxicity—are inherent to nilotinib itself, regardless of formulation.[1,5] So it's crucial that we actively monitor patients, assess risk factors, and manage therapy appropriately. Lastly keep in mind that Danziten is contraindicated in patients with hypokalemia, hypomagnesemia, or long QT syndrome.[1]

Dr. Caudle:
Now, beyond those adherence considerations, could you tell us more about how Danziten compares to Tasigna in terms of

safety and efficacy?

Dr. Mauro:
Absolutely. There's no known difference in safety and efficacy between Danziten and Tasigna.Although there's no head-to-head comparison between the two, Danziten did have to demonstrate bioequivalence as part of the 505b approval process.[1] So Danziten offers nilotinib's established safety profile. And as I mentioned earlier,Danziten demonstrates improved bioavailability, which means it may achieve the same therapeutic effect at lower doses.[1,8]

I'll also note that, while treatment-free remission has been studied across multiple BCR-ABL TKIs[9] Danziten—like Tasigna—has FDA-approved labeling that includes explicit eligibility criteria for treatment-free remission.[1,5] So clinicians and adult patients may expect the safety, efficacy, and clinical outcomes historically associated with nilotinib capsules.[1,10,11]

And now, nilotinib tablets (Danziten™) are included in the NCCN Guidelines® for CML. They acknowledge that nilotinib tablets (Danziten™) have improved bioavailability without compromising efficacy, allowing administration at lower doses and without mealtime restrictions. And the NCCN Guidelines for CML state that nilotinib products—such as Danziten and Tasigna—aren't interchangeable because of the differences in formulations, dosage forms, and strengths.[12]

Dr. Caudle:
For those just tuning in, you're listening to ReachMD. I'm Dr. Jennifer Caudle, and today I'm speaking with Dr. Michael Mauro, a paid consultant of Azurity Pharmaceuticals, about the latest FDA-approved formulation of nilotinib tablets that has no fasting restrictions on its Boxed Warning while maintaining therapeutic efficacy for patients with Philadelphia-positive CML.[1] Before we continue, let's take a moment here to review more Important Safety Information.

[Voiceover]
IMPORTANT SAFETY INFORMATION
Contraindications
Danziten is contraindicated in patients with hypokalemia, hypomagnesemia, or long QT syndrome.
Warnings and Precautions
Substitution With Other Nilotinib Products and Risk of Medication Errors: Danziten tablets may not be substitutable with other nilotinib products, including other nilotinib tablets, on a milligram per milligram basis. Confirm that the intended nilotinib product is being prescribed and dispensed.
Myelosuppression: Monitor complete blood count (CBC) during therapy and manage by treatment interruption or dose reduction.
Cardiac and Arterial Vascular Occlusive Events: Evaluate cardiovascular status, monitor and manage cardiovascular risk factors during Danziten therapy.
Pancreatitis and Elevated Serum Lipase: Monitor serum lipase; if elevations are accompanied by abdominal symptoms, interrupt doses and consider appropriate diagnostics to exclude pancreatitis.
Hepatotoxicity: Monitor hepatic function tests monthly or as clinically indicated.

Stay tuned for more Important Safety Information during this program.

Dr. Caudle:
And as we return from that Important Safety Information message, Dr. Mauro, what are some practical considerations for clinicians to keep in mind when prescribing Danziten?

Dr. Mauro:
First, let me note again that there are no head-to-head trials comparing the efficacy and safety of Danziten and Tasigna. So the efficacy and safety of Danziten has been established by adequate and well-controlled studies of nilotinib.[1] And although adult patients taking Danziten don't need to schedule meals around doses, they'll still need to avoid grapefruit products and CYP3A4 inhibitors at any time during treatment.[1]

Another consideration for clinicians thinking about prescribing Danziten is that it's not interchangeable milligram-for-milligram with other nilotinib products, including Tasigna, due to its distinct formulation.[1]

- For newly-diagnosed adult patients, the Danziten tablet dosage is 142 milligrams twice daily rather than the 300 milligram twice daily dose for Tasigna capsules.[1]
- And for adult patients with resistant disease or intolerance, the dose is 190 milligrams of Danziten twice daily in place of 400 milligrams of Tasigna twice daily.[1]

So we need to be clear on prescriptions by explicitly stating Danziten tablets and specifying the lower-dose tablets to prevent medication errors.[1]

Dr. Caudle:
You know with those practical considerations in mind, how can clinicians use shared decision-making to better understand any challenges patients may be having with adherence?

