How patient characteristics shape drug safety

Leveraging OFF-X insights to design smart clinical trials

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Explore how patient characteristics impact drug safety

Actionable insight – in minutes!

Bcl-2 inhibitor lisaftoclax has recently been approved in China for treating adults with chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL), making it the first Bcl-2 inhibitor to receive conditional approval and marketing authorization for CLL/SLL in China and the second Bcl-2 inhibitor approved globally.

We use OFF-X Translational Safety Intelligence to review its safety profile and uncover how patient condition can impact a drug's safety.

01 Evaluate the drug's safety profile

02 Benchmark against same-in-class drugs

03 Look for other drugs with a similar safety profile, across all patient conditions

04 Search for other drugs, and their targets, with a similar safety profile in our condition of interest

OUTCOME:

Uncovering, **in minutes**, an unexpected association, unique to lisaftoclax-treated CLL patients, that can help **tailor risk mitigation strategies** and select **future trial inclusion/exclusion criteria** and **safety biomarker endpoints**.

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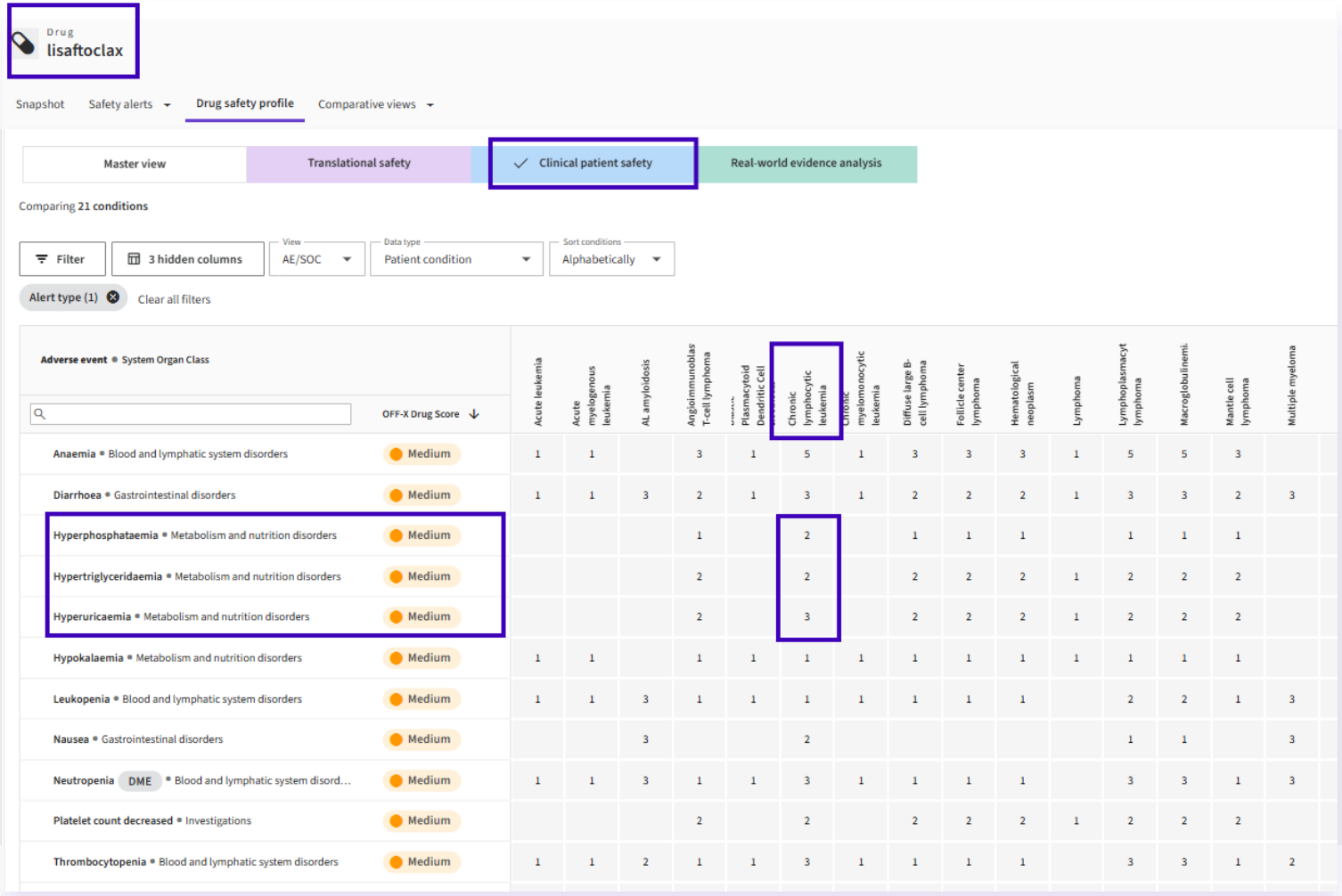
Assessing the safety profile of lisaftoclax across patient populations