Dr. Mauro:
Shared decision-making is especially important when we're considering factors that go beyond clinical data and look at treatment in the real world. One useful starting point is to check in with patients who are on medications with strict fasting requirements. Have you talked with them about the importance of fasting restrictions—and what might happen if they don't follow those instructions consistently? Have you asked them if they've missed doses because of the fasting restrictions?

From there, you can open the conversation by asking how have fasting restrictions affected their day-to-day life. You might say, "Have you found it challenging to stick to the fasting requirements?", "Have mealtime restrictions disrupted your routine in any way?"

Some patients may have found workarounds by altering sleep schedules or shifting mealtimes,[6,7] so you could follow up by asking, "Have you developed any strategies to manage these fasting requirement that have—or haven't—worked well?" For patients who find fasting requirements difficult to manage, these discussions are a chance to explore alternatives like Danziten, which may support adherence and fit more easily with their lifestyle.

Dr. Caudle:
Thank you for that. And before we close, Dr. Mauro, what would you like our audience to take away from our discussion today?

Dr. Mauro:
Well, with the FDA approval of Danziten, we can offer adult patients with Philadelphia-positive CML a treatment option with comparable efficacy to Tasigna, including the opportunity for treatment-free remission, but without the fasting restrictions that may disrupt daily life.[1]

Nilotinib tablets or (Danziten™) are now included in the NCCN Guidelines for CML,[12] so for newly diagnosed adult patients, Danziten should be part of the treatment discussion. If fasting requirements are impacting adherence for adult patients currently on Tasigna, considering Danziten as a treatment option may be appropriate.[6]

The key is that we approach treatment selection through shared decision-making. This includes educating patients on Danziten's efficacy and bioequivalence, and how removing fasting requirements with Danziten may work with their lifestyle.[1,6] And finally, let's remember to clearly specify Danziten's lower-dose tablets to prevent medication errors because Danziten is a different formulation and prescribed at a lower dose than nilotinib capsules.[1]

Dr. Caudle:
Well that's a great way to round out our discussion today. I'd like to thank my guest, Dr. Michael Mauro, for helping us better understand how Danziten is different from nilotinib capsules and can support adult patients with Philadelphia-positive CML. Dr. Mauro, it was great speaking with you today.

Dr. Mauro:
Thanks for having me.

Dr. Caudle:
Of course. For ReachMD, I'm your host Dr. Jennifer Caudle. Please stay tuned to hear Important Safety Information.

[Voiceover]
ADDITIONAL IMPORTANT SAFETY INFORMATION
Warnings and Precautions
Electrolyte Abnormalities: Danziten can cause hypophosphatemia, hypokalemia, hyperkalemia, hypocalcemia, and hyponatremia. Correct electrolyte abnormalities prior to initiating Danziten and monitor periodically during therapy.
Tumor Lysis Syndrome: Maintain adequate hydration and correct uric acid levels prior to initiating therapy with Danziten.
Hemorrhage: Hemorrhage from any site may occur. Advise patients to report signs and symptoms of bleeding and medically manage as

needed.
Fluid Retention: Monitor patients for unexpected rapid weight gain, swelling, and shortness of breath. Manage medically.
Effects on Growth and Development in Pediatric Patients: Growth retardation has been reported in pediatric patients treated with nilotinib. Monitor growth and development in pediatric patients.
Embryo-Fetal Toxicity: Can cause fetal harm. Advise females of reproductive potential of potential risk to a fetus and to use effective contraception.
Treatment Discontinuation: Patients must have typical BCR-ABL transcripts. An FDA-authorized test with a detection limit below MR4.5 must be used to determine eligibility for discontinuation. Patients must be frequently monitored by the FDA authorized test to detect possible loss of remission

Adverse Reactions
The most commonly reported non-hematologic adverse reactions (≥20%) in adult patients are nausea, rash, headache, fatigue, pruritus, vomiting, diarrhea, cough, constipation, arthralgia, nasopharyngitis, pyrexia, and night sweats. Hematologic adverse drug reactions include myelosuppression: thrombocytopenia, neutropenia, and anemia.

*These are not all the possible side effects of Danziten. Please see **Full Prescribing Information** for a full list.*

Drug Interactions
Strong CYP3A Inhibitors: Avoid concomitant use, including grapefruit juice with Danziten or reduce Danziten dose if concomitant use cannot be avoided.
Strong CYP3A Inducers: Avoid concomitant use with Danziten.
Proton Pump Inhibitors: Use short-acting antacids or H2 blockers as an alternative to proton pump inhibitors.

See Full Prescribing Information for Specific Drugs and Interactions.

Use in Specific Populations
Lactation: Advise women not to breastfeed.
Pediatric Use: The safety and effectiveness of nilotinib in pediatric patients below the age of 1 year with newly diagnosed, or who are resistant to or intolerant to Ph+ CML in chronic phase and accelerated phase have not been established.

The Important Safety Information does not include all the information needed to use Danziten safely and effectively. Please see Full Prescribing Information for Danziten.

To Report SUSPECTED ADVERSE REACTIONS, contact Azurity Pharmaceuticals, Inc. at 1-800-461-7449, or FDA at 1-800-FDA-1088 or www.fda.gov/MedWatch.

Announcer:
This medical industry feature was sponsored by Azurity Pharmaceuticals, Inc. If you missed any part of this discussion, visit Industry Features on ReachMD.com, where you can Be Part of the Knowledge.

References:

1. DANZITEN [prescribing information]: Woburn, MA: Azurity Pharmaceuticals, Inc; 2024.
2. Di Bella NJ, Bhowmik D, Bhor M, et al. The effectiveness of tyrosine kinase inhibitors and molecular monitoring patterns in newly diagnosed patients with chronic myeloid leukemia in the community setting. *Clin Lymphoma Myeloma Leuk*. 2015;15(10):599-605. doi:10.1016/j.clml.2015.06.006
3. Ibrahim AR, Eliasson L, Apperley JF, et al. Poor adherence is the main reason for loss of CCyR and imatinib failure for chronic myeloid leukemia patients on long-term therapy. *Blood*. 2011;117(14):3733-6. doi:10.1182/blood-2010-10-309807
4. Marin D, Bazeos A, Mahon FX, et al. Adherence is the critical factor for achieving molecular responses in patients with chronic myeloid leukemia who achieve complete cytogenetic responses on imatinib. *J Clin Oncol*. 2010;28(14):2381-8. doi:10.1200/JCO.2009.26.3087
5. Tasigna [prescribing information]: East Hanover, NJ: Novartis Pharmaceuticals Corporation; 2024.
6. Tan BK, Tan SB, Chen LC, et al. Medication-related issues associated with adherence to long-term tyrosine kinase inhibitors for controlling chronic myeloid leukemia: a qualitative study. *Patient Prefer Adherence*. 2017;11:1027-1034. doi:10.2147/PPA.S132894

7. Boons CCLM, Timmers L, Janssen JJWM, et al. Response and adherence to nilotinib in daily practice (RAND study): an in-depth observational study of chronic myeloid leukemia patients treated with nilotinib. *Eur J Clin Pharmacol*. 2020;76(9):1213-1226. doi:10.1007/s00228-020-02910-3
8. Radich J, Mauro M, Jain P, Diekjürgen D, Douer D. Population pharmacokinetic (PopPK) modeling for a novel nilotinib formulation. Poster CML-633 presented at: SOHO Annual Meeting; September 4-7, 2024; Houston, TX.
9. Han JJ. Treatment-free remission after discontinuation of imatinib, dasatinib, and nilotinib in patients with chronic myeloid leukemia. *Blood Res*. 2023;58:S58–S65. doi:10.5045/br.2023.2023035
10. Hochhaus A, Masszi T, Giles FJ, et al. Treatment-free remission following frontline nilotinib in patients with chronic myeloid leukemia in chronic phase: results from the ENESTfreedom study. *Leukemia*. 2017;31(7):1525-1531. doi:10.1038/leu.2017.63
11. Hughes TP, Saglio G, Kantarjian HM, et al. Early molecular response predicts outcomes in patients with chronic myeloid leukemia in chronic phase treated with frontline nilotinib or imatinib. *Blood*. 2014;123(9):1353-60. doi:10.1182/blood-2013-06-510396
12. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Chronic Myeloid Leukemia V.3.2025. © National Comprehensive Cancer Network, Inc. 2024. All rights reserved. Accessed May 13, 2025. To view the most recent and complete version of the guideline, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.