- The safety profile for lisaftoclax varies depending on the patient population.
- Interestingly, three metabolic adverse events (hyperuricaemia, hyperphosphataemia and hypertriglyceridaemia) are associated with patients with CLL – one of the approved indications for this drug—while this combination of events is not consistently observed across all other conditions.
- This table compiles safety alerts from clinical trials, allowing you to assess how the safety profile of a drug can be influenced by patient characteristics, such as condition, age, ethnicity, and gender.

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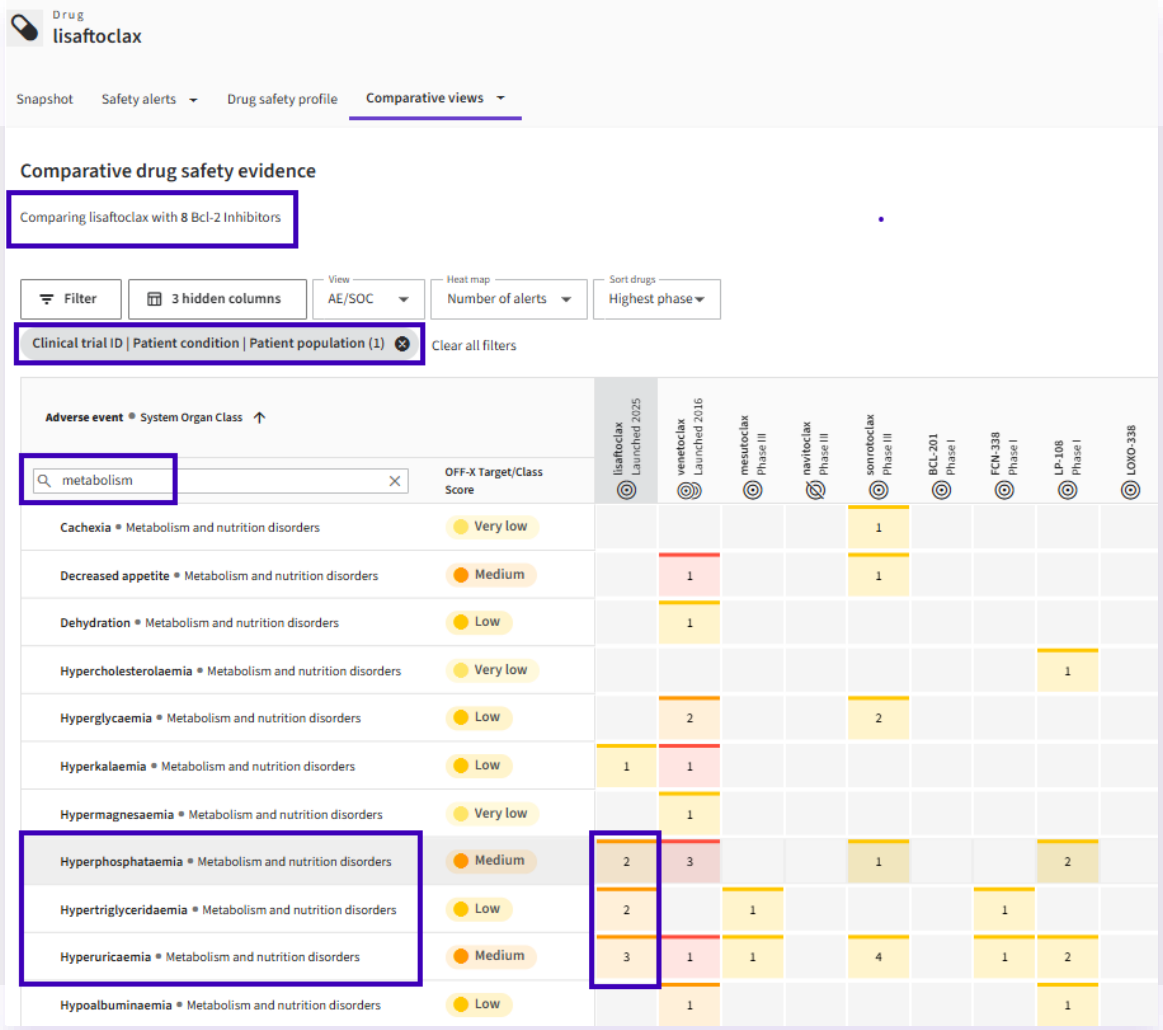
Benchmarking lisaftoclax against other Bcl-2 inhibitors



- Benchmarking a drug against others of the same class helps understand whether its risk profile is unique or reflects a broader class effect.
- In a few clicks, OFF-X provides a side-by-side comparison of adverse events reported for all Bcl-2 inhibitors in CLL patients.
- Notably, while other Bcl-2 inhibitors –including venetoclax, approved by the FDA for CLL in 2016–may share individual metabolic adverse events, only lisaftoclax exhibits the specific combination of these three, highlighting a distinctive safety signal that sets it apart.

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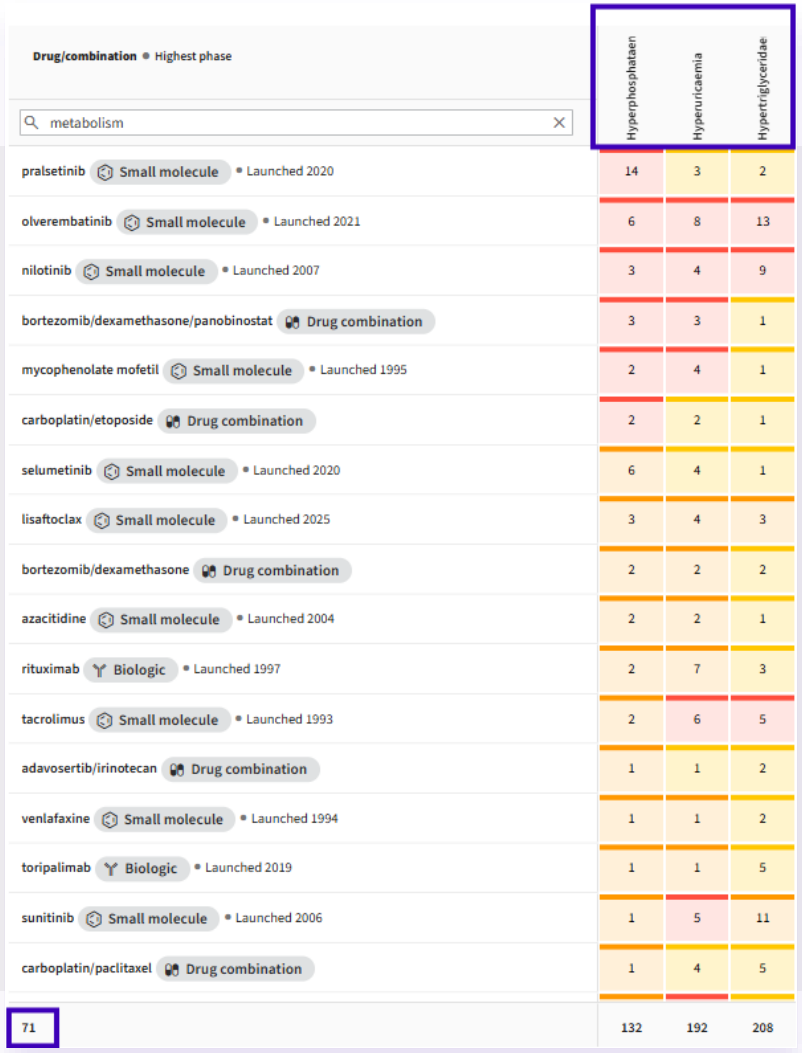
How common is this adverse event pattern?



Drug/combination • Highest phase	Hyperphosphataem	Hyperuricaemia	Hypertriglyceridae
metabolism			
pralsetinib Small molecule • Launched 2020	14	3	2
olverembatinib Small molecule • Launched 2021	6	8	13
nilotinib Small molecule • Launched 2007	3	4	9
bortezomib/dexamethasone/panobinostat Drug combination	3	3	1
mycophenolate mofetil Small molecule • Launched 1995	2	4	1
carboplatin/etoposide Drug combination	2	2	1
selumetinib Small molecule • Launched 2020	6	4	1
lisaftoclax Small molecule • Launched 2025	3	4	3
bortezomib/dexamethasone Drug combination	2	2	2
azacitidine Small molecule • Launched 2004	2	2	1
rituximab Biologic • Launched 1997	2	7	3
tacrolimus Small molecule • Launched 1993	2	6	5
adavosertib/irinotecan Drug combination	1	1	2
venlafaxine Small molecule • Launched 1994	1	1	2
toripalimab Biologic • Launched 2019	1	1	5
sunitinib Small molecule • Launched 2006	1	5	11
carboplatin/paclitaxel Drug combination	1	4	5
71	132	192	208

- By comparing adverse event patterns across drugs, researchers can distinguish true drug-related risks vs. background noise, understand biological mechanisms, uncover unexpected relationships, design safer drugs, and make better regulatory and clinical decisions.
- In a few clicks OFF-X reveals that the combination of these 3 metabolic events (hyperuricaemia, hyperphosphataemia and hypertriglyceridaemia) is rare, appearing in only 71 drugs.

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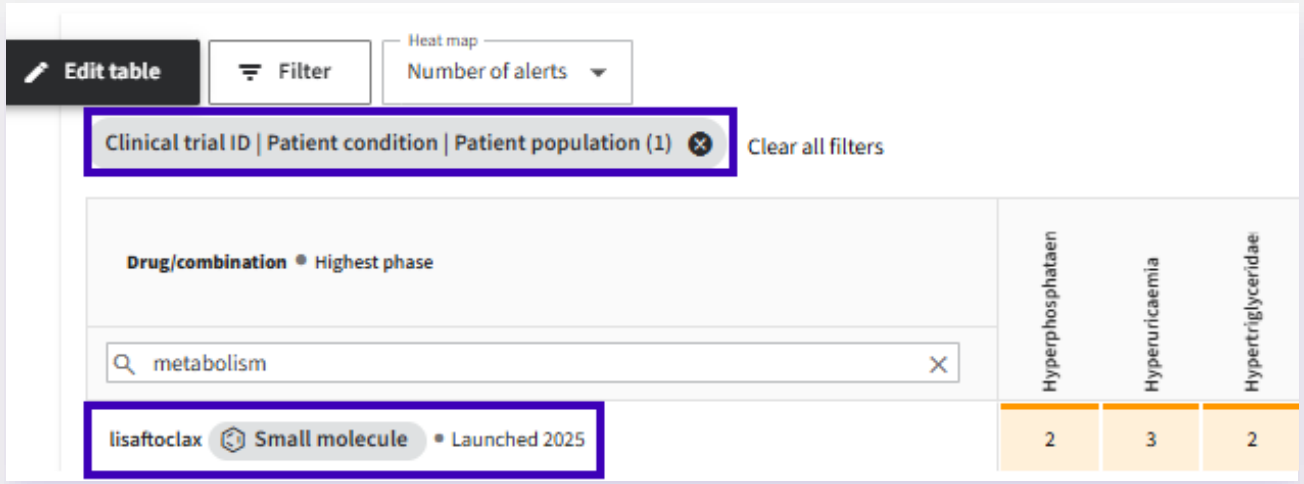
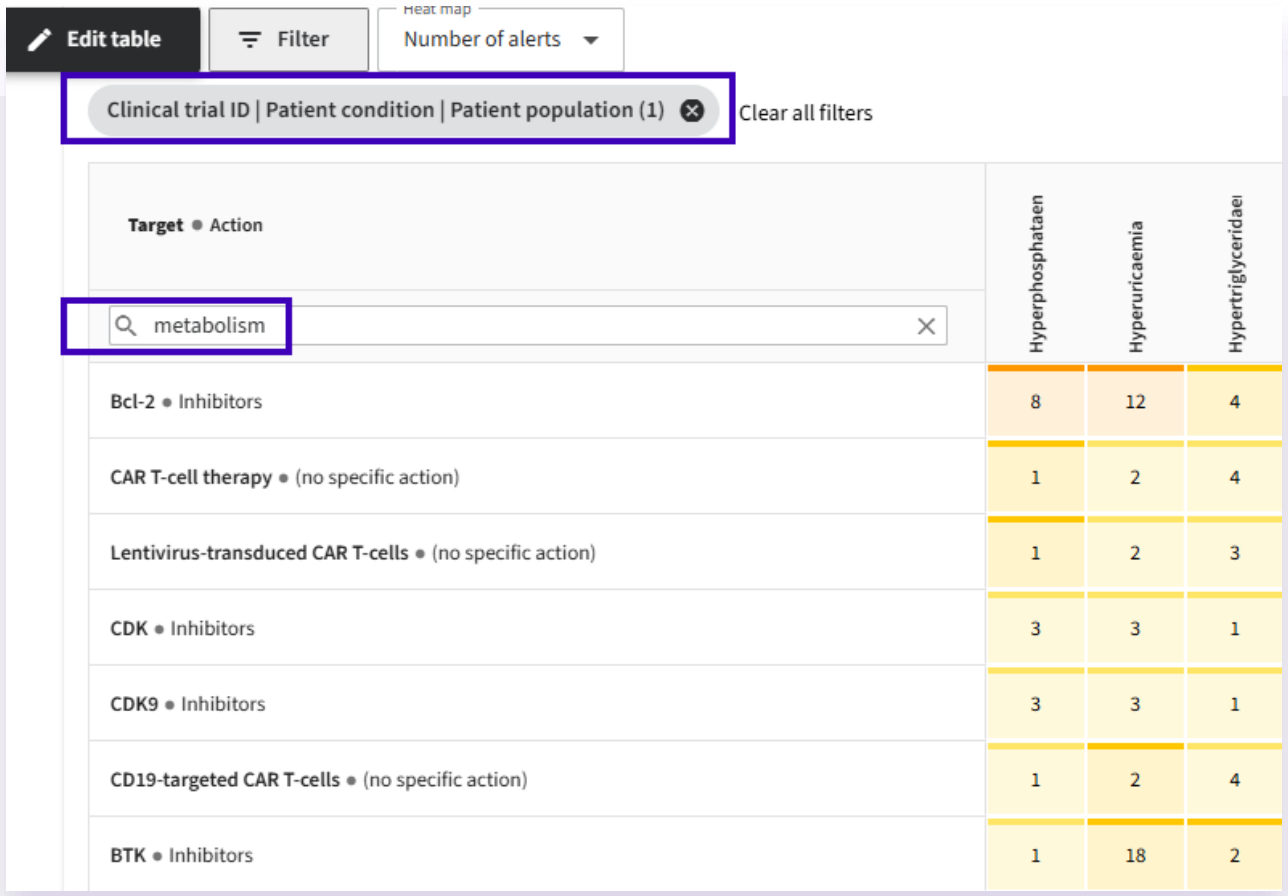
Zeroing in on CLL



- By applying a simple filter to focus on the CLL population, OFF-X quickly reveals that lisaftoclax is the only drug reporting this specific combination of metabolic adverse events.
- In minutes, OFF-X has demonstrated that this adverse event pattern is rare across all drugs and conditions, and within the CLL population, highlighting a unique safety signal for lisaftoclax in its approved indication.

Target and class-level insights



- Similarly, OFF-X visually compares adverse event patterns across targets and drug classes for specific patient populations, providing a powerful lens into underlying biological mechanisms, and can suggest whether the events are mechanism-based or are an on- or off-target effect.
- In this case, the combination of the metabolic events (hyperuricaemia, hyperphosphataemia and hypertriglyceridaemia) identified in CLL patients treated with lisaftoclax is also observed in BTK and CDK inhibitors and CAR-T cell therapies.
- This cross-target insight can guide the prioritization of mechanistic studies and next-step research.

Conclusions:

Sound evidence to guide next steps

Targeted safety monitoring: The identification of a rare combination of metabolic adverse events specifically in CLL patients treated with lisaftoclax means that researchers can design monitoring protocols that focus on these risks.

Informed trial design: Knowing that this adverse event pattern is not common in other drugs or even in other Bcl-2 inhibitors allows researchers to tailor inclusion/exclusion criteria, endpoints, and patient management strategies for future lisaftoclax trials.

Guiding mitigation strategies: OFF-X has uncovered an unexpected association that may require a mitigation strategy, thereby guiding future research efforts to understand why this adverse event pattern is observed exclusively in CLL patients treated with lisaftoclax, but not in other patients on lisaftoclax or in CLL patients receiving different drugs.

Benchmarking and differentiation

- Developers of same-class drugs can monitor lisaftoclax closely to understand what adverse events are likely to be a class effect vs. drug-specific, to inform their own trial design.
- Developers of different class drugs for the same condition can compare their safety profiles to this first-in-class drug to differentiate positioning.
- They may use findings to anticipate regulatory hurdles they could exploit or avoid.

OFF-X Translational Safety Intelligence

De-risk clinical trials with comprehensive safety intelligence and analytics

Design safe, successful clinical trials by anticipating risks for drugs in early clinical development based on members of the same class and assessing the safety profile of drugs and targets with specific patient populations and conditions.

Identify patient groups at higher risk for adverse events.

Track competitor drug and target safety profiles to better differentiate your asset.

Enable mechanistic deconvolution of unexpected safety findings.

Improve success rates by choosing optimal endpoints and biomarkers.

Trusted by the FDA

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